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Are we understanding the respiratory effects of traffic related airborne particles?

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There is convincing scientific evidence showing that ambient particulate matter (PM) is related to both short and long term health effects. Increased mortality and hospitalisation for cardiopulmonary causes have been noted in several studies evaluating the effects of PM_{10} or $PM_{2.5}$ (PM <10 or 2.5 μm in diameter).[1] However, urban air pollution consists of a complex mixture of gases and particulate agents that vary over time and through space, depending on its sources, distance and meteorological conditions.[2] Much of the scientific interest has been devoted to the toxicology of the ultrafine fraction of airborne particles (<0.1 μm).[3] These particles are usually emitted from combustion sources (eg, gasoline or diesel powered engines) or are formed from chemical conversion of gases in the atmosphere. They are relatively short lived and combine into larger particles between 0.1 and about 1 μm in diameter (accumulation mode). These particles tend to penetrate deeper in the alveolar part of the lung and have a larger surface area than larger sized particles, eliciting greater potential interaction with human tissues and a stronger inflammatory reaction. The epidemiological evidence linking ultrafine particles with respiratory health effects is still limited and controversial. In the current issue of *Thorax*, Halonen and colleagues[4] provide new and compelling evidence on the respiratory effects of particles of various sizes that will certainly stimulate further research ***(see page 635)***.

Different sized particles were measured daily in Helsinki over a period of 7 years, and a source apportionment method was applied to separate the $PM_{2.5}$ fraction from four sources (traffic, long range transport, soil and road dust, and coal/oil combustion). Daily counts of asthma emergency room visits among children, and asthma/chronic obstructive pulmonary disease (COPD) emergency room visits among adults and the elderly were collected. After careful control for time varying confounding factors, ultrafine particles, CO and NO_2 were strongly associated with asthma in children with a delay of 3–5 days. In contrast, asthma and COPD in the elderly were clearly associated with larger particles (accumulation mode, $PM_{2.5}$, coarse particles), and CO and NO_2 at immediate lag (same day). Traffic related particles had a strong delayed effect on children's emergency room visits for asthma whereas traffic related and long range transported particles had an immediate effect on asthma/COPD visits of the elderly.

There are several strengths of the paper: a new approach to study the effect of air pollution that combines specificity in the exposure assessment (daily measurements with a differential mobility particle sizer), consideration of the pollution sources and specificity in the age groups corresponding to different respiratory conditions. The authors also give interesting indications for understanding the toxicology of particulate matter. Two aspects need to be discussed in light of the differences between asthma and COPD regarding their baseline obstructive and inflammatory characteristics: the timing of the effects that characterise the response to air pollutants in patients with asthma and in COPD patients, and the difference in the size of the particles eliciting the effects.

Childhood asthma is characterised by reversible airflow obstruction, bronchial hyperresponsiveness and an underlying inflammation. The study by Halonen and colleagues[4] stresses the delayed role of ultrafine particles on this condition. There are other epidemiological observations with similar findings. Two time series studies on emergency room visits or hospitalisations for childhood asthma in the USA[5] and Copenhagen[6] support the delayed effect of ultrafine particles. The delayed effects found in these studies, including the Finnish investigation, apparently are at odds with recent

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results from a field study in London where patients with asthma walking on Oxford Street had an immediate decline in lung function in response to fine and ultrafine particles from diesel traffic, higher that those walking in Hyde Park.[7] A study by Delfino and colleagues[8] indicated an immediate increase in exhaled nitric oxide (an established biomarker of airway inflammation) in children with asthma in relation to elemental carbon and other indicators of traffic related air pollution.

As Halonen and colleagues[4] are aware, there are probably several reasons for the differences between studies that show an immediate effect on inflammation and lung function in patients with asthma and studies indicating a delayed effect on emergency room visits: there is a large underlying population distribution of asthma sensitivity and severity, asthma medication (inhaled bronchodilators and corticosteroids) may reverse the symptoms of air pollution and finally behavioural reasons may play a role, as not all families immediately recognise the severity of their child's symptoms. Nevertheless, a real lag time is likely between exposure to ultrafine particles and acute respiratory symptoms requiring emergency care because inflammatory events in the lungs develop over a range of hours to days. In addition, ultrafine particles may increase bronchial reactivity, secondary to airway inflammation, which may subsequently trigger symptoms after exposure to a variety of other environmental exposures.[9]

Unlike asthma, COPD is associated with irreversible airways obstruction and chronic airways inflammation with increasing frequency and severity of exacerbations.[10] Fine and large particles may act as inflammatory agents with an abrupt increase in airways resistance, and worsen expiratory flow limitation and dynamic hyperinflation. The declining clinical status may require prompt emergency care for more severe forms of the disease, especially when it is accompanied by cardiac dysfunction. Moreover, systemic inflammation in response to the oxidative stress induced by PM exposure has been suggested in patients with COPD[11 12] that may be responsible for acute cardiovascular morbidity. It is not surprising then that several studies have found an acute effect of PM_{10} or $PM_{2.5}$ on COPD emergency room visits or hospital care,[13–16] although in some cases an effect was not found[17] or a delayed lag was detected.[18]

As in most time series studies that measure daily variations in different air pollutants, fixed monitoring stations represent daily variations in overall population exposure. However, a differential exposure misclassification for different pollutants or size fractions may influence the results when the effects are compared. For example, vehicular traffic constitutes the most significant source of ultrafine particles near roads and the variability in exposure can be much higher than in background areas. Although Halonen and colleagues[4] indicate a reassuringly high correlation between outdoor and indoor concentrations of ultrafine particles, these results need confirmation in other areas with different environmental and urban conditions.

The possibility of generalising the findings from this study to other urban contexts is limited because of the varying nature of the pollutant mix generated from traffic. Other areas in Europe tend to have a much higher proportion of diesel powered vehicles than Nordic countries. As has been already suggested,[19] evaluating the health effects of particle size alone is difficult as it is not independent of its chemical composition. The different chemical compounds of PM (eg, transition metals) may contribute differently to the PM induced health effects. There is a need for a large data set that should include the size of the particles, their sources and their chemical composition. Although the study in Helsinki offers an important insight in this direction, it is a ''one city'' study and the results should be replicated in different contexts. Therefore, we are only approaching an understanding of the problem. What Europe clearly needs is a multi-city study, similar to the APHEA in the 1990s,[20] to evaluate the short term health effects of particles of different size, their sources and compositions.[21] The health data and ability to perform such studies are readily available, but time series of concentration levels of size fractions, chemical compositions and inventory of source contribution are not. While a large PM specialisation programme is ongoing in the USA,[22] Europe is lagging behind.

The European Union has recently approved the new annual limit for $PM_{2.5}$ (25 $\mu g/m^3$) and a revision of the $PM_{2.5}$ standard is foreseen for 2013. The EU conclusions have been controversial,[23] as adverse health effects have been detected at a much lower level of fine particles, as in the Helsinki study. There are 5 years to develop an approach that characterises sizes, properties and sources of PM, and evaluate health effects while combining epidemiological, toxicological and clinical data.

Competing interests: None.

Thorax 2008;**63**:574–576. doi:10.1136/thx.2008.096073

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Obesity and the respiratory physician

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Respiratory medicine has developed as a specialty in the wake of a number of public health milestones. The origins of many of the learned societies associated with respiratory medicine can be traced back to the epidemic of tuberculosis (TB) in the early 19th century.[1] Effective public health and effective treatment regimes reduced the prevalence and mortality of TB. The seminal work linking the role of tobacco smoking and its detrimental effects on the lung[2] was the second key finding which challenged our specialty. Public health measures and the development of new treatments are reducing the prevalence of smoking-related lung disease, although there is still much work to be done. Obesity has emerged in the opening years of this century as a major challenge to public health. The impact of obesity on the prevalence and mortality of many diseases is well documented, although there has been little attention paid to its impact on respiratory disease.

Obesity rates are rising at an alarming rate in developed and developing countries, in both sexes, in children and adults. The obesity epidemic in children is particularly concerning as today's overweight children and adolescents will become tomorrow's obese adults.[3] It has been estimated that childhood obesity observed now will lead to a reduction in life expectancy in the USA of between 2 and 5 years by the middle of this century—an effect equivalent to that of all cancers combined.[4]

Physicians recognise obesity or overweight poorly. A North American study examined the records of 424 overweight or obese patients.[5] Only 20% of patients were correctly identified by the treating physician as overweight or obese, in only 2% of cases was body mass index documented and only 16.5% of the patients received any obesity management advice (ranging from simple advice to referral for surgical management).

Obese patients provide particular diagnostic and management dilemmas to the respiratory physician, and these are explored in a series of five articles to be published over the coming months in *Thorax*. The first of these examines the epidemiology and possible aetiological links between obesity and lung disease ***(see page 649)***[6]. Much work remains to move beyond epidemiological links to an understanding of the mechanisms underlying the associations demonstrated in asthma and obstructive sleep apnoea (OSA).

OSA has a similar prevalence to diabetes in the general population and, while not all patients with sleep apnoea are overweight, excess body weight is the major modifiable risk factor for the condition. Obesity hypoventilation syndrome is a common condition, resulting in impaired quality of life and high healthcare utilisation. If recognised, it can be effectively treated.

Patients in the intensive care unit who are obese have specific and practical management issues such as specific beds required to accommodate them safely, and challenges in transport and imaging. The specific issues which affect this group of patients—including the difficulties in airway management and the recognition of abdominal compartment syndrome—are discussed, along with practical suggestions for management.

Epidemiological studies have suggested that there are links between obesity and the development of asthma. The fourth article discusses potential mechanisms for this association, including the contribution of adipokines to the asthma phenotype and the reductions in peripheral airway diameter in obesity. Obese patients with asthma use more health resources than their lean counterparts, possibly reflecting that obesity may make the asthma phenotype more resistant to treatment. Some of the commonly used drugs in respiratory medicine (eg, oral glucocorticoids) have important effects on body composition and ultimately on pulmonary mechanics, and this merits consideration in the risk/benefit ratio in their prescription.

It is known that loss of fat-free mass is a poor prognostic marker in severe chronic obstructive pulmonary disease (COPD). The effects of obesity in this condition are less well known, and this is discussed in the final article. While epidemiological studies have suggested that obesity may be protective in a number of chronic diseases including COPD, the pathophysiology of this observation is yet to be elucidated. COPD is associated with systemic inflammation and there is accumulating evidence that hypoxia may exacerbate this cascade. The final article discusses the intriguing possibility that obesity exerts different effects on various subgroups of patients with COPD and highlights areas requiring further research.

The interactions of nutrition with lung disease should be considered in everyone presenting with respiratory problems. All people with respiratory disease should have serial measures of weight on accurate well-calibrated scales, professionals should be educated in the management and recognition of obesity, patients should receive management and advice including access to well organised, readily available obesity services when required. The potential impact of obesity on pulmonary physiology should also be considered in people with other complications of obesity.

However, more important will be the urgent implementation of far-reaching public health measures designed to reduce the impact of obesity on future generations. These will include such measures as provision of routes to allow commuters to walk or cycle, regulation of advertising of junk food, access for increased physical activity, re-education of consumers regarding food choices and incentives for farmers to produce nutritious food.[7]

The combined advertising spending for Pepsi and Coca-Cola for 2004 was more

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