Clinical reviews in allergy and immunology

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The allergy epidemics: 1870-2010

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Overall Purpose/Goal: To provide excellent reviews on key aspects of allergic disease to those who research, treat, or manage allergic disease.

Target Audience: Physicians and researchers within the field of allergic disease.

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Activity Objectives

1. To trace the onset and progression of asthma and allergies from 1870-2010 and, in particular, its relation to improvements in public hygiene.
2. To understand the major theories behind the epidemic increase in asthma since 1960 and the supporting evidence for this increase.
3. To review the relevant environmental and lifestyle changes that might be associated with the increasing prevalence of allergic disease.

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Before the first description of hay fever in 1870, there was very little awareness of allergic disease, which is actually similar to the situation in prehygiene villages in Africa today. The best explanation for the appearance and subsequent increase in hay fever at that time is the combination of hygiene and increased pollen secondary to changes in agriculture. However, it is important to remember that the major changes in hygiene in Northern Europe and the United States were complete by 1920. Asthma in children did not start to increase until 1960, but by 1990, it had clearly increased to epidemic numbers in all countries where children had adopted an indoor lifestyle. There are many features of the move indoors that could have played a role; these include increased sensitization to indoor allergens, diet, and decreased physical activity, as well as the effects of prolonged periods of shallow breathing. Since 1990, there has been a remarkable increase in food allergy, which has now reached epidemic numbers. Peanut has played a major role in the food epidemic, and there is increasing evidence that sensitization to peanut can occur through the skin. This suggests the possibility that changes in lifestyle in the last 20 years could have influenced the permeability of the skin. Overall, the important conclusion is that sequential changes in lifestyle have led to increases in different forms of allergic disease. Equally, it is clear that the consequences of hygiene, indoor entertainment, and changes in diet or physical activity have never been predicted. (J Allergy Clin Immunol 2015;136:3-13.)

Key words: *Hay fever, asthma, peanut, lifestyle, hygiene, indoor environment*

The human race has come to dominate its environment so completely that any analysis of the increase or appearance of a disease has to take changes in our lifestyle into account. In the case of allergic disease changes in our environment, diet, water quality, and personal behavior over the last 150 years have played a dominant role in the specificity of these diseases, as well as in prevalence and severity. The first thing to address is when "the epidemic" started and how much the increase in different allergic diseases has occurred separately. It should be noted that some or most previous reviews have implied that the increase in allergic disease has been unimodal, but actually, that has never been a tenable analysis. Not only have increases occurred or are currently occurring at different times in different countries, but

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Abbreviation used
BHR: Bronchial hyperreactivity

also hay fever, asthma, and peanut allergy have had strikingly different time courses both in Europe and North America.

Occasional descriptions of allergic disease occurred in antiquity, such as the suggestion that one of the pharaohs died of anaphylaxis after a bee sting.[1] The first convincing description of hay fever was by John Bostock, who described his own symptoms in 1828. The first investigations of hay fever were published in the 1870s by Blackley,[2] who studied grass pollen in the United Kingdom, and Wyman,[3] who studied ragweed pollen in the United States. At that stage, the only recognized allergic disease was hay fever, and reports of an increase came from Germany, as well as the United Kingdom and United States. It is important to recognize that there were no clear reports of an increase in pediatric asthma until 1970. Furthermore, the current "epidemic" of food allergy does not appear to have started until after 1990.

This review will attempt to evaluate both the evidence for those increases and the changes that have occurred in lifestyle that could have contributed to sequential increases in different allergic diseases.

THE HAY FEVER EPIDEMIC

In 1982, Lady Simon, with a startling level of confidence about her facts, asked the author of this review, "Why did hay fever start in 1870?"[4] She then explained that her father had symptoms of allergic rhinitis and conjunctivitis in Germany in June of 1875, but after several years of symptoms, he could not find a physician who was aware of the condition. By 1890, he knew a group of such patients, but none of them had symptoms before 1870. Blackley[2] started studying the disease in Manchester, United Kingdom, in the 1860s, but his studies, including skin tests and challenge tests with grass pollen out of season, were primarily performed on himself (Fig 1). By 1900, the disease was well recognized and sufficiently severe for 2 developments.

1. Sites at which patients with hay fever could go during the season to avoid exposure to pollen were identified, and thus the island of Heligoland in the North Sea was kept free of grass pollen, and Bretton Woods Resort in New Hampshire was recognized as a retreat from the ragweed season by the United States Hay Fever Association (Fig 1).[5]
2. The earliest investigations of the effects of injections of pollen extract were carried out with the objective of establishing immunity against pollen toxin. Those experiments were published by Dunbar[6] in Germany and most significantly by Noon[7] in the United Kingdom.

The question to address is what happened in the second half of the 19th century that could have contributed to the appearance and progressive increase in seasonal allergic rhinitis. It seems likely that changes in both airborne pollen and public hygiene contributed. In England major changes in agriculture followed the reform of the corn laws in 1847.[8] That reform allowed the import of cheap wheat from Odessa in the Ukraine with the result that much of English farm land lay fallow.[9] Between 1850 and 1880, dairy herds increased, and Italian rye grass *(Lolium perenne)* was introduced, which pollinated more heavily than any of the traditional grasses.[10,11] In the United States the progressive increase in arable farming is thought to have increased the growth of ragweed. Certainly ragweed became the most import cause of seasonal rhinitis in the United States.[3,12]

Major changes in public hygiene started during the 19th century. Given the fact that the Greeks and Romans understood the need for clean water supplies, it is difficult to believe that London in 1854 and Chicago as late as 1890 were collecting "drinking water" from the same site that was used to discharge untreated sewage (Table I).[13,14] The critical studies that led to the acceptance of the relationship between sewage and enteric disease were carried out by John Snow in London, starting with the evidence about the Soho pump and cholera and following this with epidemiologic comparison in 1854 of typhoid cases among populations who obtained their water from the London River compared with those whose water came from farther up the river (Fig 2).[13,15] However, as late as 1880, there was still only limited acceptance of the germ theory of disease, even among physicians. Indeed, in 1881, President James Garfield was "murdered" by his physicians, who repeatedly probed a nonfatal gunshot wound using nonsterile instruments and fingers.[16] Starting in 1892, the city of Chicago reversed the course of the Chicago River so that sewage flowed into the Mississippi rather than into Lake Michigan, which was the source of drinking water.[14]

By 1920, chlorination of water was widespread, and all the major cities in the United States had clean water, with the result that typhoid and cholera became rare. If you look at New York City, you could argue that the critical changes in hygiene were complete by 1920 (Table II). In keeping with that, allergy became more common, and by 1946, ragweed-induced hay fever was such a severe problem in New York that the city council initiated a ragweed eradication campaign (Table II).[17,18]

Equally, in London Dr Frankland's allergy clinic had hundreds of patients in the 1950s, and he and Dr Augustin carried out the first controlled trial of immunotherapy for grass pollen hay fever.[19] In fact, the increase in allergic disease was already obvious when Dr Swineford was appointed professor of allergy and rheumatology at the University of Virginia in 1935. He had been called back from doing pathology research in Vienna to "help deal with the allergy epidemic," and he opened the first subspecialty clinic in the Medical School in 1936.[20]

THE EPIDEMIC INCREASE OF ASTHMA AMONG CHILDREN: 1960-2000

For further information, see Table III. Before 1960, most pediatrics textbooks did not regard asthma as common, let alone epidemic. During the 1960s, there were occasional reports that asthma appeared to be becoming more common, but the first convincing publication came in 1969. Smith et al[21] carried out a population-based study on schoolchildren in Birmingham, United Kingdom, which demonstrated a sharp increase in asthma between 1958 and 1968. In addition, they reported that many of the children with asthma had positive skin test responses to dust mites. Over the next few years, reports on the increasing prevalence of asthma came from several countries but predominantly from countries in which dust mites were the dominant allergen. Thus increases were reported from Australia, New Zealand, and Japan, as well as the United