Functional and reversible loss of regional pulmonary perfusion may also result from compression of lung in areas adjacent to severe emphysema. In addition, an overall reduction in lung perfusion due to cardiopulmonary interaction, partially caused by intrinsic positive end-expiratory pressure associated with dynamic hyperinflation, may also reduce DLCO.

In this study, the proportion of the lung in the severe emphysema and ME partitions accounted for individual patient changes in DLCO. The higher the baseline severe emphysema fraction of lung, the greater the increase in DLCO after LVRS. This suggests that surgical removal of severe emphysema results in excision of few capillaries, and the recruitment of previously compressed, neighboring lung and its vascular bed predominates. By contrast, the higher the baseline ME fraction of lung, the greater the decrease in DLCO. This suggests that net removal of capillaries predominates in such patients.

In this study, the change in severe emphysema volume best accounted for the improvement in exercise capacity, FEV1, RV, and TLC. This suggests that the better the surgery achieves its goal of removing severe emphysema, the better the resulting functional result. Perhaps other CT approaches that incorporate regional distribution of the emphysema would better predict response and provide a map for the surgeon.

Using another quantitative CT technique, Gierada and colleagues3 found that better outcomes after LVRS were associated with a higher severe emphysema index, upper-lobe predominance, more heterogeneity, and volume of normal-attenuation lung > 1 L. This latter feature suggests that adequate amounts of normal or near-normal lung need to be present for optimal results. McKenna and associates4 report that the best outcomes were found with a bilateral heterogeneous pattern of emphysema with upper-lobe predominance on CT and perfusion scans. Weder and colleagues5 used a simplified subjective classification of CT and found that degree of heterogeneity predicted outcome, but emphasize that even patients with homogenous patterns improved after LVRS, although to a smaller extent. In another study from the same group, multiple regression analysis found that functional improvement after LVRS was most closely correlated with preoperative hyperinflation (RV/TLC) and heterogeneity measured by CT.6 Heterogeneity on CT predicted improvement better than heterogeneity on lung perfusion scans. However, the perfusion scans were still used to guide target areas for resection in those with homogenous CT patterns. The two techniques may provide complementary information, since CT is an anatomic technique and perfusion scanning is a functional technique.

Some measure of heterogeneity is likely to be important in patient selection given a model in which decompression of normal and less-diseased lung is an important mechanism for improvement. Global pulmonary function testing measurements do not capture this, and imaging techniques are well suited to this role.

It is likely that no single parameter will adequately identify the ideal candidate for LVRS, as correlation coefficients have only been in the moderate range. It appears today that degree of hyperinflation and a heterogeneous pattern of severe emphysema are the best predictors of improvement. A consensus on the best method for describing CT severity and heterogeneity has yet to emerge. Data from the NETT trial should be helpful.

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How Much Adult Asthma Can Be Attributed to Occupational Factors (Revisited)?

Occupational asthma (OA) is a disease characterized by variable airflow limitation and/or airway hyperresponsiveness due to causes and conditions...
attributable to a particular occupational environment and not to stimuli encountered outside the workplace. Two types of OA are distinguished by whether they appear after a latency period: (1) immunologic OA, which appears after a latency period that is necessary for acquiring "sensitization"; and (2) non-immunologic OA or irritant-induced asthma.4

Recently, Blanc and Toren5 published a thorough meta-analysis with the same title as this editorial (minus the "revisited," of course). They reviewed and assessed citations from 1966 to 1999 and came to the conclusion that “occupational factors are associated with about 1 in 10 cases of adult asthma, including new onset disease and reactivation of preexisting asthma.”2 Various ways can be considered to assess the frequency of OA. These include National and Regional Statistics, workforce-based studies, and community-based studies. The advantages and pitfalls of each approach have recently been presented and discussed.3

Data taken from medicolegal statistics represent only the tip of the iceberg and can vary significantly depending on the country and appropriateness of the financial compensation. Unsatisfactory compensation may dissuade workers from making claims. Means to confirm the diagnosis may also vary. In some countries, medicolegal agencies rely on tables to assess the likelihood of OA, and objective testing is not necessarily required to the same extent.4

Sentinel projects in which physicians self-declare cases were proposed in the late 1980s. Surveillance of Work-Related Occupational Respiratory Diseases5,6 in the United Kingdom and Sentinel Event Notification System for Occupational Risks7 in six US states are the most well-known examples of such projects. The data they generate are entirely based on a physician’s diagnostic likelihood (it is not because someone has asthma and is exposed at work to a known sensitizing agent that he/she is necessarily affected by OA), usually established from a clinical questionnaire, which is a sensitive but not a specific instrument.8 As such, these data are obviously open to criticism.

Population-based surveys have lately been used to assess the risk of asthma attributable to the workplace. Blanc9 found that 15% of American adult asthmatics reported that their asthma was worse at work. More recently, Kogevinas and coworkers10 estimated that the risk of asthma attributable to the workplace was 5 to 6.7% of adult asthmatics, depending on the criteria used. The attributable risk was slightly lower (3.1%) in a similar study carried out in New Zealand.11 These data mean that OA is not necessarily required to the same extent.4

Surveys have been carried out in high-risk workplace. Several cross-sectional surveys, all of which suffer from the healthy worker effect, have been carried out. Generally, the prevalence of OA is slightly <5% for high-molecular-weight agents and between 5% and 10% for low-molecular-weight agents.12 Longitudinal studies have only rarely been carried out. In one such study, we looked at nearly 800 apprentices in animal-health technology, pastry making, and dental hygiene, all of whom were exposed to high-molecular-weight agents and had been prospectively assessed.13 We found that the incidence-density of sensitization was 7.9 per 100 person-years in apprentices exposed to laboratory animals, 4.2 in those exposed to flour, and 2.5 in the group exposed to latex. More recently, we found that the incidence-density of OA (defined by significant changes in bronchial responsiveness to methacholine and skin reactivity to a program-derived allergen) in the group of animal-health apprentices was 2.7 per 100 person-years (D. Gautrin; personal communication; September 2000).

Other possibilities are to determine the proportion of asthmatic subjects seen in a general or specialized practice for whom OA can be suspected. This is the approach favored by Tarlo and coworkers in the article in this issue of CHEST (see page 1309). These authors found that out of 731 adult asthmatic subjects seen in a secondary and tertiary asthma clinic, 435 had adult-onset of asthma; of these, 310 were employed at the time of the visit. Fifty-one of the 310 subjects (16%) reported that their asthma was worse at work. The particular interest of this study lies in the fact that the authors tried to estimate the likelihood of OA in these 51 subjects by more objective evidence, though the investigational tools were clearly incomplete for many subjects. Sixteen subjects (5%) of the 310 adult-onset asthmatic subjects who were employed at the time of the visit had probable OA. Almost 50% had aggravation of underlying personal asthma, which is not OA. In the latter instance, it is highly probable that better control of the underlying asthmatic condition would have allowed these workers to continue to work. Furthermore, the estimate is based on the number of patients with a history of current work. It is known that subjects with OA are left with permanent asthma in 75% of cases even after complete removal from exposure.14 Therefore, a percentage of the asthmatic subjects included in the study by Tarlo and coworkers might have had OA due to previous and not to current exposure at work. Current asthma might have been related to a previous job.

Although there might have been a referral bias in the study by Tarlo and coworkers (physicians who referred their patients to this clinic were probably
acknowledged that this was a specialized asthma clinic with a specific interest in OA), and the diagnosis of OA was only partially based on objective testing, the finding that approximately 5% of asthmatic patients might well have OA is entirely compatible with figures derived from population-based surveys and cross-sectional surveys in high-risk workplaces. The message to be remembered, then, is that 5% of all asthmatic subjects may have their asthma caused by their workplace. They are therefore worth being investigated for this condition with objective testing.

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Deep Vein Thrombosis and Pulmonary Embolism

A Single Disease Entity With Different Risk Factors?

In recent years, deep vein thrombosis and pulmo
nary embolism, its major complication, have been increasingly considered as a single disease entity, namely venous thromboembolism. Indeed, both au
tropic and clinical studies have shown that approxi
mately 90% of pulmonary emboli arise from the deep veins of the lower limbs. Moreover, an asymp
tomatic pulmonary embolism can be found in about half the patients presenting with a symptomatic proximal deep vein thrombosis. Finally, deep vein thrombosis and pulmonary embolism share many risk factors, such as age, major surgery or trauma, cancer, immobilization, pregnancy, oral contracep
tives, and hormone replacement therapy.

In 1993, in a landmark study, Dahlbäck et al identified a functional anomaly in certain families that predisposed to deep venous thrombosis, which they named resistance to activated protein C. Shortly thereafter, it was shown that this anomaly was due to a mutation of factor V, named factor V Leiden, that reduced its normal capacity to be inactivated by activated protein C, thus creating a hemostatic im
balance in favor of thrombosis. More recently, a mutation of prothrombin, prothrombin G20210A, was also shown to be more frequent in patients with deep vein thrombosis than in the general population. Hence, it seemed logical that these inherited thrombophilic defects would also predispose to pulmo
nary embolism. Intriguingly, a study performed in consecutive nonselected patients admitted for suspected pulmonary embolism found no difference between the prevalence of factor V Leiden in pat
tients in whom pulmonary embolism was ruled in or out. This series was criticized because factor V Leiden was diagnosed by a functional test and not by DNA analysis. However, in the past few years, this finding has been repeatedly confirmed, the study by Margaglione et al, published in this issue of CHEST (see page 1405), adds to this growing body