

Epidemiology of allergic rhinitis

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It is increasingly important to study the epidemiology of allergic rhinitis (AR), as a series of observations have indicated that we in the western countries at present have a very high and increasing prevalence rate of AR. The study of the relationship between the various factors determining the frequency and distribution of AR is important in order to identify and, if possible, to eliminate the factors which account for the high frequency of AR.

In this article we shall present the results of published prevalence studies and discuss the diagnostic problems and the determinant factors of relevance for the interpretation of the prevalence studies. Finally, we shall speculate on the possible reasons for the "hay fever epidemic".

Diagnostic problems

AR is usually classified as seasonal allergic rhinitis (SAR) and perennial allergic rhinitis (PAR).

SAR, or hay fever, is particularly well suited for epidemiological studies for a number of reasons. 1) There is an obvious causal relationship between allergen exposure and all symptoms. 2) The typical seasonal occurrence of the symptoms renders the case history reliable. 3) It is easy to confirm the diagnosis by skin testing with potent allergen extracts. 4) The degree of exposure to allergen can be quantified by the daily pollen count, and it can be compared from place to place and from time to time.

However, there are some problems in making a well-defined diagnosis of AR in epidemiological investigations, which can be exemplified by the following study. In Danish medical students we found a positive skin test to pollen in 24%, but only 15% had ever had symptoms, and only 8% had received treatment. Thus, the results of an epidemiological

study may vary considerably depending upon 1) whether skin testing is performed (asymptomatic allergy and AR), 2) only a questionnaire is used (symptomatic AR and non-AR), or 3) whether patients seeking medical advice are studied (severe cases of AR and non-AR).

During the last decades a series of studies on the prevalence of AR have been published from different countries (Table 1). Most studies are exclusively based on a questionnaire, and allergy testing has been performed mainly in the studies of university students. When allergy testing is not used, "AR" includes SAR, PAR and non-AR. SAR is the most frequent of these diseases, but their relative contribution to the total prevalence figures in different studies is not known. Hagy & Settipane (23) found a 4 to 1 ratio between SAR and PAR, which may be representative for most studies in temperate zones.

PAR is more difficult to study than SAR, as an assessment by history of a causal relationship between symptoms and allergen exposure is unreliable. Mite-allergic patients can not, and animal-allergic patient will not associate sneezing bouts with allergen exposure. In addition, it is difficult to distinguish PAR from other forms of chronic rhinitis. Thus, published data on PAR may be less reliable than those on SAR.

Determinant factors

As seen in Table 1, there are considerable differences between the reported prevalence rates of AR. This may reflect both sampling and methodological differences, as well as true differences between the study populations. Below we shall describe some of the determinant factors which can influence the prevalence rate of AR.

Table 1. Published accumulative prevalence rates for allergic rhinitis.

Location (reference)	Year of publication	Age	Prevalence (percent)
Switzerland (1)	1970	5-6	0.5
Switzerland (2)	1984	4-6	1.1
Tasmania (3)	1984	7	6.8
Sweden (4)	1977	7	7.4
Sweden (5)	1995*	7	5.5
Sweden (5)	1995**	7	8.1
Tokelau (6)	1980	0-14	14
New Zealand (6)	1980	0-14	28
Maldives (7)	1979	0-15	20.4
Norway (8)	1985	8-14	5.4
Finland (9)	1991	3-18	6.0
Florida (10)	1978	5-16	12.1
Denmark (11)	1993	5-16	10.5
Estonia (12)	1995	10-12	7.4
Norway (13)	1995	13	17.8
Sweden (14)	1994	14	17
Switzerland (1)	1970	15	4.4
Switzerland (2)	1984	15	6.1
Finland (15)	1980	15-17	22
USA (16)	1964	14-18	19
Finland (17)	1970	10-19	2.7
Switzerland (18)	1989	15-24	16
USA (19)	1974	16-24	15.5
USA (20)	1959	Students	12
USA (21)	1962	Students	5.7
USA (22)	1968	Students	13.9
USA (23)	1969	Students	19.7
Finland (24)	1979	Students	28

* Study performed 1979

** Study performed 1991

Age

The age of a study population is an important factor for the result, as seen in Table 1. The incidence of SAR peaks between the ages of 10 and 15 and declines substantially after age 35 (19, 25). The symptoms of SAR tend to persist into adulthood (26), decline in middle age, and almost disappear in old age (27). This spontaneous "cure" of the clinical disease, but not of the allergic sensitization, deserves a detailed study of the underlying immunological mechanisms. In old age even accumulated prevalence rates decrease, because people tend to forget their former symptoms (19). Thus, AR usually develops in school age or adolescence and the highest prevalence rates are found in studies of young adults.

Sex

AR is in some, but not all, studies more frequent in boys than in girls, but the difference disappears in adolescence (13, 19, 28).

Positive skin test

As mentioned above, not all patients who exhibit a positive response on skin-prick testing have clinical symptoms related to the allergen in question, but the larger the wheal response, the greater the likelihood that these subjects will subsequently develop rhinitic symptoms on specific allergen exposure. A serial study of university students identified that 71% of students with a 4+ skin wheal response to pollen had developed seasonal symptoms within a 7-year follow-up period, compared with 23% for those with a 1+ response and 7.7% of those with an initial negative response (23).

Genetic predisposition

The significance of a family history of atopic disease for the development of AR in the single individual is well known and documented (14). The higher concordance rate of AR in monozygotic than in dizygotic twins confirms the role of a genetic predisposition (29, 30). However, the genetic effects on allergen-specific sensitization and on occurrence of clinical disorder are relatively weak, as the concordance for sensitization to grass pollen is 15% in dizygotic twins and 40% in monozygotic twins (30).

Early onset of AR is more likely to occur in persons with a family history of atopic disease, but after childhood, the genetic influence on the occurrence of atopy tends to decrease. Late onset of AR often occurs in adults who have no atopic background and who only develop a single allergy (31, 32).

Races and ethnic groups

Differences between studies of populations are more likely to be due to environmental than to genetic factors, since no racial or ethnic differences have been found in the prevalence of AR in studies of groups matched for social status and environmental conditions (6, 21). Although AR appears to be relatively uncommon in Africa, black university students in the United States have about the same prevalence of hay fever as other races (31).

Socio-economic status

The most usual survey methods, which rely heavily on the individual's recognition of hay fever symptoms, are likely to be influenced by the sophistication of the group being studied. This suspicion is apparently supported by the consistently higher prevalence rates of SAR recorded for university students than for the population as a whole (23) and for high-income groups as compared to low-income

groups (19). However, a difference in the number of positive skin tests to aeroallergens cannot be explained as reflecting a recognition or reporting bias. Nathanson & Rhyne (33) compared the skin test results of children divided on the basis of social class. They found the highest rates of positive reactions for all aeroallergens in the upper social class, and this was highly significant for ragweed, grass and house dust. Barbee et al (34) found a correlation between positive skin tests, and the levels of education and income, which is encouraging for students with hay fever.

Month of birth

A series of studies have shown that birth 1–3 months before the birch and grass pollen seasons slightly but significantly increases the risk of hay fever (35, 36). This observation is theoretically interesting, as it confirms the existence of a vulnerable period early in life when the initial priming of the immune system for IgE isotype switching takes place, promoting the later clinical sensitization and development of disease (37).

Allergen exposure

Potent aeroallergens are ubiquitous, but there are considerable regional differences. Usually patients are initially exposed to the sensitizing allergen early in life, but first-time exposure can occur when the patient moves to another region or country. This happens, for example, when foreign students are going to study in the United States, where they are exposed to ragweed pollen for the first time. During the second to fifth year following their arrival in the midwestern United States, as many as 19% of 161 foreign students developed ragweed hay fever, whereas only 1.6% of a control group of native students had the new onset of ragweed hay fever during this period of time (30). This observation indicates that the simple mono-allergen disease, hay fever, may be less dependent upon priming events during the “vulnerable period” in infancy than are the patients, starting their “allergy march” with food allergy and atopic dermatitis and continuing with airway allergy, asthma and PAR.

Airway infection

It is currently believed that early childhood respiratory infection, especially RSV bronchiolitis, may predispose to wheeziness and asthma (38). However, there seems only to be one publication of 11 children from 1979 (39) which favours the statement that airway infection also may facilitate allergic sensitization. There are no epidemiological data to indi-

cate that airway infections have any influence on the development of AR.

Parenteral smoking

The important role of parenteral smoking for the development of childhood wheeziness and asthma has been definitely proven by several studies (38, 40), and it is speculated that this important indoor pollutant also can act as an “adjuvant”, facilitating allergic sensitization (41). However, the experimental evidence in favour of this statement is, in our opinion, not convincing and there are no data linking smoking to the development of AR.

Breastfeeding

Numerous studies have evaluated the impact of breastfeeding on the subsequent development of atopic allergic disease. Although the results have varied, the balance of evidence appears to favour the hypothesis that early feeding with cow's milk or solids increases the risk of developing food allergy and atopic eczema but not the risk of developing AR (41–44). However, Saarinen & Kajosaari (45) recently reported that exclusive breastfeeding for 6 months, in a group of high-risk children, dramatically reduced the occurrence of AR at age 17 years. This finding, at variance with other reports (41–44), needs confirmation before definite conclusions can be drawn. However, its potential significance for prevention is obvious.

Rural and urban areas

As originally pointed out by Charles Blackley in 1873 (46): “There is the curious phenomenon that hay fever is apparently less common in rural than in urban areas.” Not all rural versus urban comparisons have found a difference in the occurrence of AR, but whenever there is a difference it is toward less AR in the rural environment (31, 32, 47, 48). Judging by high pollen counts in rural areas and much outdoor exposure, a rural child will meet more allergen than his urban friend. It has been hypothesized that those regularly exposed to grass develop tolerance to pollen allergens, but this hypothesis does not agree with the frequently reported dose-response relationship between allergen exposure and the risk of allergic sensitization (41).

Developed and developing countries

Allergic diseases are beginning to be recognized in developing countries, particularly where traditional lifestyles are becoming eroded by western influences (40, 32). A good example to illustrate this

phenomenon is a study from New Zealand by Waite and coworkers (6). In 1966 the New Zealand government undertook to resettle in New Zealand 1000 of 1950 Tokelauan islanders after their atoll near Samoa was devastated by a hurricane. Comparing children up to 14 years of age who remained on the island with those moved to New Zealand, 14% on Tokelau had AR as compared with 28% in New Zealand.

Helminthic infection

The possible influence of helminthic infection on the allergic reactivity of tropical populations is complex and can consist of both non-specific potentiation of IgE synthesis against environmental allergens and of suppressive effects that are due to both mast-cell saturation and inhibition of specific IgE synthesis (49). However, to date there is no convincing evidence that helminthic infection significantly influences the prevalence rate of AR.

Air pollution

Outdoor air pollution, especially exhaust from diesel cars, is a frequently quoted "adjuvant factor" for allergic sensitization and a suspected cause of the high prevalence rates of AR in industrialized countries. This statement is, however, mainly based on experimental *in vitro* evidence (50) and on a single report from Japan of an increased frequency of SAR in patients living near motorways (51). These findings have not gained support from a well-controlled study of more than 7000 children in the reunified Germany (52). In Leipzig, where there was a considerably higher degree of air pollution than in Munich, the prevalence rates of AR and of positive skin tests to aeroallergens were significantly lower (2.4% and 18.2%) than in Munich (8.6% and 36.7%). In another large epidemiological study, there was a higher prevalence of AR in a lightly polluted city in Sweden than in a heavily polluted city in Poland (53). Thus, the evidence in favour of air pollution having a significant "adjuvant" effect on allergic sensitization are not convincing.

Increasing prevalence rate

Recent large-scale surveys in general practice have indicated that the prevalence of AR, at least as judged by patients attending their family doctors for treatment, has almost doubled from 1970 to 1981 (25). These observations are supported by a report of Åberg (48), who studied the computer records of Swedish conscripts examinations in 1971 and in 1981 regarding the prevalence of AR. The material comprised 55,000 18-year-old males in each cohort.

During the 10-year period the prevalence of AR increased from 4.4 to 8.4%. In a more recent study, Åberg et al (5) found that the prevalence rate of AR in 7-year-old children had increased from 5.5% in 1979 to 8.1% in 1991.

Although there are no comprehensive longitudinal studies to prove that AR has actually increased in frequency, and increasing awareness and recognition of allergic diseases no doubt influences the published data, the available evidence strongly suggests a progressive increase in the incidence of atopic disease in industrialized western countries since the turn of the last century, particularly in the last decades. Similar data are available for asthma and atopic dermatitis (41), and also for AR and the other atopic diseases in Hong Kong and other rapidly developing countries in the Far East (54).

Reasons for increased prevalence of AR?

The above data are alarming and represent a considerable challenge to allergologists, who are responsible for advising the authorities on which measures to take in order to stop the increase in atopic allergic diseases. Generally, the authorities and the lay people believe that we know how to prevent these diseases, but unfortunately, this is not the case and we should have the courage to admit it.

So far, the most well formulated and best immunologically founded hypothesis attempting to explain the epidemic of atopic allergic diseases is proposed by Patric Holt from Australia (37). According to this hypothesis, a causative factor may be a lack of exposure to microbial antigens and infections during the first months of life. Microbial antigens primarily induce the development of Th1 cells, and the domination of Th1 memory cells for a particular antigen can effectively "lock out" subsequent Th2 reactivity and thus protect against allergic sensitization. In popular terms, the two green strings of purulent secretions, seen more or less permanently under the noses of poor children in the old days, and today in countries with a low socio-economic standard, may yield some protection against the development of AR.

It is tempting to speculate that it is an effect of an affluent lifestyle on the immune system, which constitutes the risk factor. Good nutrition with optimal amounts of proteins, iron, zinc, vitamin C, vitamin B6 and B12 of the pregnant mother and the newborn is known to increase the resistance to infections (55). Maybe such optimal nutrition can also render the immune system "supernormal", exhibiting sensitive and efficient responses, not only to microbial antigens, but also to innocent pollen proteins.

Unfortunately, the above hypotheses, considering allergy as a sign of wealth and health, render

preventive measures difficult. Apparently, we can choose between being "poor and infectious or rich and allergic".

Conclusions

The overall estimates of the prevalence of allergic rhinitis in western countries are 20–30% skin-test positive, 15–20% symptomatic, and perhaps 10% using treatment. As hay fever lasts for about one third of a lifetime, it means that approximately 3% of the total population needs treatment in a given pollen season. There can be little doubt that the prevalence of AR has increased over the last decades in many western countries, and a similar increase occurs when native populations move to a westernized society. The increased risk for developing allergic rhinitis, associated with a western lifestyle, cannot be explained by an increased exposure to potent aeroallergens. It has been postulated that increased outdoor and indoor air pollution, acting as "adjuvant" for the allergic sensitization, is the cause of the increased prevalence rates of airway allergy. This popular hypothesis is, in our opinion, based on thin evidence, and it has not been supported by recent and well-controlled epidemiological studies. We have to admit our ignorance of the cause or the causes of the present epidemic of allergic rhinitis. Apparently, there exists a powerful environmental factor which seems so intimately associated with an affluent western lifestyle that it may render effective prevention difficult or even impossible. We are not aware of the existence of any modern western society having a low or a decreasing prevalence rate of allergic rhinitis.

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