

that ablation of CIN may help promote a type-specific immune response not available when the lesion, and its large viral load, are excised. High recurrence rates in older women and in women previously treated for CIN are consistent with the notion that such women have a decreased ability to clear the virus. Unfortunately, specific HPV typing was not done in Mitchell and colleagues' study, so whether ablative procedures enhance a type-specific immune response remains unknown.

Clearly, the preference of the clinician and patient and cost considerations, not concern over potential differences in efficacy or complications or fertility, should dictate choice of treatment of CIN, but the issue that will continue to confront clinicians is whether low-grade lesions (CIN1, mild dyskaryosis) should be treated even though most are self-limiting.¹⁷ Management guidelines have increasingly included non-treatment of low-grade lesions as an option if the patient is likely to attend reliably for follow-up, but concern over being held responsible for a progressive lesion continues to drive intensive follow-up protocols that may not be cost-efficient. At the end of the day, whatever will enable each woman to feel most normal may be the best choice.

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Air pollution and asthma: the dog that doesn't always bark

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Over the past decade there has been a renaissance in studies of air pollution. This renewed interest has been driven partly by the development of more sensitive techniques to analyse time-series data, which have shown that there are still clear adverse effects on mortality rates from current levels of air pollution. These effects are seen largely in elderly people and are related to cardiovascular and respiratory causes of death.

With this evidence of extreme sensitivity to air pollutants among some sections of the population, the difficulty in establishing consistent evidence for a link between air pollution and asthma, an association that the lay public and many scientists take as self-evident, seems paradoxical. A disease that is almost defined by an increased sensitivity of the airways to almost any stimulus ought to be clearly associated with air pollution.

However, despite many instances of associations between exacerbations of asthma and increases in air pollution, there are many failures to find these associations. The most spectacular are from some of the major air-pollution episodes. In the great London smog of 1952, John Fry was struck by the lack of any effect on asthmatic children in his practice, although his observations¹ are now little cited and largely forgotten. In 1985, in the last severe smog to affect Europe, there was also a stark contrast between the increased rates of mortality from and hospital admission for stroke, cardiovascular disease, and chronic obstructive lung disease and a lack of any effect on asthma in the affected areas.² Studies of such events can be insensitive to some changes because they rely on routinely collected information and not on direct observation of symptoms and lung function. However, the recent PEACE study, which is the most comprehensive study to date of the association between concentration of airborne particles and exacerbations of respiratory disease in children, did not show any consistent relation between these two variables across 14 centres in Europe.³

One potentially important explanation might simply be technical. Perhaps in the negative studies the measurements were not accurate enough, or the studies were too small to show the expected effects. Alternatively, the effects that were there may have been overwhelmed by other contemporary events, such as infections, which, uncontrolled for in the analyses, may have disguised the real effects. This explanation does not, however, seem very likely. Other explanations are that the air pollutant or pollutants that are being studied are not defined and measured precisely enough, or that the response to them is modified by as yet unidentified important factors. There is currently great interest in characterising particulate air pollution more precisely and identifying the factors that make it toxic.

Today's *Lancet* carries a report of another study of air

pollution on the respiratory health of children with airway disease. The investigators asked a large sample of children in the Netherlands to complete a diary recording symptoms and peak-flow values each day for three winters. The report gives the results for four sets of children defined by whether they had bronchial hyper-responsiveness, atopy, neither, or both. The conclusion from the study is that only those who have both atopy and bronchial hyper-responsiveness are susceptible to the effects of increased air pollution. Among children who had one risk factor, only those with a high IgE concentrations seemed at all susceptible. Does this finding help in the explanation of past results?

Many studies have shown interactive effects between air pollutants and allergic responses both in animals⁴ and in human beings.⁵ These effects may explain a link between atopy and air pollution, but by themselves they do not account for the lack of a response to air pollution in some studies.

A further clue may come from studies undertaken in Barcelona, Spain. Here, there were also epidemics of asthma, which were initially linked to concentrations of nitrogen dioxide in the atmosphere.⁶ As is now well known, the cause of these epidemics was contamination of the air with soy-bean allergen from ships unloading in the harbour.⁷ The reason for the initial confusion was that the types of weather that trap allergen trap all pollutants. The epidemics of asthma did not occur whenever there was an air-pollution episode, but only when these episodes coincided with the unloading of soy bean from ships in the harbour.

The effects seen in relation to air pollution in general are very much smaller than the effects seen during the epidemics in Barcelona or in other episodes of asthma linked to large-scale allergen exposure.⁸ However, there is further evidence from Barcelona that, on non-epidemic days, very much lower exposure to allergen also produced adverse effects.⁹ One question that needs to be answered is whether allergen concentrations in air explain why only those children with high IgE concentrations were affected by increases in air pollution in the Dutch study.

Asthmatic people respond very strongly to inhaled allergen, and there are studies apart from those in Barcelona that imply that sensitised individuals do respond to ambient concentrations of allergens. Others have shown increased mortality rates or increased morbidity on days with high spore counts in the air,¹⁰⁻¹³ and acute respiratory arrests have been shown to be more common in the "alternaria season" in the USA in people with the relatively rare sensitivity to this mould (*Alternaria alternata*).¹⁴ However, measurement of allergen is far from straightforward and measurement of pollen and mould counts by themselves may not be an adequate test. The problem with allergen is that it takes many forms, and there may be important allergens in the air about which little is known. For instance, scientists in Denver have, perhaps surprisingly, reported the presence of latex allergen in the fine particles of ambient air.¹⁵

The implications of the findings from the Dutch study for policy may be important. Although very little is known about the allergenicity of outdoor air, the likelihood of control of outdoor allergens in the same way as of other pollutants is small, so reliance may have to be placed on measures to make individuals less

susceptible rather than on control of exposure. Meanwhile, control of other forms of air pollution remains important, to reduce the effects on older people who have cardiovascular risk factors or chronic obstructive lung disease, and to reduce any interactive effects with allergen in the atopic population.

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Treatment of IgA nephropathy

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IgA nephropathy is one of the commonest types of glomerulonephritis in many parts of the world, accounting for 15-20% of all glomerulonephritis in western Europe and 30-40% in Japan, but less than 10% in North America.¹ These differences may be related to ethnic and environmental factors but are also due to varying indications for renal biopsy. The true incidence may be severely underestimated because necropsy studies and histological examination of kidneys donated for transplantation indicate that 2-4% of the population may have glomerular mesangial IgA deposits. For most of the subset recognised clinically, the prognosis is good. However, 20-30% of patients will develop progressive renal failure over the 20 or so years from the time of initial diagnosis, and 1-2% of adult patients with IgA nephropathy enter end-stage renal failure each year. Spontaneous remissions in adult patients are unusual, occurring in less than 4%. Since the natural history of