
Prevalence of atopy and asthma in eastern versus western Europe: why the difference?

Paolo M. Matricardi, MD

Learning Objectives: This article reinforces the reader's knowledge of the epidemiology of allergy and asthma in eastern versus western European countries and the ability to recognize the different hypotheses formulated to explain the rising trend of allergic asthma in Europe.

Data Sources: Articles in English comparing the epidemiology of allergy in eastern versus western Europe published before December 31, 2000.

Results: Significant higher prevalences of atopy and allergic asthma were observed in the early 1990s among populations living in western compared with eastern European countries. Changes in lifestyle after the fall of the communist system were associated with an increasing trend of atopic sensitization and hay fever in former East Germany after only 6 to 8 years after the Germany reunification. It has been hypothesized that a similar "converging" trend in the prevalence of allergic asthma and of bronchial hyperresponsiveness may take longer periods.

Conclusions: The prevalence of allergic asthma has increased decades earlier in western Europe with respect to eastern Europe. This is probably attributable to changes in lifestyle that had already occurred rather than to air pollution. The factors of a western lifestyle (diet, hygiene, varied allergen exposure) that have determined the difference in allergic asthma prevalence across Europe have yet to be identified.

Ann Allergy Asthma Immunol 2001;87(Suppl):24-27.

INTRODUCTION

Allergic asthma was very rare in Europe until the 20th century; thereafter it became so frequent as to prompt the term "postindustrial revolution epidemic."¹ Several studies have demonstrated an increase in the prevalence of asthma estimated with the same methodology in cohorts born in different years in various European countries: United Kingdom,²⁻⁴ Finland,⁵ France,⁶ Italy,⁷ and Sweden.⁸ The rising trend is part of a generalized increase in atopic conditions characterized by mucosal eosinophilic inflammation, allergic rhinoconjunctivitis, and atopic eczema. A clear example emerges from a study conducted in Aberdeen (Scotland) schoolchildren (8 to 13 years) who were administered the same questionnaire in 1964, in 1989, and in 1994.^{9,10}

The prevalence of asthma increased from 4.1 (1964) to 10.2 (1989) to 19.6% (1994). Similarly, hay fever increased from 3.2 to 11.9 and to 12.7%, and atopic eczema from 5.3 to 12.0 to 17.7%, which is indicative of an underlying increase in susceptibility to atopy.^{9,10}

Epidemiologic Studies Comparing Eastern with Western European Countries

This epidemic trend was not observed to the same extent in eastern European countries. In the pioneering studies by Von Mutius et al,^{11,12} the prevalence of atopy or asthma was examined among 9- to 11-year-old children living in former West Germany (Munich, n = 5,030) compared with East Germany (Leipzig and Halle, n = 2,623): atopic sensitization (West vs East) was 36.7% versus 18.2% (odds ratio [OR] 2.6; $P < 0.0005$); current asthma was 5.9 versus 3.9 (OR 1.5; $P < 0.0005$); current hay fever was 8.6% versus 2.7% (OR 3.4; $P < 0.0005$).^{11,12} Similarly, among 10- to 12-year-old children liv-

ing in Sweden (rural Sundsvall), the prevalence of atopic sensitization was higher than in those living in Poland (Konin) (24.2% vs 13.7%; OR 1.72; $P < 0.05$).¹³ The prevalence of atopy-related disorders was higher in Finland and Sweden compared with Estonia, Latvia, and Poland,¹⁴ or in Italy compared with Albania.¹⁵ Conversely, eastern Europe had a higher prevalence of bronchitis when compared with western Europe.¹¹

Converging Trend after the Fall of the Communist System

In the 1990s, populations living in eastern Europe started to progressively change their lifestyle, by assimilation of several aspects of a "western lifestyle." It was therefore anticipated that this natural experimental model would be useful to test the hypothesis that westernization was linked to an increase of atopic diseases.¹⁶ As expected, increases in the prevalence of atopic sensitization and hay fever, but not of asthma and bronchial hyperresponsiveness, were observed in a 5-year period in Leipzig (former East Germany).¹⁷ In keeping with these observations, the prevalence of atopic sensitization and of hay fever among 9- to 11-year-old children was not lower in Dresden (former East Germany) than in Munich (former West Germany) 5 years after the reunification.¹⁸ However, the prevalence of physician-diagnosed asthma and bronchial hyperresponsiveness was lower in Dresden than in Munich.¹⁸ These observations suggested that either environmental factors influencing atopy and hay fever differ from those causing allergic asthma, or that unknown factors linked to westernization must exert their influence very early in infancy to cause asthma later in life.^{17,18}

Institute of Neurobiology and Molecular Medicine, Italian National Research Council, Rome, Italy.

Received for publication April 1, 2001.

Accepted for publication in revised form September 25, 2001.

HYPOTHESES ON THE CAUSES OF WEST VERSUS EAST DIFFERENCES

The causes of the rising trend of asthma must be identified to devise primary prevention strategies and new therapeutic approaches. Thus far, the epidemic trend has been attributed to pollution,¹⁹ diet,²⁰ allergen exposure,²¹ and hygiene.^{22,23} The different prevalences of allergic asthma in western and eastern Europe is a valuable paradigm for investigations of the epidemic trend of the disease.

Pollution

Pollution was considered an inducer of allergic sensitization and allergic asthma, especially after the report by Ishizaki et al²⁴ that sensitization to cedar pollen was more frequent among the residents of an area exposed to automobile exhaust than among the residents living in a cedar forest with less intense automobile traffic. Pollen grains dispersed in a polluted atmosphere can interact with other suspended substances and facilitate the capacity of pollen allergens to induce immunoglobulin E sensitization.^{19,25,26}

Thus, pollutants can influence the way a pollen, once inhaled, is processed. In particular, T cell responses to major allergen proteins may be skewed in a type 2 T helper cell direction in the presence of pollutants such as diesel exhaust particles (DEP).²⁷ This hypothesis and its corollary that pollution may be responsible for the epidemic trend of allergic asthma was challenged by studies performed in Germany after reunification.¹¹ Populations living in heavily polluted areas in the former East Germany (Leipzig) had a lower risk of developing allergic asthma compared with those living in the former West Germany (Munich). However, only levels of sulfur dioxide and total suspended particles were higher in Leipzig, whereas DEP were more abundant in the Munich atmosphere.¹¹ It was therefore proposed that the "eastern" (or type I) kind of outdoor pollution (more sulfur dioxide and total suspended particles) could cause respiratory infections and symp-

toms of irritation, whereas the "western" kind (or type II) of pollution (DEP, ozone, and nitrogen dioxide) could be linked to allergic sensitization and respiratory allergies.¹⁹ The alternative hypothesis was that other factors linked to a western lifestyle were responsible for the higher prevalence of atopy and asthma in West Germany, and that pollution could act mainly as a trigger or an aggravating factor in susceptible patients.²⁸

Allergen Exposure

In Munich, children were more frequently sensitized not simply to one allergen, but to almost all the allergens used in the screening procedures: mite, cat, mixed grass pollen, birch pollen, and hazel pollen.¹¹ This suggests that allergen exposure was probably not a critical factor determining differences in the prevalence of sensitization. In principle, one could not exclude that West German children were more exposed to mite or cat allergen, but major differences in exposure to grass, birch, and hazel pollens were very unlikely. Some years later, Hirsch et al²⁹ tested the hypothesis that low indoor exposure to house-dust mite (HDM) allergen in East Germany had contributed to the lower prevalence of allergic asthma. They found that the mean concentration of HDM group I allergen in mattresses and carpets of 634 East German dwellings was 2.16 $\mu\text{g/g}$ and 0.48 $\mu\text{g/g}$, respectively, shortly after the reunification of Germany. These values did not differ significantly from those obtained in West Germany using similar methodologies. Consequently, it was concluded that the differences in prevalence of allergic asthma between the two countries was not related to HDM exposure.²⁹

Diet

Westernization is characterized by profound changes in dietary habits; thus, it is conceivable that ingestants might be implicated in changes in disease patterns.²⁰ Accordingly, the increasing trend in allergy and asthma cases has been attributed to: 1) increased salt intake³⁰; 2) decreased consumption of

antioxidants (eg, vitamin C)³¹; 3) bottle feeding practices³²; and 4) increased consumption of vegetable oils (margarine).³³

An increased consumption of margarine as opposed to fats of animal origin (butter) after reunification has been implicated in the "converging" trend in the epidemiology of atopy and hay fever between the two Germanys.¹⁷ An ecologic association between the consumption of *trans* fatty acids and the prevalence of childhood asthma has also been recently reported.³³

Similarly, decreased consumption of antioxidants such as vitamin C in the diet has been considered a potential cause of atopy and asthma epidemic in western Europe.^{31,34} A large Italian study has recently identified an association between the intake of fresh fruit rich in vitamin C and wheezing symptoms in children.³⁵

Hygiene

A higher prevalence of allergic asthma has also been attributed to changes in interactions between humans and the microbes of their ecosystem inherent in the western lifestyle.^{22,23} In modern societies, allergies spread among new cohorts according to gradients dictated by hygiene and by the individual degree of genetic predisposition to atopy. Collectively, these concepts are known as the "Hygiene hypothesis."^{22,23} This theory, unlike others (pollution, increased allergen exposure, nutrients), explains the epidemic in evolutionistic terms,³⁶ and its biologic plausibility is supported by an overwhelming amount of *in vivo* and *in vitro* evidence.^{23,37} This theory has been challenged by conflicting data and some inconsistencies, discussed in detail elsewhere.³⁸ The differences in the prevalence of allergic asthma between western and eastern Europe represent a valuable opportunity to investigate this hypothesis.

The composition of intestinal microflora was very different in infants living in European countries with a low (Estonia) versus a high (Sweden) prevalence of atopy. *Lactobacilli* and *Eubacteria* predominated in the intestinal microflora of Estonian infants, whereas

Clostridia occurred more frequently in Swedish infants.³⁹ It was also observed that allergic 2-year-old children were colonized less often by *Lactobacilli* and harbored higher counts of aerobic bacteria (coliforms, *Staphylococcus aureus*) than nonallergic children.³⁹ This suggested that bacteria colonizing the gastrointestinal tract may modulate the tendency to atopic sensitization to airborne allergens, and that differences in microbial composition in intestinal microflora may be a critical factor in the higher prevalence of allergic asthma in western versus eastern Europe.³⁹

Individuals who have been reared in poor hygiene conditions can be identified from the presence of infectious agents in their serum (eg, hepatitis A virus). Using this strategy, we found that poor hygiene was inversely associated with respiratory allergies in a group of Italian military cadets.⁴⁰ The inverse association between atopy and hepatitis A virus antibodies was confirmed in a general population sample.⁴¹ It was also observed that atopy was inversely related to other orofecal/foodborne infections (*Toxoplasma gondii* and *Helicobacter pylori*), but not to a series of airborne viruses.⁴² Thus, a high turnover of microbes at mucosal surfaces, including the gut, may "train" our mucosal immune system to interact safely with nonmicrobial antigens.^{42,43} An ecologic association between the prevalence of antibodies against hepatitis A virus and atopy or allergic asthma has never been investigated. However, it is interesting to note that in Albania, the European country with the lowest prevalence of asthma (according to International Study of Asthma and Allergies in Childhood phase I studies), the prevalence of positive serology for hepatitis A virus among adults is well over 80% (A. Priftanji, personal communication, December, 2000).

CONCLUSION

Questions raised by the epidemiologic trend of allergic asthma across Europe still wait for precise answers. Available data tend to support the hygiene and the diet hypotheses over other hy-

potheses. However, information coming from Europe should be interpreted in light of information arising from epidemiologic studies on allergies and asthma performed in non-European countries. Interestingly, rising trends in severe asthma cases have been observed in poor, and presumably less hygienic, urban areas of US cities ("inner-city asthma").⁴⁴ In contrast, serum immunoglobulin E responses toward airborne allergens are not infrequent in rural, unhygienic areas of developing countries, where helminths are highly prevalent.⁴⁵ Therefore, hypotheses that may explain geographical patterns of allergic diseases and asthma in Europe may be challenged by data coming from non-European populations.⁴⁰

REFERENCES

1. Emanuel MB. Hay fever, a post industrial evolution epidemic: a history of its growth during the 19th century. *Clin Allergy* 1988;18:295-304.
2. Morrison-Smith J. The prevalence of asthma and wheezing in children. *Br J Dis Chest* 1976;70:73-77.
3. Whincup PH, Cook DG, Strachan DP, Papacosta O. Time trends in respiratory symptoms in childhood over a 24 year period. *Arch Dis Child* 1993;68:729-734.
4. Burr ML, Butland BK, King S, Vaughan-Williams E. Changes in asthma prevalence: two surveys 15 years apart. *Arch Dis Child* 1989;64:1452-1456.
5. Venn A, Lewis S, Cooper M, et al. Increasing prevalence of wheeze and asthma in Nottingham primary schoolchildren. *Eur Respir J* 1998;11:1324-1328.
6. Haahtela T, Lindholm H, Bjorksten F, et al. Prevalence of asthma in Finnish young men. *BMJ* 1990;301:266-268.
7. Ronchetti R, Villa MP, Barreto M, et al. Is the increase in childhood asthma coming to an end? Findings from three surveys in schoolchildren of Rome, Italy. *Eur Respir J* 2001;17:881-886.
8. Aberg N. Asthma and allergic rhinitis in Swedish conscripts. *Clin Exp Allergy* 1989;19:59-63.
9. Ninan TK, Russell G. Respiratory symptoms and atopy in Aberdeen schoolchildren: evidence from two surveys 25 years apart. *BMJ* 1992;304:873-875.
10. Omran M, Russell G. Continuing increase in respiratory symptoms and atopy in Aberdeen schoolchildren. *BMJ* 1996;312:34.
11. von Mutius E, Martinez FD, Fritzsche C, et al. Prevalence of asthma and atopy in two areas of West and East Germany. *Am J Respir Crit Care Med* 1994;149:358-364.
12. Von Mutius E, Fritzsche C, Weiland S, et al. Prevalence of asthma and allergic disorders among children in united Germany: a descriptive comparison. *BMJ* 1992;305:1395-1399.
13. Braback L, Breborowicz A, Dreborg S, et al. Atopic sensitization and respiratory symptoms among Polish and Swedish schoolchildren. *Clin Exp Allergy* 1994;24:826-835.
14. Bjorksten B, Dumitrescu D, Foucard T, et al. Prevalence of childhood asthma, rhinitis and eczema in Scandinavia and eastern Europe. *Eur Respir J* 1998;12:432-437.
15. The ISAAC Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. *Lancet* 1998;351:1225-1232.
16. Nowak D, Wichmann HE, Magnussen H. Asthma and atopy in western and eastern communities—current status and open questions. *Clin Exp Allergy* 1998;28:1043-1046.
17. von Mutius E, Weiland SK, Fritzsche C, et al. Increasing prevalence of hay fever and atopy among children in Leipzig, East Germany. *Lancet* 1998;351:862-866.
18. Weiland SK, von Mutius E, Hirsh T, et al. Prevalence of respiratory and atopic disorders among children in the east and west of Germany five years after unification. *Eur Respir J* 1999;14:862-870.
19. Behrendt H, Friedrichs KH, Kramer U, et al. The role of indoor and outdoor pollution in allergic diseases. *Prog Allergy Clin Immunol* 1995;3:83-89.
20. Weiss ST. Diet as a risk factor for asthma. *Ciba Found Symposium* 1997;206:244-257.
21. Woolcock AJ, Peat JK, Trevillion LM. Is the increase in asthma prevalence linked to increase in allergen load? *Allergy* 1995;50:935-940.

22. Strachan DP. Epidemiology of hay fever: towards a community diagnosis. *Clin Exp Allergy* 1995;25:296–303.
23. Martinez FD, Holt PG. Role of microbial burden in aetiology of allergy and asthma. *Lancet* 1999;354:12–15.
24. Ishizaki T, Koizumi K, Ikemori R, et al. Studies of prevalence of Japanese cedar pollinosis among the residents of a densely cultivated area. *Ann Allergy* 1987;58:265–270.
25. Behrendt H, Becker WM, Friedrichs KH, et al. Interaction between aeroallergens and airborne particulate matter. *Int Arch Allergy Appl Immunol* 1992;99:425–428.
26. Behrendt H, Becker WM, Fritzsche C, et al. Air pollution and allergy: experimental studies on modulation of allergen release from pollen by air pollutants. *Int Arch Allergy Immunol* 1997;113:69–74.
27. Frew AJ, Salvi SS. Diesel exhaust particles and respiratory allergy. *Clin Exp Allergy* 1997;27:237–239.
28. Magnussen H, Jorres R, Nowak D. Effect of air pollution on the prevalence of asthma and allergy: lessons from the German reunification. *Thorax* 1993;48:879–881.
29. Hirsch T, Range U, Walther KU, et al. Prevalence and determinants of house dust mite allergen in East German homes. *Clin Exp Allergy* 1998;28:956–964.
30. Burney P. A diet rich in sodium may potentiate asthma. Epidemiologic evidence for a new hypothesis. *Chest* 1987;91(Suppl):143S–148S.
31. Soutar A, Seaton A, Brown K. Bronchial reactivity and dietary antioxidants. *Thorax* 1997;52:166–170.
32. Kramer MS. Does breast feeding help protect against atopic disease? Biology, methodology, and a golden jubilee of controversy. *J Pediatr* 1988;112:181–190.
33. Weiland SK, von Mutius E, Husing A, Asher MI. Intake of *trans* fatty acids and prevalence of childhood asthma and allergies in Europe. *Lancet* 1999;353:2040–2041.
34. Seaton A, Godden DJ, Brown K. Increase in asthma: a more toxic environment or a more susceptible population? *Thorax* 1994;93:470–475.
35. Forastiere F, Pistelli R, Sestini P, et al. Consumption of fresh fruit rich in vitamin C and wheezing symptoms in children. SIDRIA Collaborative Group, Italy (Italian Studies on Respiratory Disorders in Children and the Environment). *Thorax* 2000;55:283–288.
36. Rook GA, Stanford JL. Give us this day our daily germs. *Immunol Today* 1998;19:113–116.
37. Romagnani S. Regulation of the development of type 2 T-helper cells in allergy. *Curr Opin Immunol* 1994;6:838–846.
38. Matricardi PM, Bonini S. High microbial turnover rate preventing atopy: a solution to inconsistencies impinging on the Hygiene hypothesis? *Clin Exp Allergy* 2000;30:1506–1510.
39. Sepp E, Julge K, Vasar M, et al. Intestinal microflora of Estonian and Swedish infants. *Acta Pediatr* 1997;86:956–961.
40. Matricardi PM, Rosmini F, Ferrigno L, et al. Cross-sectional retrospective survey of prevalence of atopy among Italian military students with antibodies against hepatitis A virus. *BMJ* 1997;314:999–1003.
41. Matricardi PM, Rosmini F, Rapicetta M, et al. Atopy, hygiene, and anthroposophic lifestyle. *Lancet* 1999;354:430.
42. Matricardi PM, Rosmini F, Riondino S, et al. Exposure to foodborne and orofecal microbes versus airborne viruses in relation to atopy and allergic asthma: epidemiological study. *BMJ* 2000;320:412–417.
43. Wold AE. The hygiene hypothesis revised: is the rising frequency of allergy due to changes in the intestinal flora? *Allergy* 1998;53(Suppl):20–25.
44. Platts-Mills TA. Changes in the 20th century environment: do they explain the increase in asthma? Proceedings of the 54th Annual Meeting of the AAAAI, March 13–18, 1998; Washington, DC.
45. Yemaneberhan H, Bekele Z, Venn A, et al. Prevalence of wheeze and asthma and relation to atopy in urban and rural Ethiopia. *Lancet* 1997;350:85–90.

Requests for reprints should be addressed to:
 Paolo M. Matricardi, MD
 CNR-Istituto di Neurobiologia e Medicina
 Molecolare
 Via di Pietralata, 190
 00158 Rome, Italy
 E-mail: matricardi.pm@mclink.it