ABC of allergies

The epidemiology of allergic disease

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Atopy is defined as the production of specific IgE in response to exposure to common environmental allergens, such as house dust mite, grass, and cat. Being atopic is strongly associated with allergic disease such as asthma, hay fever, and eczema, but not everyone with atopy develops clinical manifestations of allergy and not everyone with a clinical syndrome compatible with allergic disease can be shown to be atopic when tested for specific IgE to a wide range of environmental allergens. This is particularly so for asthma.

Asthma is arguably the most serious of the allergic diseases in that it is disabling (causing more than 100 000 hospital admissions each year in England and Wales) and occasionally fatal. In 1995, 137 people aged under 45 died as a result of asthma. Although concern has been expressed that death certificates may overestimate or underestimate asthma mortality depending on diagnostic fashion, significant misclassification with other forms of chronic obstructive lung disease in this age group is unlikely. In the early 1960s asthma mortality increased dramatically in many countries. The increase was attributed to the excessive use of non-selective β agonists, which were subsequently withdrawn from the market. More recent increases in asthma mortality reported from Britain, France, and the United States may be related to increased prevalence or severity of asthma or inadequate health care. Evidence for the latter comes from audits and confidential inquiries that show inadequate treatment of asthma in the months leading up to death and during the fatal attack and the observation of higher mortality in populations recognised as often receiving poor health care (socioeconomically deprived people in Britain; black people in the United States). In England and Wales asthma mortality rose between the mid-1970s and the mid-1980s but declined steadily during the early 1990s.

Hay fever and eczema are important causes of morbidity, being responsible for a substantial proportion of health service use, particularly in primary care, and reduced quality of life.

Prevalence

Time trends

The prevalence of diseases associated with atopy has increased in many parts of the world over the past 20 to 30 years. In the United Kingdom the prevalence of diagnosed asthma and symptoms strongly suggestive of asthma in children has increased at a rate of about 5% a year. Increases of a similar magnitude have been observed in Sweden, Switzerland, Norway, the United States, Australia, New Zealand, and Taipei. Some of this apparent rise may have occurred in response to greater public awareness of asthma and a greater tendency of parents to report wheezing illnesses in their children and to attend their doctor for treatment of asthma.

Few serial surveys have examined an increase in objective markers for asthma, although the prevalence of exercise induced bronchial constriction has increased in Welsh schoolchildren over 15 years, suggesting that the increase in reported symptoms reflects a genuine change in health status. Few reported serial surveys have examined the prevalence of asthma in adults, although the proportion of military recruits with asthma has increased in Finland, Sweden, and Israel.

Age standardised asthma mortality, England and Wales, 1969-94 (both sexes, 15-64 years)

Changes in prevalence of asthma and wheeze, according to surveys conducted 1956-93 worldwide

Change in prevalence of wheeze, asthma, exercise induced bronchial constriction, hay fever, and eczema in children in south Wales between 1973 and 1988

Change in prevalence of sensitisation to common allergens in schoolchildren in Japan and Switzerland

Most of the surveys that have shown increases in the prevalence of asthma have also shown increases in the prevalence of other allergic diseases, such as hay fever and eczema. In the United Kingdom, results from the three national birth cohorts (samples of people born in 1946, 1958, and 1970) have shown a marked increase (5.1%, 7.3%, and 12.2% respectively) in the prevalence of eczema as reported by the mother in children aged under 5.

The rising prevalence of allergic disease has resulted in increased use of health services. For asthma, hospital admissions (particularly among children aged under 5 years), consultation with general practitioners, and the use of drug treatment all rose sharply during the 1980s. Consultations with general practitioners for managing hay fever also increased.

The increased prevalence of all allergic diseases suggests that the prevalence of atopy has increased. Epidemiological information from Switzerland and Japan shows that the prevalence of atopy is increasing in children. In both these studies the increase in the prevalence of atopy was due to an increase in sensitisation to a variety of allergens and not dominated by an increase in sensitisation to one particular allergen. In Britain no evidence exists that exposure to allergen has increased—in fact grass pollen levels have steadily decreased over the past 20 years and pet ownership has probably not changed. At present the extent to which changes in the prevalence of atopy and changes in allergen exposure explain the time trends in allergic disease is unknown.

Geographical distribution

Until recently the methods used for assessing the prevalence of allergic disease were not standardised and comparisons of disease prevalence between countries were flawed. Two major research initiatives, the European Community respiratory health survey (ECRHS) and the international study of asthma and allergies in childhood (ISAAC) have developed and executed standardised protocols for the assessment of disease prevalence in many different countries in adults and children.

The European Community respiratory health survey has shown wide geographical variation in the reported prevalence of symptoms highly suggestive of asthma, treatment for asthma, and current hay fever or nasal allergies in adults. In general, symptoms are more common in New Zealand, Australia, the British Isles, and the United States than in mainland Europe, although there is wide variation even within some countries. The distribution of atopy (for these purposes defined as sensitisation to house dust mite, grass, cat, or *cladosporium* species) shows a similar distribution, with marked variation between countries, although the extent to which variation in atopy explains variation in symptoms is still under investigation.

Areas with high (red) and low (blue) prevalence of asthma (top), hay fever and nasal allergies (centre), and sensitisation to any one of house dust mite, cat, timothy grass, or *cladosporium* species (bottom), according to results of the European Community respiratory health survey (white circles represent areas that participated in the study but which did not have a particularly high or low prevalence)

Prevalence (percentage) of self reported asthma symptoms in past year in children aged 12-15 years in five centres participating in the international study of asthma and allergies in childhood

	Bochum, Germany	West Sussex, UK	Wellington, New Zealand	Adelaide, Australia	Sydney, Australia
Sample size	1928	2097	1863	1428	1519
Wheeze in past year	20	29	28	29	30
Severe attack of wheezing in past year	6	7	11	10	13

The international study of asthma and allergies in childhood, which has not yet been fully reported, has shown that severe asthma is more common in children living in New Zealand and Australia than in those living in West Sussex and in Bochum, Germany.

Risk factors

Genetics

Total IgE concentration, the production of specific IgE, and bronchial hyperreactivity are all under some degree of genetic control. Chromosome 5 has been implicated in the regulation of total IgE concentration, chromosome 11q linked to the atopic phenotype (high total IgE concentration or specific IgE to a common allergen), and chromosome 14 linked to eczema; specific HLA haplotypes are linked to the development of IgE to some allergens (for example, specific allergens from rye grass are associated with DR3). Although genetic susceptibility to allergic disease is important, it is unlikely that either the large geographical variations in disease prevalence between peoples of similar genetic background, or the increase in allergic disease over the past few decades can be explained by genetic factors.

Age and sex

The incidence of asthma is higher in children than in adults. Longitudinal surveys suggest that children with mild disease are likely to become asymptomatic as teenagers, whereas those with more severe disease will have symptoms that persist throughout life. To some extent this "ageing" effect explains why in some cross sectional studies allergic disease is less common in adults than in children, but these observations may also reflect an increased propensity for asthma and atopy in those born later in the century.

More boys than girls have atopy, asthma, and hay fever, although these differences become less apparent later in life. At all ages, males have higher total IgE concentration than females.

Infection

More than 80% of asthma exacerbations in children are of viral origin. This epidemiological observation equates well with most clinical experience, but consensus is weaker over the role of infection in the pathogenesis of atopy and allergic disease.

Children who grow up in large families, especially if exposed to older siblings, are likely to experience more childhood infections than those who come from small families. Because the prevalence of allergic disease, in particular hay fever, and sensitisation to common allergens is lower in those who grow up in large families or who have older siblings, high rates of infection in childhood may protect against the development of atopy and allergic disease.

Secular changes in family structure and maternal smoking do not fully explain the increase in wheezing, hay fever, or eczema in adolescents.

Smoking

- People who smoke have higher total IgE concentration and are more likely to become sensitised to allergens in the workplace than people who do not.
- The association between smoking and sensitisation to common allergens, however, is not clear, with several reports of lower rates of sensitisation to common environmental allergens and less hay fever in smokers
- This may be explained to some extent by the "healthy smoker" bias (the tendency of those with allergic disease not to smoke) but may also reflect a genuinely reduced incidence of some forms of allergy among smokers
- Smoking is an important risk factor for bronchial hyperreactivity—a feature of asthma—but its association with asthma remains uncertain
- Children whose mothers smoke during pregnancy have reduced lung function and more wheezing illness during childhood but do not seem to have more allergic diseases

Prevalence of hay fever in young adults by family size, number of older siblings, and number of younger siblings

Exposure to allergens

The development of sensitisation to an allergen requires exposure to that allergen. Exposure early in life may be associated with a higher risk of sensitisation than exposure later in life, but no evidence exists yet that reducing allergen load in the home of young children reduces sensitisation or the development of allergic disease.

Once sensitisation has occurred, repeated exposure to that allergen is likely to trigger symptoms. Epidemics of asthma have occurred when high levels of allergen have been present in ambient air. In Barcelona outbreaks of asthma identified through sudden increases in emergency admissions for asthma resulted from unloading of soy beans at the local harbour. The epidemics were prevented by reducing the ambient allergen load by installing filters at the top of the storing tower. In Britain a severe thunderstorm in 1994 was associated with the largest ever outbreak of asthma. Many of the epidemic cases had previously experienced only hay fever, and asthma was probably precipitated in these grass sensitised individuals by the release during the thunderstorm of small aerosolised particles of grass allergen from grass pollen in the air. In Britain more deaths from asthma occur during the summer and early autumn than during the winter. This seasonal pattern is not observed in deaths from asthma in elderly people and may be another manifestation of the importance of allergens on the severity of asthma, particularly in young people.

In Britain most people with allergic disease are sensitised to house dust mite, and this allergen has been implicated as the most important allergen for both the development and exacerbation of asthma and eczema. In other countries sensitisation to cat, grass, or moulds may be a more important cause of disease.

More than 300 agents have been identified as occupational allergens. Occupational exposure to allergens may cause eczema, rhinitis, or asthma. Occupational exposure to agents known to cause asthma may be responsible for as many as 1 in 15 cases of adult onset asthma in some populations.

Diet

Over the past 20 years diet has dramatically altered in most developed countries. Sensitivity to food, particularly to milk, eggs, and fish, is not uncommon in childhood; in adults, though "intolerance to foodstuffs" is frequently reported, it is rarely observed on formal challenge. Withdrawal of allergenic foods may reduce the severity of some allergic disease. Other dietary factors such as electrolytes (sodium and magnesium), nature of fatty acids in the diet (in particular oily fish), and antioxidants have all been identified as possibly increasing the severity of asthma.

The data in the second graph are from Burr et al (*Arch Dis Child* 1989;64:1452-6); in the third graph are from Nakagomi et al (*Lancet* 1994;343:122-3) and Gassner et al (*Schweiz Rundschau Med* 1992;81:426-8); in the fourth graph are from Strachan D (*Clin Exp Allergy* 1995;25:296-303); and in the second table are from Meredith S (*J Epidemiol Community Health* 1993;47:459-63). The first table and the final graph are adapted with permission from Pearce et al (*Eur Respir J* 1993;1455-61) and the Office for National Statistics' *Health of Adult Britain*, respectively.

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The ABC of allergies is edited by Stephen Durham, honorary consultant physician in respiratory medicine at the Royal Brompton Hospital, London. It will be published as a book towards the end of 1998.

Odds of dying from asthma by month compared with odds of dying in January (England and Wales, 1958-91)

Incidence (95% confidence interval) of occupational asthma (cases per million workers per year) in some high risk occupational groups

Occupational group	Incidence
Coach and other spray painters	658 (508 to 839)
Chemical processors	364 (274 to 475)
Plastics workers	337 (248 to 448)
Bakers	334 (248 to 440)
Laboratory technicians and assistants	188 (139 to 247)
Workers in welding, soldering, and electronic assembly	175 (138 to 218)

Further reading

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