examination to the next.[10] This kind of noise reduction may be less important in cross sectional studies such as the one by Dawkins *et al*,[8] and it may even introduce new errors. An increase in total lung volume is an inherent part of the emphysematous process and, by eliminating that aspect of the disease, volume adjustment may in fact weaken the correlation between CT lung density and other measures of disease severity (unpublished data). Thus, adjustment of lung density for lung volume is not always to be recommended.

The two studies published in this issue of *Thorax* underline the urgent need for standardisation and international agreement on recommendations for lung density measurement based on CT scanning. However, provided CT lung density can be standardised and validated against traditional clinical outcome variables, it may prove to be a new measurement that is objective, specific, and sensitive for monitoring the effect of new drugs on the progress of emphysema in future randomised clinical trials.

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Asthma and obesity

Asthma and obesity: where are we now?

S Chinn

The importance of the reported association between obesity and asthma is still unclear

An association between asthma and overweight or obesity was first reported in adults in the 1980s.[1 2] The papers were concerned with chronic disease in general and excited little attention in the respiratory field at the time. In children concern had been over growth retardation in those with asthma.[3] In 1984 Somerville *et al*[4] reported a weak association between symptoms of asthma and increasing weight for height, but again this provoked little interest.

In the last 5 years there have been numerous reports of an association in adults and in children—too many to cite directly.[5 6] Even since the later of these two reviews there have been further reports in children,[7] in adults,[8] and specifically in women.[9] The lack of earlier reports does not necessarily imply that the association is recent because, when the prevalence of obesity was lower, there was less power to detect a raised prevalence or incidence in obese subjects. However, in addition to this indirect evidence, there is some direct evidence for the association being recent in origin. In a study of children aged 5–11 years in Britain carried out over 23 years, in contrast to the weak association in the 1977 data cited above, a strong association was found in data collected in 1994.[10] In adults there is evidence for an association between asthma and obesity in Britain as early as 1982, but no other reports to show whether the relation existed earlier.[6] Obesity, defined as a body mass index (BMI) of 30 or more, had already reached 14% in adults in the US by the early 1970s,[11] a figure comparable to that reached in England in 1993,[12] so it seems likely that the association, if present, could have been detected in the US earlier than the 1980s.

THE EVIDENCE

Confounding

Studies in adults have found associations between reported asthma or symptoms (rather than doctor diagnosed asthma) and BMI and, in a few studies, height and weight were also self-reported. This has led to some scepticism that the association is spurious or due to confounding[13] or, at most, the result of increased perception of symptoms among those who are overweight.[14] Schachter *et al* found an association between symptoms and medication for asthma and increasing BMI, but not airway responsiveness (AHR), in 1971 adults aged 17–73 years,[14] and in this issue of *Thorax* they present similar findings in 5993 children aged 7–12 years.[15]

The association is not simply due to concomitant trends in asthma and obesity, as suggested by Wilson.[13] The association is not ecological but is found in individual data and, while in the UK the trends in BMI and asthma have been concurrent in children, the trend in BMI does not explain the trend in asthma due to the recent nature of the association.[10] Wilson's alternative explanation was that it was due to confounding. Confounding can never be completely ruled out in observational studies, but the factors suggested by Wilson—gastro-oesophageal reflux and obstructive sleep apnoea—are not potential confounders but intervening variables on putative causal pathways.[13]

Increased perception

That the association may be due to increased perception of symptoms in obese individuals is much more difficult to rule out. Indeed, it can be assumed

that part of the association is due to perception as lung function decreases with increasing BMI within individuals,[16 17] although in cross sectional data an increase in lung function may be seen at lower BMI and a decrease only at higher values.[18] The question is whether the association is entirely due to increased perception. The conclusions of Schachter *et al* were based on finding no trend of increasing AHR with greater BMI.[14 15] However, in 11277 participants in the European Community Respiratory Health Survey (ECRHS) a statistically significant trend was found even after adjusting for lung function,[19] and a case-control study of men in the Normative Aging Study found a U-shaped relation with greater AHR at high and low BMI, also adjusted for lung function.[20]

There is other evidence for not dismissing the association as being entirely due to increased perception. In children, case-control studies comparing those with diagnosed asthma and those without showed that the asthmatic children had greater mean BMI.[21 22] Furthermore, at least six longitudinal studies have shown an increased incidence of asthma in overweight or obese children and adults.[6 7] A delayed effect is more difficult to explain away than an immediate one by increased perception. In these studies incidence was calculated in those disease or symptom free at baseline. The lack of an agreed definition of asthma, and the difficulty of differentiating true incident asthma from recurrence of quiescent asthma, have provoked criticism of this approach.[23] However, the studies do make the reverse causation hypothesis—that lack of exercise in asthmatic patients promotes obesity—an unlikely explanation. These studies also provide evidence against the mechanical effects of obesity being the sole explanation, by the same argument as against increased perception and against a combination of perception and mechanical effects alone.

Studies of change in symptoms in obese asthmatic patients who lose weight have the potential to overcome the above scepticism. The one randomised controlled trial of 38 obese patients showed a reduction in symptoms and improvement in health status in the treated group compared with the control group, and an increase in lung function.[24] However, at high BMI a reduction in weight is likely to increase lung function irrespective of symptoms,[16 17] so this may not have convinced the sceptics. Airway responsiveness was not measured. A large trial including AHR as an outcome could provide evidence that the change in reported symptoms is not entirely due to reduced perception with weight loss, although on its own it cannot determine whether obesity is a cause of asthma.

Dietary factors

Review articles have considered many possible explanations apart from confounding, mechanical effects, and perception.[5 6] Obesity may modify the immune system, female sex hormones may play a role, physical inactivity may independently promote obesity and asthma, and a large number of dietary factors may be implicated.[5] In the randomised controlled trial weight reduction was achieved through a diet which was modified in content as well as in calories,[24] and surgical reduction may lead to dietary changes. It may be feasible to collect dietary data in asthmatic patients motivated to lose weight, but a large study will be required to disentangle the candidate explanatory factors.

Sex differences

A number of studies have found an association between the prevalence or incidence of asthma in women but not in men, prompting a discussion of the mechanisms involving female sex hormones. However, the finding was not universal and, in the ECRHS, the association between AHR and obesity was, if anything, greater in men,[18] but associations between symptoms and obesity were almost identical in men and women.[25] Part of the explanation for this heterogeneity in the findings may be in study size and methodology. In order to conclude a different effect in men and women, a statistically significant interaction is required. It is not sufficient to observe a statistically significant relation in one group and not in the other, but studies may lack the power to detect an interaction.[26] A number of studies have not reported a test of interaction but analysed data for men and women separately on a priori grounds because of the previous reports of differing associations. Others have reported a combined effect, so the evaluation of the evidence for and against a sex difference is quite difficult. In addition, some of the larger studies of adults showing a greater association in women analysed reported height and weight[27 28] which may have different validity in men and women. Only a large study with the power to detect an interaction effect can answer the question, but the interaction may genuinely differ between studies if the association is due to multiple mechanisms with difference contributions in different places.

Schachter *et al* found an association between BMI and atopy in girls,[15] while Jarvis *et al* found no association with atopy in men or women, and no interaction between BMI and atopy on symptoms.[25] Huang *et al* found an association between high BMI and both atopy and AHR in girls but not boys in Taiwan,[29] the association with atopy explaining that with AHR. An association between BMI and atopy was reported in a study in Finland but no symptom data were included.[30]

WHERE ARE WE NOW?

The scientific community is divided over the importance of the reported association between obesity and asthma, over whether the association is confined to women and girls or not, and whether atopy is also associated and perhaps on a causal pathway. In addition, there are a number of plausible mechanisms with little or no evidence for or against their role. Only large studies which include AHR as an outcome are likely to add further to the debate. However, we can surely all endorse the plea made by Redd and Mokdad[23] not to delay intervention programmes to tackle the obesity epidemic while we argue over the mechanisms for an association with asthma.

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Air pollution and lung cancer

Air pollution and lung cancer: what more do we need to know?

A J Cohen

Further work is needed to quantify the effect of outdoor air pollution on lung cancer

Lung cancer accounts for 1.2 million deaths yearly worldwide, exceeding mortality from any other cancer in the developed countries.[1] The vast majority are caused by tobacco smoking, but environmental causes of cancer, including air pollution, have long been a concern also.[2] Outdoor air pollution has received particular attention lately as research has proliferated linking exposure, even at low ambient levels, to a wide range of adverse health effects including increased mortality and morbidity from non-malignant cardiovascular and respiratory disease and lung cancer. In response, international agencies such as the World Health Organization and governments in Europe, the US and Canada have reviewed existing air quality standards and, in many cases, moved to strengthen them. In the developed countries, where air quality has generally improved in recent decades, the scientific basis and public health efficacy of these actions have been questioned by industries whose emissions are regulated and others. In this context, reports linking air pollution and lung cancer are likely to attract attention and generate controversy. The publication of the paper by Nafstad and colleagues in this issue of *Thorax* is an occasion to consider both the contribution of this study to the evidence linking air pollution and lung cancer and what additional research may be needed.[3]

Exposure to outdoor air pollution has been associated with small relative increases in lung cancer in studies conducted over the past four decades.[4] The epidemic of lung cancer emerging in the 1950s in the US and Europe motivated early research on the role of air pollution, including studies of migrants and urban-rural comparisons but, as the role of cigarette smoking became increasingly clear, interest in air pollution waned. However, recent prospective cohort and case-control studies which have taken into account tobacco smoking, as well as occupational and other risk factors, have continued to report increases in lung cancer associated with air pollution.[5–7] The American Cancer Society (ACS) study, which included 10 749 lung cancer deaths, reported that each 10 $\mu g/m^3$ increment of fine particles ($PM_{2.5}$) was associated with an 8–14% increase in lung cancer.[7] A causal interpretation is buttressed by other evidence. Urban air contains known and suspected human carcinogens such as benzo[α]pyrene, benzene, and 1,3-butadiene, together with carbon based particles onto which carcinogens may be adsorbed, oxidants such as ozone and nitrogen dioxide, and oxides of sulphur and nitrogen in particle form. Increased lung cancer has also been reported among workers occupationally exposed to components of urban air pollution such as polycyclic aromatic hydrocarbons and diesel exhaust.[8 9]

In light of this evidence, the question is arguably not ''Does air pollution cause some lung cancers?'', but rather ''How many excess cases is it likely to cause?''. The answer to this question, and another—''Which pollutants, emitted by which sources, may be responsible?''—can potentially inform regulatory action to improve air quality and public health.

The current evidence suggests that lung cancer attributable to air pollution may occur among both smokers and non-smokers, and therefore both residual confounding and effect modification of the air pollution relative risk due to cigarette smoking must be considered. Nafstad *et al*[3] report the relative risks of air pollution adjusted for cigarette smoking, but adjustment may not have controlled completely for potential confounding. The authors acknowledge that their study, like most other cohort studies, has information on cigarette