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The burden of childhood asthma

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Abstract

Paediatric asthma is a major clinical concern worldwide and represents a huge burden on family and society. It accounts for a large number of lost school days and may deprive the child of both academic achievement and social interaction. Childhood asthma also places strain on healthcare resources as a result of doctor and hospital visits and the cost of treatment. The prevalence of asthma varies worldwide, possibly because of different exposure to respiratory infection, indoor and outdoor pollution, and diet. Certain risk factors appear to predispose children to developing asthma and atopic disease, including incidence and severity of wheezing, atopy, maternal smoking, and number of fever episodes. This paper discusses the burden, prevalence, and risk factors associated with paediatric asthma.

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Keywords: asthma; disease prevalence; burden of disease; risk factors

Asthma is the most common chronic disease in children. The prevalence is increasing although the reasons why are poorly understood. Paediatric asthma is a major global health problem, which exerts a substantial burden on the family, healthcare services, and on society as a whole. A national survey of over 17 000 households in the United States showed that the annual burden experienced by 2.7 million children affected with asthma comprised 7.3 million days when the patient was restricted to bed, 10.1 million days of school absence, 12.9 million contacts with a doctor, and 200 000 hospitalisations resulting in 1.9 million days of hospital admissions.[1] Furthermore, asthma can considerably impair the child's ability to enjoy and partake in activities such as playing a musical instrument and sporting events,[2] and even affect sleep patterns and their academic and career success because of poor school attendance associated with asthma attacks. In addition, cancellation of social events because of illness and sibling rivalry may affect families of the asthmatic child.

The common characteristics of asthma include bronchospasm, variable airway narrowing, bronchial hyperresponsiveness, and airway inflammation, but its diagnostic definition is still not clearly defined. Asthma prevalence studies lack consistency, possibly because of the ill defined diagnostic criteria and non-standardised study protocols. Consequently, an international study was performed using a standardised protocol for each centre.[3]

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Prevalence of childhood asthma and associated symptoms

The ISAAC study compared the prevalence rates of asthma and atopic disease in 155 centres in 56 countries worldwide, and was conducted over a period of one year in 721 601 children aged either 6–7 years or 13–14 years.[3] Overall, the prevalence of asthma tended to be greater in English speaking countries, but the international pattern was suggestive that environmental factors may have played a role in the prevalence of childhood asthma.

Evidence from the ISAAC study also showed that the distribution of childhood asthma varies between global populations from less than 2% to approximately 33% of the population. Prevalence reaches 17–30% in the UK, New Zealand, and Australia, whereas areas of low prevalence (1–7%) include Eastern Europe, China, and Indonesia.[3] Furthermore, the prevalence also appears to vary within countries. For example, across India it ranges from less than 5% to approximately 20%.[3]

It is unclear why the variation in the prevalence of asthma is so large. One theory involves a greater understanding of hygiene and healthcare in the western world, which may lead to a different exposure to infection early in life. Consequently, this may render the immune system susceptible to an atopic response.[4] Childhood respiratory disease,[5] allergen exposure,[6] dietary changes,[7 8] and socioeconomic differences[9] may also play a role in the variation.

Ethnic origin may also play a role in the prevalence of asthma. This was confirmed in a recent study conducted in German children, of which 7% were either of Turkish nationality born in Germany or had moved there during the first year of life.[10] The prevalence of asthma, atopy, and bronchial hyperresponsiveness were lower in Turkish children than in native German children. Multivariable analysis failed to highlight any of the risk factors assessed, although other factors that were not evaluated, such as diet may explain the difference between the populations. A genetic factor is unlikely to be involved, as the prevalence of asthma in Turkish children living in Germany was lower than that reported in Turkey. Alternatively, some type of selection bias associated with immigration, for example, only healthy Turkish people chose to move to Germany, may be implicated.

Following the reunification of Germany in 1989, various epidemiological comparative studies examined whether environmental and cultural differences play a role in disease prevalence in the former East and West Germany. Children who lived in the former East Germany have a significantly lower prevalence of asthma and hay fever (fig 1), despite being

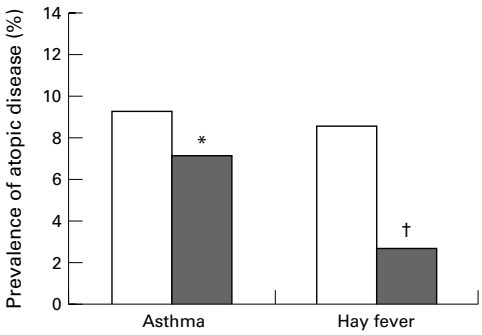

*Figure 1 Prevalence of atopic diseases in Munich, Leipzig, and Halle. Open and closed columns refer to Munich and Leipzig/Halle. Statistical comparisons were performed: *p < 0.05; †p < 0.0005 (data from von Mutius et al[11]).*

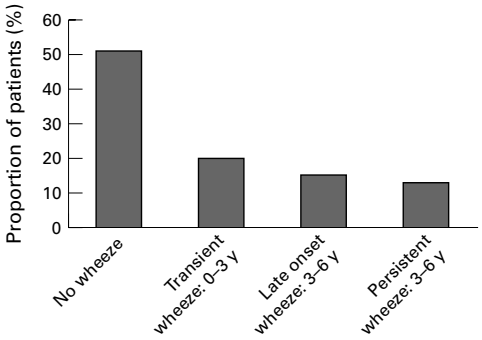

Figure 2 Patterns of wheezing in 1246 newborn babies during the first six years of life (data from Martinez et al[14]).

exposed to higher levels of atmospheric pollution.[11] In contrast, the prevalence of bronchitis, frequent cough, and wheeze were greater in the former East than the West, possibly because of the prevalence of viral infection in day care and/or to higher pollution levels in the East. However, by the mid 1990s, the prevalence of childhood hay fever and atopic sensitisation increased in the former East part of Germany, while the prevalence of asthma remained stable.[8] The findings further indicate that factors affecting the onset of asthma may be prevalent during the early infant years, whereas the development of hay fever and atopic sensitisation appears to be under the control of factors associated with the post-infancy age.

Wheezing illness in childhood

Approximately 70% of wheezing episodes during the first year are associated with viral respiratory infection,[12] of which respiratory syncytial virus, rhinovirus, and influenza B virus were the most frequently cultured.[13] Several studies have investigated the relation between childhood respiratory disorders, their prognosis, and the development of asthma. Martinez and colleagues[14] studied 1246 newborn babies during the first six years of life and examined the pattern of wheezing and its associated factors. By the age of 6, 52% of children had never had any wheezing compared with 20% who had transient early wheezing before the age of 3, 15% began to wheeze after the age of 3 (late onset wheezers), and 14% experienced wheezing throughout their first six years (fig 2). Furthermore, 60% of those children who wheezed before the age of 3 were reported to be wheeze free by the age of 6. When the incidence of wheezing with respect to age was evaluated, certain risk factors were found to be associated with transient, late onset and persistent wheezing.

Risk factors associated with transient wheezing included small airways and impaired lung function at birth, whereas maternal asthma, atopy, and male sex appeared to predispose for both late onset and persistent wheezing. Impaired lung function at 6 years, increased IgE concentrations at 9 months, maternal smoking, and eczema during the first year of life were also linked to persistent wheezing (table 1). Impaired lung function at 6 years probably reflects the chronic nature of persistent wheezing. Martinez and colleagues[14] suggested that children may have become sensitised below the age of 1, thus contributing to persistent wheezing, as IgE concentrations at the age of 9 months correlated with persistent wheezing.

Stein and colleagues[15] examined the relation between lower respiratory tract illness before the age of 3 and the prevalence of atopy and wheezing in childhood. Of the 1246 children enrolled at birth, 888 were followed up over the first three years of life. The results showed that those children who experienced a lower respiratory tract infection because of respiratory syncytial virus had a greater risk of subsequent wheezing in the first six years of life, but this risk had disappeared by the age of 11. In addition, no association was found between the incidence of respiratory syncytial virus infection and the subsequent development of allergic disease.

Table 1 Factors associated with different wheezing patterns in the first six years of life in 1246 children (data from Martinez et al[14])

	Transient	*Late onset*	*Persistent*
Maternal asthma	—	Yes	Yes
Higher prevalence in boys	—	Yes	Yes
Atopy	—	Yes	Yes
Lung function impaired	At birth	—	At the age of 6 years

Transient—children who wheezed only under the age of 3.
Late onset—children who wheezed only after the age of 3.
Persistent—children who wheezed throughout the first six years.

Relation between infantile fever and childhood asthma

Infection with rhinoviruses, respiratory syncytial virus, parainfluenza virus, or coronavirus causes 50–60% of exacerbations among asthmatic patients; however, the type of infection may vary within asthmatic populations.[16 17] For example, rhinovirus is more common in older children, adults, and atopic patients and the severity of infection dictates both the extent of bronchial hyperresponsiveness and the severity of the asthma attack.[16] Furthermore, higher viral titres strongly correlate with a more severe exacerbation of asthma.[18–20]

The relation between childhood asthma and respiratory infection also impacts on the risk of hospital admission. During the autumn and winter months in the upper hemisphere, the incidence of upper respiratory tract infection

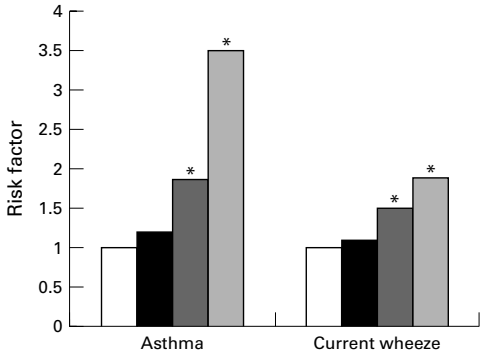

*Figure 3 Association between risk of asthma in school age children and frequent fever in infancy. Frequency of fever was recorded as never (open columns), 1–2 times (closed columns), 3–4 times (dark grey columns), or ⩾5 times (light grey columns). *p < 0.05 v children with fever frequency of never (data from von Mutius et al[23]).*

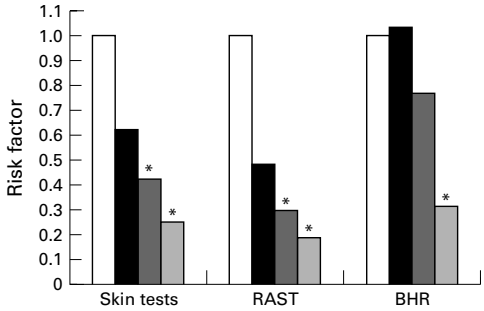

*Figure 4 Association between the risk of atopy, as determined by positive skin prick test or radioallergosorbent test (RAST), or the risk of bronchial hyperresponsiveness and frequent fever in infancy among asthmatic children. Frequency of fever was recorded as never (open columns), 1–2 times (closed columns), 3–4 times (dark grey columns), or ⩾5 times (light grey columns). *p < 0.05 v children with fever frequency of never (data from von Mutius et al[23]).*

increases in parallel with the increased incidence of asthma exacerbations requiring hospitalisation.[21 22]

One study, in which fever was assessed as a potential risk factor for developing asthma, showed that children who had experienced at least three episodes of fever within their first year were significantly more likely to develop asthma and current wheeze than those who had never had an episode of fever ($p < 0.05$; fig 3).[23] Asthmatic children who experienced at least three episodes of fever had a significantly reduced risk of developing atopy at school age; those who experienced at least five episodes also had a significant reduced risk of bronchial hyperresponsiveness at school age ($p < 0.05$ *v* children with a fever frequency of never; fig 4).[23] When the risk of asthma was evaluated in children with or without either atopy or bronchial hyperresponsiveness, there was a strong correlation between the frequency of fever and the prevalence of asthma in non-atopic children (fig 5).[23] These data indicate that children who experience frequent infections early in their life are more susceptible to the development of non-atopic asthma and recurrent wheeze at school age. However, these individuals were less likely to be symptomatic at school age, indicating that a subset of the population who experienced frequent early

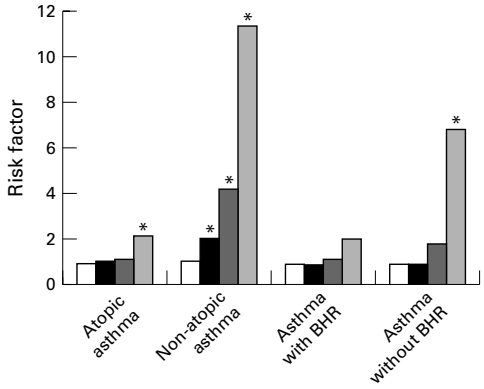

Figure 5 Risk of asthma with and without atopy/bronchial hyperresponsiveness with frequent fever episodes in infancy. Frequency of fever was recorded as never (open columns), 1–2 times (closed columns), 3–4 times (dark grey columns), or ⩾5 times (light grey columns). p < 0.05 v children with fever frequency of never (data from von Mutius et al[23]).

childhood infections have a better prognosis and are less related to the atopic asthmatic phenotype.

Symptom reduction in adolescence

Asthmatic children who develop and continue to have atopic sensitisation have a worse prognosis than wheezers with virus induced illness.

Many studies have revealed that when asthmatic children reach adolescence, symptoms may disappear in up to 75% of patients who wheezed before the age of 7.[24–26] In contrast, many adults who had childhood asthma and/or wheezing but who appear to have outgrown it, may still experience respiratory symptoms.[27 28] Patients with persistent wheezing are less likely to be symptom free as adults.[24] However, lack of medical attention and poor use of medication to relieve symptoms may explain why the prevalence of wheezing remains high in adolescence.[28]

Burrows and colleagues[29] reported that bronchial hyperresponsiveness to methacholine also lessened with age in children aged 9–15 years who underwent a skin prick test to various allergens, including the house dust mite, dog, cat, and aspergillus. The results showed that allergen sensitivity, determined by the diameter of the skin wheal, was proportional to methacholine induced bronchial hyperresponsiveness. A follow up analysis showed that bronchial hyperresponsiveness decreased with age in children who were non-atopic and in those who were only mildly affected.

Conclusions

Paediatric asthma exerts a tremendous burden not only on families but also on healthcare resources for the management of exacerbations of asthma. Early detection and treatment of childhood asthma may contribute to reducing this burden, and inhaled corticosteroids are an important tool in this regard. Increased understanding of risk factors should enable existing therapies to be better targeted, while facilitating the development of new treatment options.

Controlled management of paediatric asthma should improve the child's ability to participate in extracurricular activities, resulting in huge social benefits.

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