Effect of air pollution on the prevalence of asthma and allergy: lessons from the German reunification

An increase in the prevalence of bronchial asthma has been reported in many countries,[1 2] but there is still no conclusive explanation for these observations. The possible contribution of air pollution to atopy and bronchial asthma has gained increasing attention in recent years, and this topic has been addressed in several extensive reviews.[3–7] Many detailed experimental and epidemiological reports are now available which have focused on the effects of sulphur dioxide (SO_2), airborne particulates, nitrogen dioxide (NO_2), and ozone on the airways of asthmatic subjects and normal populations. We will briefly summarise the effects of these pollutants on respiratory health to improve the understanding of the epidemiological data that have become available following the German reunification. Reunification offered the opportunity to compare two populations that have been exposed to highly different levels of air pollution.

Several controlled exposure studies have shown that asthmatic subjects are more sensitive to the bronchoconstrictor potency of SO_2 than are healthy subjects. Bronchoconstriction can occur in some asthmatic individuals[8] during exercise at concentrations as low as 700 $\mu g/m^3$ and is observed in many[9] at about 1400 $\mu g/m^3$. In contrast, healthy volunteers[10] do not experience bronchoconstriction below concentrations of about 2700 $\mu g/m^3$. Pollution episodes in the Meuse valley (Belgium) in 1930, in Donora (USA) in 1948, and in London in 1952 demonstrated detrimental effects on respiratory mortality related to high levels of SO_2 (daily average about 4000 $\mu g/m^3$), acid aerosols, and smoke. This was particularly true for patients with pre-existing asthma (in Meuse and Donora) or bronchitis and asthma (London). Several epidemiological investigations have confirmed the positive association between respiratory morbidity and SO_2 or particulate matter at much lower levels in both adults and children. For example, a positive relationship between wheeze, peak flow impairment, and bronchodilator use on the one hand, and SO_2 levels (highest daily average, 105 $\mu g/m^3$), smoke (range 2–120 $\mu g/m^3$), and particulate matter on the other, has recently been found in children with chronic respiratory symptoms.[11] Even moderately elevated concentrations of SO_2 and particulate matter during winter time may therefore have an impact on respiratory diseases in susceptible populations.

Much experimental and epidemiological work has also been performed on the respiratory effects of NO_2. At concentrations of 200–500 $\mu g/m^3$ this pollutant has been shown to cause an increase in bronchial responsiveness to external stimuli in some subjects with asthma,[12–15] although other authors were unable to detect such effects at these[16] or much higher concentrations.[17] Similarly, in healthy subjects an increase in airway responsiveness has been observed at about 4000 $\mu g/m^3$ NO_2 by some[18] but not by others. No consistent effects on airway tone have been reported at these or lower concentrations.[19] Several cross sectional studies have revealed a higher prevalence of respiratory symptoms in children and adults from homes where gas was used for cooking (implying peak NO_2 levels of 400–800 $\mu g/m^3$), suggesting an effect of indoor NO_2 on respiratory health.[20] In addition, an association between the annual average concentration of NO_2 (11–51 $\mu g/m^3$) and the duration of symptomatic respiratory episodes has been reported in a random sample of preschool children.[21] At present, however, studies do not permit unique conclusions to be drawn on the role of NO_2, nor do they clearly indicate whether subjects with asthma are more susceptible to the adverse effects of NO_2 than normal subjects.

In experimental settings ozone has been shown to cause impairment of lung function at levels of 160–240 $\mu g/m^3$ during prolonged exercise[22] whereas the effective concentrations during shorter exposures[23] range between 400 and 800 $\mu g/m^3$. The typical functional changes following exposure to ozone are a transient restrictive ventilatory impairment and an increase in bronchial responsiveness to methacholine and histamine. Only few data from controlled exposure studies in asthmatic subjects are available,[24] some of them suggesting a slightly increased ozone sensitivity when compared with healthy individuals.[25] In a large sample of subjects we found that interindividual variation in acute alterations of lung function and airway responsiveness after ozone breathing were much more pronounced than differences in response between healthy subjects and patients with rhinitis or asthma.[26] Epidemiological studies have shown positive associations between respiratory illness and ambient ozone levels mainly in children, recent studies coming from Tennessee,[27] California,[28] Austria,[29] and Mexico.[30] They indicate that long term exposure to high ambient ozone concentrations (45% of days > 120 $\mu g/m^3$) may be associated with persistent bronchial hyperresponsiveness.[29] Changes in lung function on a daily basis relate in a negative fashion to ambient ozone levels[28 30] and an individual response may[30] or may not[27] be dependent on pre-existing airway disease.

The German reunification in 1989 provided a challenging opportunity to study two genetically similar populations who, over more than 40 years, have been exposed to different levels of environmental pollution as well as different living conditions. The East German industralised areas, especially in Saxony and Thuringia, are characterised by high concentrations of SO_2 and particulate matter—for example, average monthly levels of SO_2 and particulate matter in Leipzig and Erfurt (East Germany) during winter were about 300 $\mu g/m^3$ and 120 $\mu g/m^3$, respectively, whereas the values in a moderately industralised city in West Germany such as Munich were always below 50 $\mu g/m^3$ (SO_2) and 80 $\mu g/m^3$ (particulate matter). Conversely, NO_2 levels tended to be higher in the West German than in the East German cities. Several investigations are still under way and few data have yet been published in international journals; we will therefore briefly review the trends indicated by the available data.

Krämer and coworkers[31] performed a cross sectional study on respiratory symptoms and doctors' diagnoses in more than 4000 preschool children in several towns in East and West Germany. First results indicate higher prevalences of "frequent cough" and lower prevalences of doctor diagnosed asthma and rhinitis in children from the East German cities than in children from West Germany. These findings are compatible with a recent study reported by von Mutius *et al*[32] in which

6081 children in Leipzig (East Germany) and Munich (West Germany) were asked for their lifetime prevalence of asthma and allergic disorders, and bronchial responsiveness was assessed by cold air inhalation challenge. The lifetime prevalence of doctor diagnosed asthma was 7·3% in Leipzig and 9·3% in Munich, and prevalence of wheezing was 20% and 17%, respectively. The prevalence of diagnosed bronchitis was higher in Leipzig (30·9%) than in Munich (15·9%). No difference was found in the prevalence of bronchial hyperresponsiveness to cold air. Interestingly, hay fever (2·4% *v* 8·6%) and typical symptoms of rhinitis (16·6% *v* 19·7%) were reported less frequently in Leipzig than in Munich. In 7200 randomly selected subjects aged between 20 and 44 years in the two German centres of the EC Respiratory Health Survey—Erfurt (East Germany) and Hamburg (West Germany)—the answers to screening questions revealed a similar tendency.[33] Of the subjects from Erfurt 1·3% reported an attack of asthma within the last year and 13·2% answered positively when asked whether they had suffered from nasal allergies such as hay fever. The respective figures for Hamburg were considerably higher at 3·0% and 22·8%. These data will be compared with the results of lung function tests, methacholine challenges, skin tests, and specific IgE determinations. If one considers that the question on, for example, asthma has a specificity of 90% with respect to positive histamine challenge,[34] our figures lend support to the perplexing impression that the true prevalence of asthma seems to be lower in East than in West Germany. The final evaluation will take into account the influences of individual risk factors such as smoking, occupational exposure, and other epidemiologically relevant predictors for respiratory disease.

An explanation remains to be found for the apparently higher prevalence of atopic and asthmatic disorders in West than in East Germany. Since asthma in children and adolescents is most often of atopic origin and is closely linked to bronchial hyperresponsiveness, the studies from East and West Germany suggest that long term exposure to high levels of SO_2 and particulate matter does not increase the prevalence of asthma or allergy. Animal studies which have shown facilitated allergic sensitisation after low level SO_2 exposure[35] possibly do not adequately reflect the conditions met in human subjects.

The higher prevalence of allergic sensitisation in West Germany is further supported by the data on IgE antibodies against important indoor allergens such as *Dermatophagoides pteronyssinus, D. farinae*, and cat which have been obtained in 901 vocational pupils from Leuna (East Germany) and Duisburg (West Germany). The prevalence of antibodies against these mites and cat was more than fivefold and threefold, respectively, higher in Duisburg than in Leuna.[36] No such differences were found in sensitisation against outdoor allergens such as rye, Timothy grass, birch, and mugwort. One may therefore speculate that "western" housing styles[2] with decreased ventilation, higher humidity, and probably higher numbers of pets may be more important for the prevalence of asthma and atopy than "classical" outdoor pollutants such as SO_2 and particulate matter. These speculations may also provide a clue to the extraordinarily high rates of asthma and atopy found in New Zealand, a country which also seems to have a perfect climate for allergens. If this line of reasoning is true, measures must be taken to reduce the indoor allergen burden and thereby decrease the risk of atopy and asthma.[37] As an alternative explanation it is tempting to relate the increased prevalence of allergic disorders in Western cities to the much heavier traffic exhausts.

It has been hypothesised that the allergenicity of antigens could be enhanced by pollutants. Ishizaki and coworkers[38] found the highest incidence of cedar pollinosis among residents living along an intercity main road with heavy automobile traffic, whereas residents in the cedar forests with less automobile traffic showed a lower incidence. It is not clear, however, that confounding factors have been adequately taken into account. Krämer and coworkers[39] reported an elevated frequency of positive RAST classes to pollen allergen in those children exposed for more than one hour per day to traffic. Others have reported a more frequent sensitisation to aeroallergens in polluted than in non-polluted regions, and specific IgE levels were higher in subjects from urban areas than in those from rural areas.[40] It has recently been shown experimentally that short term inhalation of 240 $\mu g/m^3$ ozone tended to increase bronchial responsiveness to inhaled allergens in a small group of asthmatic subjects.[41] Such an effect has not been found at the level of the nose,[42] suggesting different susceptibility or different mechanisms at these levels. Although animal studies suggest that allergic sensitisation could be increased by previous exposure to ozone,[4] this effect has not been consistently observed after long term exposure to high ozone concentrations.[29]

What can be learned from these studies? Asthmatic patients show increased susceptibility to the adverse respiratory health effects of most air pollutants. This is true for SO_2 and probably, to a lesser extent, for NO_2 and ozone. The question whether air pollution can cause asthma and atopy is not yet resolved. Studies from East and West Germany suggest that SO_2 and smoke do not increase allergic sensitisation under real life conditions.[31–33] If ozone exposure was a major risk factor for atopy and asthma a substantially higher rate of these disorders would be expected in cities like Los Angeles, which is not the case. Multicentre cross sectional studies which cover a broad variety of risk factors for atopy and asthma such as the EC Respiratory Health Survey are therefore clearly warranted and will shed light on the still open question as to what extent indoor and outdoor factors are relevant for the prevalence and severity of these disorders. Skilful combination of epidemiological studies and controlled human exposure experiments seems to be more promising than further extension of data derived from laboratory animal studies.

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