ground. There was also an association between cigarette smoking and irregular opacities. Other factors such as bronchitis, age, and exposure to coal dust were involved in the development of irregular opacities.

Asbestosis is the classic pneumoconiosis that presents with basilar irregular opacities on the chest radiograph. Histologic studies in asbestosis reveal peribronchial, irregularly distributed fibrosis. Most of the prevalence studies of asbestosis among asbestos workers showed smokers with asbestosis had an increased frequency of basilar irregular opacities compared to non-smokers. In addition, chest radiographic evidence of basilar irregular opacities resembling those seen in asbestosis and histologic evidence of interstitial fibrosis were more frequently seen on the chest radiographs and lungs of cigarette smokers without dust exposure.

Irregular, basally distributed radiographic opacities occurred in higher prevalence among cigarette smoking granite workers exposed to low levels of silica. Before these irregular opacities can be accepted as evidence of a response to silica, correlation between these chest radiographic abnormalities, post-mortem histologic examination, and dust analysis will be necessary.

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The Optimal Treatment of Malignant Pleural Effusions
A Continuing Dilemma

Malignant pleural effusions are a common and often morbid problem in patients with advanced cancer. The optimal treatment of malignant pleural effusions remains controversial. While nonsclerosing cytotoxic intrapleural chemotherapy has occasionally been used to treat both the effusion and the underlying malignancy, the usual approach is to inject a sclerosing agent into the pleural space after draining the effusion by tube thoracostomy. Tetracycline is the most widely accepted sclerosant, but many other agents have been used, attesting to the fact that no single agent is uniformly satisfactory.

The information on pleurodesis for malignant pleural effusions is derived mainly from small retrospective series. The few reported prospective clinical trials leave a great deal to be desired in their study design. Problems with these trials include small numbers of patients; loosely defined eligibility criteria; variable criteria for assessing response; lack of central review of chest radiographs to verify response rates; lack of long-term follow-up; and lack of randomized comparison to other forms of treatment. There has also been considerable variation in the doses and the methods of administration used for sclerosing agents. By and large, published literature in this area serves more to confuse than to enlighten us.

In this issue (see page 1528), Ruckdeschel and coauthors report their experience with a prospective multi-institutional trial designed to compare bleomycin pleurodesis to tetracycline pleurodesis for the treatment of malignant pleural effusions. To be eligible for this trial, patients were required to have a cytologically positive pleural effusion or a positive pleural biopsy, could not have had previous intrapleural therapy, and had to be ECOG performance status 0-2. Concurrent radiotherapy to the chest or recent changes in systemic chemother- or hormonotherapy were not allowed. Radiographic evidence of reexpansion of the affected lung following chest tube drainage was required. Eligible patients were randomized to receive either 60 units of bleomycin or 1 g of tetracycline intrapleurally. Specific guidelines were set for the administration of these agents. Patients were classified as having recurrent disease if they had radiographic evidence of any fluid reaccumulation following complete drainage of the pleural space and reexpansion of the lung. The two patient groups were compared for the rates of recurrence at 30 and 90 days after treatment and for the time to recurrence within 90 days. Toxicity was similar between the two arms of
this study. The rate of recurrence was significantly lower and the time to recurrence significantly longer in the bleomycin arm compared to the tetracycline arm.

Patients with malignant pleural effusions pose some special problems with respect to the design of clinical trials. They have a limited life expectancy even if they have a good performance status at the time of entry into the study. As the authors point out in their discussion, about half of the patients die within three months. Thus, large numbers of patients must be entered into a study in order to have statistically adequate numbers of patients available to analyze response rates. Many of these patients require ongoing radiotherapy or systemic treatment for disease in extrathoracic sites. The numbers of patients in whom such treatment can be withheld or stabilized in order to evaluate pleurodesis as the sole variable is limited. Patients with malignant pleural effusions often have underlying pulmonary parenchymal disease, bulky pleural disease, or some degree of a "trapped" lung, which makes it difficult to interpret radiologic response after pleurodesis. Ideally, such patients should be excluded from a clinical trial, and central review of all chest radiographs should be performed by a radiologist in order to control for these variables. Unlike other clinical trials, studies of malignant pleural effusions have no standard way of measuring response. The definition of response has varied greatly in previously published studies from using no radiographic evidence of any pleural fluid reaccumulation, to attempting to quantitate the amount of pleural fluid seen on chest radiograph as a partial or a complete response, to simply recording whether patients redeveloped symptoms.\(^2\)\(^{-11}\) The latter is an unacceptable method of assessment in a clinical trial, particularly in patients who have many other causes of dyspnea. Unfortunately, the issue of how best to define response remains unsettled. Finally, since the management of malignant pleural effusions is primarily palliative, clinical trials should carefully examine the toxicity and cost of treatment and the need for retreatment in patients who have a recurrence of disease. Ruckdeschel and coauthors did not include central radiology review and did not examine the costs of treatment or the need for retreatment. They have clearly tried, however, to select a homogeneous group of patients. They have also set clear-cut eligibility and treatment guidelines and have chosen the simplest and most reproducible measurement of recurrence.

In spite of some flaws in study design, this trial represents an important effort to evaluate the management of a major clinical problem in an organized and objective manner. This approach has been deplorably infrequent in the past. Treatment for malignant pleural effusions remains suboptimal, with a 40 per-cent recurrence rate in the better treatment arm of this trial. Other methods of managing this problem should be evaluated in the future, using guidelines similar to those set forth in this study.

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A Team Approach to Nicotine Dependency Treatment

Smokers who continue to smoke in the presence of disease meet at least one of the criteria for nicotine dependency. The Diagnostic and Statistical Manual of Mental Disorders, revised 3rd edition (DSM-111-R), published by the American Psychiatric Association, lists nicotine dependence under psychoactive substance use disorders. The diagnostic code for nicotine dependence is 305.10. Health professionals should become aware of the diagnostic criteria listed on pages 167 and 168 of the manual. Smokers who meet the DSM-III criteria will answer "yes" to at least three of the following:
1. Substance often taken in larger amounts over a longer period of time than person intended.
2. One or more unsuccessful efforts to cut down on or to quit smoking.

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