The epidemiology of atopic dermatitis

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Atopic dermatitis is the most common chronic inflammatory skin disease and is a major cause of morbidity and suffering. This review examines its differing prevalence worldwide, its aetiology, and genetics.

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Atopic dermatitis (AD) affects up to one in five children in the UK. While it is often perceived as a minor problem it can cause considerable disruption to the lives of sufferers and those who care for them. It involves significant cost for the family and health-care systems (Fennessy et al, 2000).

WHAT IS ATOPIC DERMATITIS?

AD is synonymous with eczema; this literally means 'to boil out' (from the Greek). It is an erythematous condition with scaling, vesiculation and crusting, which is typically very itchy. Histologically the main characteristic of AD is spongiosis.

In order to describe the epidemiology of AD a precise and robust set of diagnostic criteria are required. There have been several attempts to produce such criteria but the only criteria that have been validated both in a hospital and community setting are those published by Williams et al in 1994. These state that the diagnosis of AD requires an itchy skin condition in the last 12 months plus three or more of the following:

- History of flexural involvement
- History of asthma or hay fever
- History of generalized dry skin
- Onset of rash before the age of 2 years (not applicable if child aged under 4 years)
- Visible flexural dermatitis.

SEVERITY OF AD

The effects of AD range from dry skin and mild irritation to a generalized, severe, disabling skin condition. It is therefore necessary to somehow express severity as part of an epidemiological description of the condition. One definition described in the literature uses sleep disturbance as a parameter (Williams et al, 1999).

The Nottingham group (Emerson et al, 2000) evaluated AD by using three measures of severity:

- Chronicity – for what proportion of the last year has the individual had AD?
- Intensity – how many nights of sleep are disturbed per week?
- Extent – what percentage of the body is involved?

A community-based sample looked at with the above scoring system showed the distribution of severity shown in *Figure 1*.

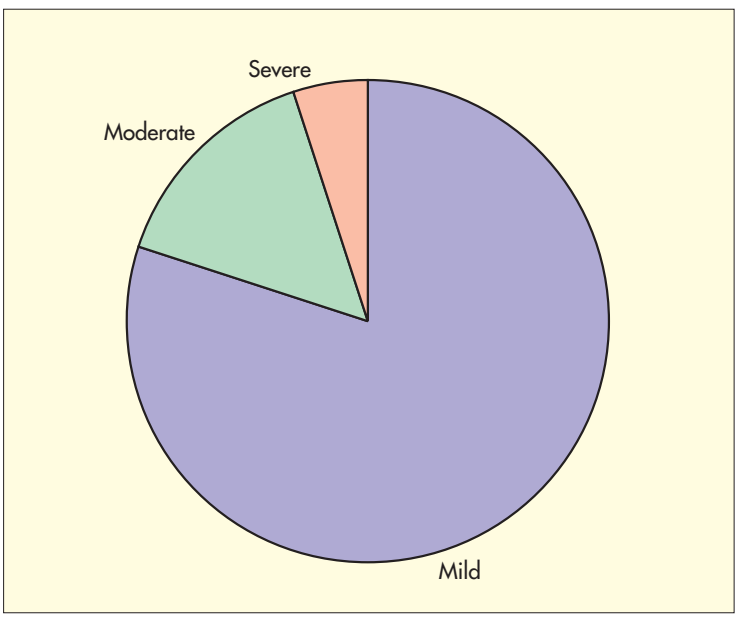
PREVALENCE BY AGE

AD affects all ages but is primarily seen in children. Observations from a cohort born in 1958 (Williams and Strachan, 1998) showed:

- A prevalence of AD of 12.6%
- Onset of AD by 7 years of age in 66%
- In 65% AD had resolved by 7 years of age
- In 74% AD had resolved by 16 years of age.

It is recognized that a proportion of those who clear their AD in childhood may relapse in adult life.

Figure 1. Severity of atopic dermatitis in the community.



WORLDWIDE PREVALENCE OF AD

The prevalence of AD varies markedly across the world. Williams et al (1999) have shown that prevalence varies from just above 1% to just below 20% in children aged 6–7 years. Their findings are shown in *Figure 2*. The percentages quoted relate to AD diagnosed according to recognized criteria.

Population migration results in a change in prevalence of AD from the rate in the country of origin to the country of residence (Worth, 1962).

PREVALENCE WITHIN DIFFERENT AREAS OF THE UK

As well as varying from country to country AD varies within different regions. In the UK it is more common in the north Midlands, London, and the south east (Williams and Strachan, 1998). There is no difference in the prevalence between races in a single city in the UK (Neame et al, 1995).

CHANGES IN PREVALENCE OVER TIME

AD is increasing in frequency over time. A study of Scottish school children showed a prevalence of 5.3% in 1964 and 12% in 1986 (Ninan and Russell, 1992). A study of British cohorts over time (Ninan and Russell, 1992) shows a similar rise: 5.1% in 1946, 7.3% in 1958 and 12.2% in 1970. Reasons suggested for the increasing prevalence include:

- Decreased rates of breast-feeding
- Earlier introduction of weaning foods
- Widespread use of food additives
- Changes in the formulation of infant formulas
- Environmental factors favouring the expression of AD in those who are genetically susceptible.

However, no direct relationship has been shown for any of the above factors.

SOCIOECONOMIC STATUS

AD is one of the few diseases that is more common in higher socioeconomic class (SEC). In the UK it is almost twice as common in children

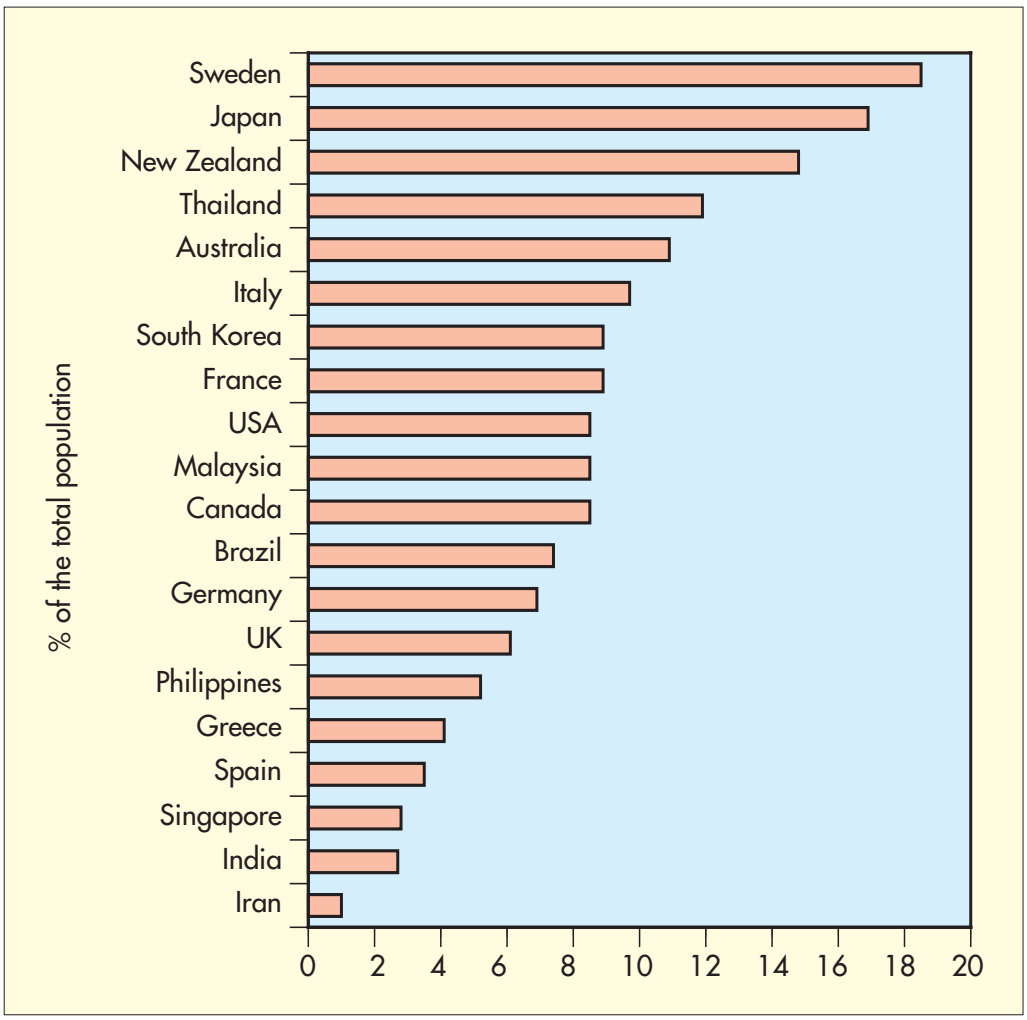


Figure 2. Prevalence of atopic dermatitis in 6–7-year-olds.

brought up in households of high SEC compared with children living in low SEC households (Williams and Strachan, 1998).

There is also a temporal change in the effect of SEC – in 1946 AD was less prevalent in high SEC children than low SEC children. By 1958 the position had reversed and this remained the case in 1970 (Taylor et al, 1984).

ASSOCIATED CONDITIONS

One-third of children aged 5–7 years with AD also have asthma or hay fever. Children with severe AD are more likely to develop asthma. The following are also more common in children with AD:

- Mollusca contagiosa
- Viral warts
- Hyperreactivity to insect bites
- Migraine
- Recurrent herpes simplex infections
- Glue ear and recurrent ear infections.

SYMPTOMATOLOGY OF AD

Sleep disturbance is said to occur in 10–30% of preschool children without AD but in 63% of children with AD. This increases to 86% during exacerbations and decreases to 26% when the AD is well controlled (Lawson et al, 1995). Children with AD also have increased clinginess and dependency on carers and 54% may have evidence of behavioural problems (Daud et al, 1993). Also, children with AD miss more school than their peers and are often socially marginalized at school.

AD has an effect on economic status; 27% of mothers of children with AD are able to work outside the home compared with 65% of mothers of children without AD (Daud et al, 1993). Severe financial problems occur in 11% of families that include a child with AD.

AD also has a significant effect on the family life of sufferers. Treatments may take up to 2 hours a day, leaving a parent little time to spend with other children. Relationship problems occur in a higher proportion of families with children with AD than in comparable families without AD (Lawson et al, 1995).

GENETICS

AD is a genetic disorder based on the interactions between an unknown number of genes and environmental factors. In a family with an affected child there is usually a family history for eczema or one of the other atopic disorders, asthma and rhinitis. Twin studies of AD have shown concordance of 0.72–0.86 in monozygotic and 0.21–0.23 in dizygotic twin pairs, indicating the presence of strong genetic factors in the development of the disease (Cookson et al, 2002).

Candidate genes include those that have been shown to influence immunoglobulin E (IgE) responsiveness: β chain of the high-affinity receptor for IgE (chromosome 11); the interleukin 4/5 cluster (chromosome 5); interleukin 4 receptor (chromosome 16); HLA-DR (chromosome 6) and the T-cell receptors α/δ (chromosome 14), and those that are associated specifically with AD: mast cell chymase (14q11), SPINK5, the Netherton's gene (5q31) (Cookson et al, 2002).

Two genome-wide screens have been carried out: the first study in families of German and Scandinavian children with AD found linkage to a region on chromosome 3q21; the second screen of British families found three regions of linkage on chromosomes 1q21, 17q25, and 20p. All four loci are closely coincident with regions known to contain psoriasis susceptibility genes. The implication is that these genes have general effects on dermal inflammation and immunity.

One important region is on chromosome 1q21 which overlies the human epidermal differentiation complex, and these genes are involved in the regulation of epidermal differentiation (Cookson et al, 2002).

The genetics underlying AD are complex and seems to involve multiple genes with varying functions: some genes that relate to IgE responsiveness, some that affect the barrier function of the skin, and others that have a more general affect on skin inflammation. Unravelling the genes involved will hopefully lead to a better understanding of the pathophysiology of AD.

THE EFFECT OF IGE

IgE is a monomeric immunoglobulin. It binds to Fc receptors on the surface of mast cells, triggering the release of inflammatory mediators. It normally exists at levels below that of other immunoglobulins. Levels are markedly elevated in 80% of patients with AD. About 10% of patients with AD have a normal IgE with no specific IgE reactivity, which suggests that IgE responsiveness is a phenomenon of AD rather than a primary causative factor. Cord blood IgE has been shown to be a helpful predictor of AD (Karmus et al, 2001).

PRIMARY PREVENTION

Exclusive breast-feeding in the first 3 months of life has been shown to reduce the incidence of

AD if there is a family history of atopy. This effect is lessened in the general population (Gdalevich et al, 2001). The affect of antenatal maternal allergen avoidance has not been shown to be significant when a meta-analysis is performed. There is, however, evidence that decreasing allergens while breast-feeding may reduce the incidence of AD (Kramer, 2000). Allergens avoided included cows' milk and eggs.

Early exposure to high concentrations of house dust mite correlates with decreased levels of AD, as does early exposure to pets (Gehring et al, 2001; Nafstad et al, 2001). Exposure to a diverse range of solid foods at the weaning stage is associated with a higher incidence of AD (Ferguson et al, 1982). Babies born prematurely of very low birth weight have a significantly lower prevalence of AD at 1 year of age than matched controls born at term. It has been postulated that early exposure to antigens may cause tolerance rather than sensitivity (Buhree et al, 1999).

CONCLUSION

AD affects up to 20% of the childhood population. At its worst it is a severely disabling illness. It is hoped that a further understanding of the epidemiology and genetics of the disease will in turn allow more effective treatment and perhaps prevention. HM

Conflict of interest: none.

KEY POINTS

- Atopic dermatitis is the most common chronic inflammatory skin disorder.
- It affects up to 1 in 5 children.
- The majority of children cease to suffer with atopic dermatitis by 16 years of age.
- Prevalence is increasing over time.
- It has a marked effect on personal and family life.

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