

ABC of asthma

Prevalence

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Genetics

Our understanding of the genetics of asthma has recently advanced considerably. A familial link has been recognised for some time together with an association with allergic rhinitis and allergic eczema. The familial link with atopic disorders is strongest in childhood asthma and with the link to maternal atopy. Earlier investigations were helped by studies of isolated communities—such as in Tristan da Cunha, where the high prevalence of asthma can be traced to three women among the original settlers.

Genetic studies

Early studies of genetic links within families with more than one member with asthma suggested a strong link to certain genetic regions of interest, particularly 5q and 11q. Further studies in different populations did not replicate all the early findings, and it became evident that, as in other common conditions, the genetic links were not simple. Several issues have been identified, and there seem to be differences in the links between ethnic groups. Susceptibility seems to be determined by several genes that have an effect in different aspects of asthma. There has been steady progress moving from areas of broad linkage to candidate asthma genes. Again, findings have not always been replicated in different populations. Genes have been identified that are linked to the Th2 cytokine signalling pathway, Th2 cell differentiation, airway remodelling, innate and adaptive immune responses, and IgE levels. Most of the work relates to the presence of asthma. Different asthma phenotypes, the natural course and severity of asthma, and interaction with environmental influences are being investigated.

Future investigations

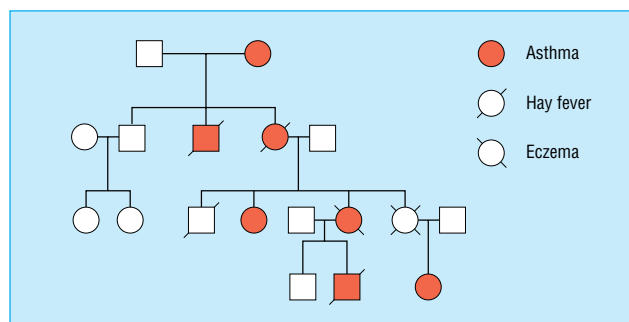
Future investigations in the genetics of asthma may teach us more about susceptibility and progression in asthma. Genetic influences may also underlie different responses to treatment and raise the promise of matching treatment to a patient's individual response and the production of new treatments aimed at influencing specific genes and their products.

Early environment

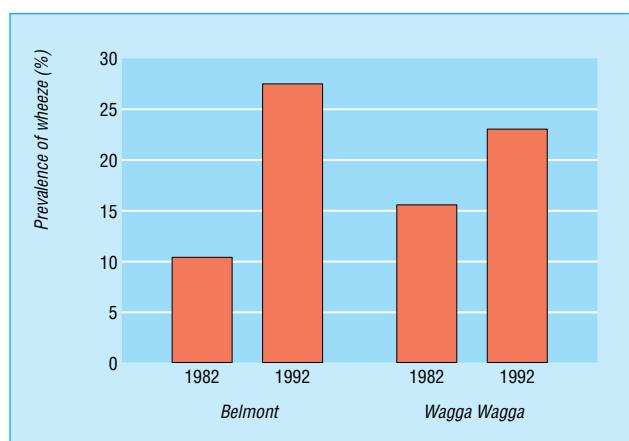
Genetic susceptibility alone does not account for the development or persistence of asthma. Genetic susceptibility is linked to environmental exposure. Early environmental influences before and soon after birth may be particularly important. The type and extent of exposure to allergens and infections may influence the development of the immune process and the likelihood of the development of asthma.

The hygiene hypothesis links to this balance of the parts of the immune system. Asthma is less likely to develop in children with older siblings. The hypothesis is that processes such as earlier exposure to infections from older siblings and commensal gut bacteria may help the maturation of the immune system and the switch to a Th1 lymphocyte phenotype rather than the Th2 phenotype. The Th1 cellular immune responses are related to protection against many infections while Th2 responses favour atopy. The theory was supported by evidence that asthma and allergies are less common in children brought up on farms and in close contact with animals.

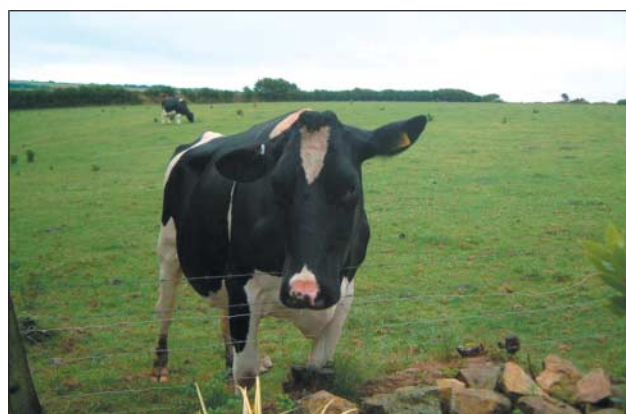
This article is adapted from the 5th edition of the *ABC of Asthma in Adults*, which will be published later this year



Family tree of an atopic family



Increase in prevalence of wheeze in children aged 8-10 in two towns in New South Wales between 1982 and 1992. The counts of house dust mite in domestic dust increased substantially over the same period (Peat JK, et al, *BMJ* 1994;308:1591-6)



Early exposure to animals seems to reduce the risk of subsequent asthma

The hypothesis has been extended to suggest that, as well as immune maturation in infancy, the degree of competence of the immune system achieved at birth may be important. The influences on this are poorly understood but might be related to the prenatal cytokine environment.

Genetic factors and clinical course

Atopic people are at risk of asthma and rhinitis. They can be identified by immediate positive results on skin prick tests to common allergens.

The development of asthma depends on environmental factors acting with a genetic predisposition. The movement of racial groups with a low prevalence of asthma from an isolated rural environment to an urban area increases the prevalence in that group, possibly because of their increased exposure to allergens such as house dust mites and fungal spores or to infectious agents, pollution, and dietary changes.

Family history—The chance of a person developing asthma by the age of 50 is 10 times higher if they have a first degree relative with asthma. The risk is greater, the more severe the relative's asthma. Breast feeding has been suggested to reduce the risk of a child developing atopic conditions such as asthma because it restricts the exposure to ingested foreign protein in the first few months of life. Conflicting results have been published, and it may require considerable dietary restriction by the mother to avoid passing antigen on to the child during this vulnerable period. Overall, although infant wheezing may be less common in breastfed infants, there is no good evidence that asthma is less prevalent. Nevertheless, the many other benefits of breast feeding indicate that it should be encouraged.

Smoking in pregnancy—Maternal smoking in pregnancy increases the risk of childhood asthma; exposure during the first few years of life is also detrimental. Studies of paternal smoking have produced similar but less certain trends.

Weight control—Obesity is associated with an increased likelihood of asthma. Regular exercise to maintain fitness and control weight is sensible advice for people with asthma.

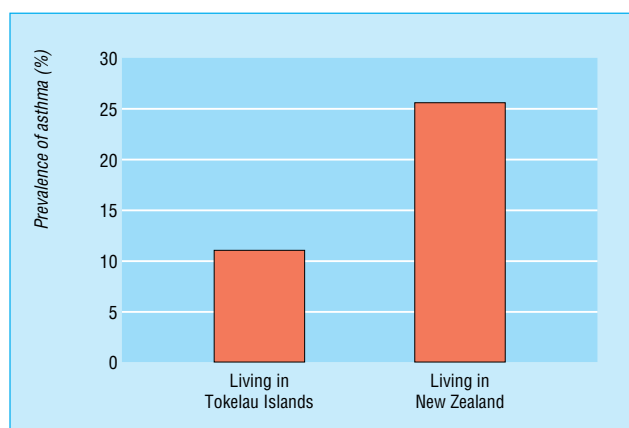
Diagnostic criteria in epidemiological studies

For epidemiological purposes, a common set of criteria is the presence of symptoms in the past 12 months and evidence of increased bronchial responsiveness. Phase 1 of the international study of asthma and allergies in childhood (ISAAC) looked at prevalence of symptoms in 13-14 year olds in 155 centres worldwide. Prevalence rates differed over 20-fold, and ISAAC phase 2 will explore these differences. The Odense study in children found 27% with current symptoms of asthma but only 10% had asthma diagnosed. Different diagnostic tests, such as methacholine responsiveness, peak flow monitoring, and exercise testing, did not correlate well with each other. Each test was reasonably specific, but individual sensitivities were low. The combination of peak flow monitoring at home and methacholine responsiveness produced the best results.

Prevalence figures

The reported prevalence depends on the definition of asthma being used and the age and type of the studied population. Regional variations exist, particularly in developing countries, where rates in urban areas are higher than in poor rural districts.

For clinically important asthma, many countries have broad prevalences of around 5% in adults and 10% in children, but



Prevalence of asthma in Tokelauan children aged 0-14 still in the Tokelau Islands or resettled to New Zealand. Asthma, rhinitis, and eczema were all more prevalent in islanders who had been settled in New Zealand after a hurricane. (Waite DA, et al, *Clin Allergy* 1980;10:71-5)



Smoking in pregnancy increases the risk of asthma in the child

The Odense study confirms that no single physiological test is perfect and that different tests may detect different clinical aspects of asthma. A positive result on any test combined with a typical history would confirm the diagnosis of asthma

definitions based on hyper-responsiveness or wheeze in the past 12 months produce rates of around 30% in children. Although the label of asthma may have been used more readily in social classes I and II in the past, more recent figure for young adults across Europe indicate a higher prevalence in lower socioeconomic groups, regardless of atopy.

Most studies using equivalent diagnostic criteria across the 1970s to 1990s showed that the prevalence of asthma was increasing. More recent studies show that this increase has reached a plateau or even reversed in developed countries. A recent study showed a decline from 29% to 24% in the symptom of wheeze in the previous year in Australian primary school children. ISAAC showed a similar decrease from 34% to 28% for 12-14 year olds between 1995 and 2002. Interestingly, the label of asthma, especially mild asthma, was being used more over this time.

During the past 10 years admissions to hospital for asthma and emergency room attendances have fallen, especially in children. This may be linked to better control through appropriate treatment. The pattern in developed countries suggests that prevalence peaked around 1990. Although there has been an increasing tendency to use the label of asthma, the true prevalence and the frequency of more serious asthma is showing signs of a reduction.

In children aged around 7 more boys are affected than girls (sex ratio 1.5:1 to 2:1), but teenagers boys do better than girls, and by adulthood the sex incidence has become about equal.

Changes in prevalence

Several explanations were suggested for the increase in prevalence. The strong genetic element has not changed so any true increase, other than in changes in detection or diagnosis, must come from environmental factors. No single explanation is likely as the possible factors do not apply equally to all the populations experiencing the change in prevalence.

Change in the indoor environment—The advent of centrally heated homes with warm bedrooms, high humidity, and soft furnishings probably increases exposure to house dust mites. This may be part of the explanation but does not fit with changes in developing countries.

Smoking—Maternal smoking during pregnancy and infancy is associated with an increased prevalence of asthma in childhood. The increase in smoking among young women in recent years may play some part in the increase in prevalence. Smoking by people with asthma increases its persistence.

Family size—The reduction in family size, with the increased risk in first born children, plays a small part.

Pollution—Symptoms of asthma are made worse by atmospheric pollution such as nitrogen oxides, sulphur dioxide, and small particulate matter. However, outdoor environmental pollution levels do not correlate with changes in prevalence. Indoor pollution from nitrogen oxides, organic compounds, and fungal spores may be more important.

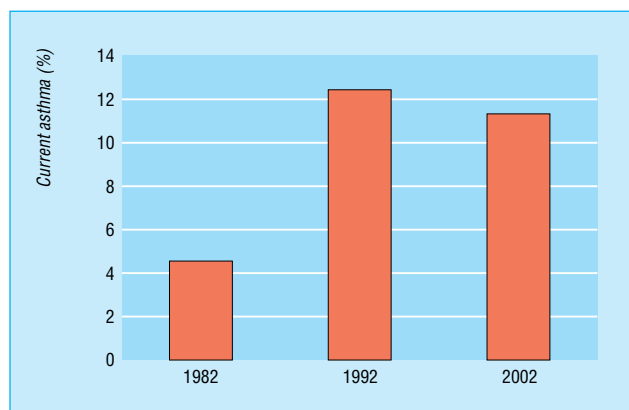
Diet—Some studies have shown relations between diet and asthma related to higher salt intake, low selenium, or reduced vitamin C, vitamin E, or certain polysaturated fats. The effects of dietary intervention, however, have not supported or refuted this as a major contribution.

The picture of the pregnant woman is published with permission of Faye Norman/Science Photo Library.

The ABC of Asthma in Adults is edited by John Rees, consultant physician, Guy's, King's and St Thomas's School of Medicine, London SE1 9RT, john.rees@kcl.ac.uk

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Prevalence of asthma in Australian children aged 8-11 has shown that the prevalence has reached a plateau (adapted from Toelle BG, et al, *BMJ* 2004;328:386-7)

Possible explanation for changes in prevalence of asthma

- Indoor environment
- Smoking
- Family size
- Pollution
- Diet



Outdoor pollution increases symptoms in people with asthma

Further reading

- Anderson HR, Ruggles R, Strachan DP, Austin JB, Burr M, Jeffs D, et al. Trends in prevalence of symptoms of asthma, hay fever, and eczema in 12-14 year olds in the British Isles, 1995-2002: questionnaire survey. *BMJ* 2004;328:1052-3
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