outdoor pollution mixture. Ozone in England does not seem to play a role in lung function.

Previous studies do not provide enough evidence to relate the effects of air pollution conclusively to one or the other specific spirometric measures, although there are some indications of larger effects on the markers of the small airways.[4] Forbes *et al* provide data only on FEV_1 and the FEV_1/FVC ratio, showing no association for the ratio after adjusting for smoking and social class. Larger misclassification in the measurement of FVC than FEV_1 in the general population studies may explain these results in part.

The larger size and improved exposure assessment in the study of Forbes *et al* reinforce the knowledge of a deleterious effect of current levels of air pollution on lung health in Europe. However, the cross-sectional nature of these studies does not solve important questions regarding the most relevant age period and exposure time windows of susceptibility. It is impossible to know if the effects on the lung function level in adulthood reflect growth deficits experienced during childhood and whether these subjects entered the lung function decline phase with a reduced lung function. The largest effects observed by Forbes *et al* were among the oldest people (>75 years). Nevertheless, this does not imply an effect during the decline phase since it could result from a cohort effect because of higher historical air pollution levels for this age group. It is possible that air pollution behaves like smoking in adulthood, which accelerates lung function decline, and that changes in smoking resulted in changes in the slope of decline. In any case, there is a need to extend follow-up studies to children and to perform large follow-up studies through to adolescence in order to quantify the magnitude of the effect of air pollution in accelerating lung function decline not only for a better knowledge of the origins of COPD, but also to assess the population impact of air pollution and the potential consequences of its reduction.

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Can traffic-related air pollution cause asthma?

John R Balmes

Traffic-generated pollution contains particles and gases (eg, oxides of nitrogen) that are known to have health effects.[1] Concentrations of pollutants emitted by motor vehicles are highest within 150 m of roadways and remain raised up to 300 m from roadways, but fall off markedly beyond that range.[2 3] Exposure to the mixture of traffic-generated pollutants may be more relevant to human health than exposure to any single ambient air pollutant, making epidemiological investigations of traffic effects a key component of research into the public health impact of air pollution. However, assessment of exposure to traffic-related air pollution can be problematic. Exposure to traffic can be estimated with complex dispersion models of pollutants from local freeway and non-freeway sources, but the data inputs required for such modelling are not always available. A frequently used simpler approach has been to estimate residential distance to roadways.

A number of studies have found an increased prevalence of asthma or asthma symptoms in children who live near roadways with high traffic counts.[4–8] One large British study that focused on traffic within 150 m of children's homes found a gradient in risk that increased markedly with decreasing residential distance to a main road.[7] A large study in southern California showed an increased prevalence of asthma and wheeze in children living within 75 m of a major roadway.[9] Another study by Jerrett *et al* that analysed data from the same southern California cohort was able to demonstrate an association between the incidence of asthma and exposure to traffic-related pollution.[10] A recent review summarised the evidence for traffic pollution as a risk factor for both asthma exacerbation and onset as strong.[11]

In contrast to the relatively rich literature for children, little has been published on the effects of traffic-related pollution on asthma in adults. Although several previous studies in adults with asthma have found that exposure to traffic—as measured by distance of residence from nearest major roadway—was associated with asthma symptoms, health care utilisation or decreased lung function,[12–14] the study by Künzli and colleagues[15] reported in this issue of *Thorax* is the first to show convincing evidence that exposure to traffic-related particulate matter increases the risk of adult-onset asthma (***see page 664***). When the paper by Künzli *et al* is taken together with the study by Jerrett *et al*,[10] we now have evidence in both children and adults that traffic-related pollution can cause as well as exacerbate asthma.

Given the robust effects observed on asthma outcomes in other studies of both children and adults, it is somewhat surprising that distance to roadway was not associated with the risk of new-onset asthma in over 2700 non-smoking Swiss

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adults in the analysis by Künzli *et al*.[15] The authors speculate that they did not find an effect of distance to roadway because their study design was longitudinal, and this variable did not change over time for most subjects. Moreover, they contend that the modelled traffic-related particulate matter exposures which they assigned to their subjects captured the spatial and temporal heterogeneity of individual exposures better than can be achieved with distance to roadway metrics. They suggest that this greater heterogeneity of exposure allowed their analysis to achieve statistical significance despite the relatively small number of new cases of asthma in the SAPALDIA cohort. Similar reasoning can be applied to the study by Jerrett *et al* which captured spatial heterogeneity in traffic exposures by using nitrogen dioxide concentrations measured immediately outside the children's homes as a proxy for the traffic-related pollution mixture.[10]

Perhaps the greatest research challenge regarding the impact of traffic-related pollution on asthma is to determine what specific constituents of the mixture are responsible for the observed effects. While diesel exhaust particles have clearly been shown to induce both cytotoxic and immune adjuvant responses in toxicological studies[16] as well as acute lung function decrements in subjects with asthma,[17] it has been difficult to distinguish diesel effects from those of other components of the traffic mixture in epidemiological studies, largely due to an inability to assess exposure properly. Until we develop better exposure assessment methods, we will be unable to meet this challenge. Without good data about the causative agents in the traffic pollution mixture, our ability to control exposures to protect the health of people with asthma will continue to be handicapped.

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Pulmonary infection in Wegener's granulomatosis and idiopathic pulmonary fibrosis

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Friederich Wegener's original paper "On generalised septic vessel disease" suggests he thought it likely there was an infectious cause for the condition which now bears his eponym.[1] The characteristic pathological features of Wegener granulomatosis (WG) are: a necrotising granulomatous inflammation of the respiratory tract with vasculitis affecting both arteries and veins; focal necrotising glomerulonephritis; and a varying degree of systemic vasculitis—the so-called "Wegener's triad".[2] The granulomatous inflammation is conspicuous for the absence of any obvious microorganism, although granulomatous infections can sometimes be misdiagnosed as WG.[3] During the 70 years since Wegener's description there have been some remarkable advances in both the diagnosis and treatment of this condition and in our understanding of its pathogenesis. However, the precise nature of the initiating factor(s) remains elusive.

What we do know is that there is a strong association between WG and the human leucocyte antigen (HLA)-DPB1*0401 allele, suggesting that there is an inherited predisposition for the condition.[4] Interestingly, there is also an association with α-1 antitrypsin deficiency.[5] We also know that virtually all patients who subsequently develop the systemic disease have circulating antineutrophil cytoplasmic antibodies (ANCAs) and these are mainly directed against proteinase-3 (PR3), the so-called "Wegener's autoantigen"—a serine protease which regulates cell proliferation, differentiation and death.[6] This antibody has proved to be a useful biomarker for the diagnosis of WG,[7 8] although less so for the likelihood of relapse.[9] Furthermore, our increasing knowledge of its biological properties has provided new insights into the pathogenesis of WG. Specifically, whilst PR3 is the target antigen for ANCAs, the observation that elevated levels of PR3 at sites of granulomatous inflammation correlate with increased tumour necrosis factor α (TNFα) has led to the hypothesis that PR3 is directly involved in the modulation of cytokines associated with an aberrant immune response (see Csernok *et al*[10] for a review).

Following tissue injury, increased levels of PR3, released from activated or dying neutrophils, might act as a danger/alarm

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