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SECTION 3
PLEURAL EFFUSIONS

Exudative pleural effusions etiologically related to prior asbestos exposure have been described in recent years. Assessment for an effusion is now part of the ILO U/C radiographic work chart (Chapter 3). Pleural effusions related to asbestos exposure may be secondary to bronchogenic carcinoma, mesothelioma, cor pulmonale due to pulmonary fibrosis, or so-called benign asbestos effusion.

This additional entity, "benign asbestos effusion," has been described by many authors.[1–3] The criteria for diagnosis are prior history of asbestos exposure, absence of any other predisposing cause for the effusion, and spontaneous remission of the effusion. Excluded are those patients with an asbestos exposure history and carcinoma, mesothelioma, or cor pulmonale due to severe pulmonary fibrosis or in whom some other identifiable cause such as lymphoma is detectable. Acceptance of the entity of benign asbestos effusion is widespread, thus Becklake[4] writes, "The justification for this diagnosis increases, and asbestos exposure can reasonably be added to the long list of causes of benign *recurrent* pleural effusion." Fletcher and Edge[5] state, "The only occasion when benign asbestos pleurisy with effusion can be diagnosed with confidence is when a chronic effusion is persistently negative for tuberculosis on culture, when no other cause can be found, and where the condition spontaneously improves."

In the author's opinion, the diagnosis of benign asbestos effusion is fraught with hazard. It cannot be made without a long-term follow-up to ensure that spontaneous complete resolution of a single or multiple episode of pleurisy has occurred. Even in such cases, an occult cause such as thromboembolic disease may be responsible. More worrisome is that an effusion may be present for months or years, culminating in a diagnosis of mesothelioma. In addition, the pleural cavity in health contains a small amount of pleural fluid, with a protein content similar to that of interstitial fluid. The amount is sufficiently great that it may be demonstrated by lateral decubiti radiographs in 4 percent of healthy persons; this technique will detect amounts of fluid greater than 3–5 ml.[6]

CLINICAL FEATURES

Bearing in mind the author's skepticism expressed above, the following reflects current published descriptions mentioned in the references.

The effusion may be unilateral, bilateral, or recurrent. Regression of an

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Fig. 2-43. *Shipyard worker who complained of dull chest pain. Right decubitus showing pleural effusion; no plaques are visible.*

effusion on one side may be followed by a contralateral occurrence. Up to separate episodes in 1 patient are recorded. The effusion may recur over years without evidence of mesothelioma development. In others, a mesothelioma may be accompanied by a pleural effusion on the contralateral side, apparently benign in that the radiographic appearance on that side may be normal. If the effusion is prolonged, the prognosis with regard to eventual development of mesothelioma must be guarded. The onset is usually insidious but occasionally acute. By definition the effusion must resolve without specific treatment. The effusions are small and usually need lateral decubiti radiographs for adequate visualization (see Figs. 2-43 and 2-44). Pleuritic chest pain is present in patients with acute onset, whereas only a dull ache may be present in patients with insidious effusions, and some patients are asymptomatic. Physical signs vary with the amount of fluid, and in acute cases there may be fever, usually low grade. Digital clubbing may be present in prolonged effusions, especially if there is much accompanying parenchymal fibrosis. Dry crepitations due to associated interstitial fibrosis may be heard.

Over 500 benign asbestos effusions have been recorded as of 1977. Gaensler and Kaplan[1] report 21 percent of their asbestos patients to have had a pleural effusion, and in their series of 91 pleural effusions of various etiologies, 13 percent were believed related to asbestos exposure as compared with the following:

Congestive failure	
Malignancy	
Infection	
Collagen disease	
Pulmonary infarct	
Chronic interstitial pneumonia	



Fig. 2-44. *Left decubitus view in steep Trendelenburg and expiration shows mobile pleural effusion, fibrotic changes, and panlobular emphysema in left lower lobe of ex-shipyard worker. Again, no plaques are seen. The white streaks are artifacts.*

Laennec's cirrhosis	2%
Undetermined	9%

In their series, a single episode of effusion was seen in 6 patients, two to four episodes in 5 patients, and a persistent effusion in 1 patient. Unlike Gaensler and Kaplan, the author subscribes to the opinions of Fletcher, Edge, and Becklake that a definition of benign asbestos pleural effusion must include complete resolution. In Gaensler and Kaplan's series the effusion was unilateral in 3 patients and bilateral (simultaneously or in sequence) in 9. The interval between the last asbestos exposure and the development of pleurisy has varied from a few months to 31 years,[2] while duration of exposure has been from 3 to 38 years.[1]

When the effusion has an acute onset, it may be accompanied by fever, leukocytosis, fast sedimentation rate, and general systemic symptoms. A few may show a positive latex agglutination test for rheumatoid factor; circulating antinuclear antibodies are usually absent. Many other diseases may thus be simulated. Analysis of the exudate is of limited value (see below); if the effusion is prolonged, a limited thoracotomy should be performed to examine pleural and parenchymal biopsy material for asbestos fibers and fragments using specialized techniques and, more important, to exclude other causes by appropriate histological and microbiological examinations.

PLEURAL FLUID ANALYSIS

Asbestos related pleural fluid is an exudate with a protein content v... from 3.4 to 7.5 gm/100 ml.[3] Red blood cells may be absent, but counts ... range of 5,000 to 50,000 cells per cubic millimeter are usually present ... inflammatory cell content: polymorphonuclear leukocytes, monocytes ... phocytes, and eosinophils are variable; eosinophils in some patient ... lymphocytes in others are disproportionately frequent. Asbestos fibers or ... ments have not been reported in the exudate.

Pleural exudates will usually have a pleural fluid-to-serum protein ra... greater than 0.5, a pleural fluid LDH (lactic dehydrogenase) of greater ... 200, and a pleural fluid-to-serum LDH ratio of greater than 0.6. Simultan... use of both pleural fluid protein and LDH levels better differentiates exu... from transudates than do the previously used pleural protein level of 3.0 ... 100 ml.[7] Exhibitive cytology of the exudate is necessary to exclude an un... lying malignancy, especially mesothelioma and bronchogenic carcinoma ... those with a history of asbestos exposure. The cytological identification ... benign and malignant mesothelial cells and their differentiation from cells s... from a carcinoma or from a mesothelial reaction are difficult. It is especi... important to note that atypical macrophagelike cells, similar to cells found in proven mesothelioma, may be found. In 2 of 6 patients who initially were thought to have benign pleural effusions and in whom such cells were found, the eventual clinical course was that of mesothelioma.[8] A progression ... many years of apparently benign asbestos effusion to mesothelioma has been noted by others.[9, 11] To repeat, an effusion in a person with prior asbestos exposure that does not remit cannot be considered as a benign asbestos effusion, and even then, some other cause may be responsible (see Fig. 2-...

PATHOLOGY

The underlying lung usually shows some degree of fibrosis; the visceral pleura is thickened (see Fig. 2-46); the parietal pleural usually has some degree of lamellar thickening, but localized plaque formation large enough to be apparent radiographically is usually absent.

The visceral pleura may be as thick as 15 mm and is white in appearance. There is gross hyaline connective tissue proliferation, with well-formed collagen fibers arranged in bundles and an occasional cleft lined by flattened cells. If papillary formation is present, the possibility of a developing mesothelioma cannot be discounted. Cellular infiltration is usually slight, and if great, other etiologies need careful consideration.[13] Blood vessels are usually scanty ...



Fig. 2-45. *Left pleural effusion and plaques in an ex-shipyard worker. A small mesothelioma was present on the right. Because of the small size of the mesothelioma, it was thought unlikely to have produced mediastinal lymphatic obstruction, and the etiology of the left effusion was therefore in doubt. The left pleural aspirate did not contain any cells.*



Fig. 2-46. *Lateral view of chest of an ex-shipyard worker. Oblique arrows indicate thickening of visceral interlobar fissure; horizontal arrows point to anterior mediastinal parietal pleural calcification.*

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occasionally are frequent and help explain the sanguineous nature of some effusions.

The parietal pleura may show a diffuse thickening, but localized pl[aque] formation on the side of the effusion occurs in a minority of cases. [Cal]cification of plaques is rare. Parietal pleural plaques, calcified or [non]-calcified, may be present on the unInvolved side.

The underlying lung is invariably abnormal. There are varying degrees of pulmonary fibrosis. Minimal involvement may entail pleural thickening and edema of interlobular septa and extension of pleural fibrosis into the sep[ta]; more severe involvement is characterized by increased collagen formation in the interstitium of the lung and obliteration of alveoli and bronchioli by fibrosis. A fuller account is given in Chapter 2, Section 2 on pulmonary fibrosis.

Although asbestos fibers and particles are not apparent in the exudate, they may be detected in the affected pleura and lung. Specialized techniques may be needed.

All the main types of asbestos fibers have been associated with benign asbestos effusion.[10-12,16] The author has not read of pleural effusion developing in experimental animals subjected to asbestos inhalation.

RADIOLOGY

In the identification of an asbestos-related exudate, decubiti views in *expiration, with a Trendelenburg tilt, are frequently essential, since volumes* of fluid are usually small. As mentioned previously, small amounts of pleural fluid may be demonstrated in normal persons with this technique.[6] When the exudate is recurrent, a prior episode may have resulted in obliteration of costophrenic angle and subsequent effusions may not be clearly apparent initially. Lamellar diffuse thickening of the parietal or visceral pleura may simulate an effusion, but in these instances the costophrenic angles are usually not obliterated. Thickening of interlobar fissures may be a sequel of a previous effusion or may be due to asbestos exposure without an effusion. Interlobar visceral pleural thickening due to "dry" asbestos pleurisy without a current effusion is most common in the minor fissures and is always associated with parietal pleural changes.[17]

The "biological markers" of calcified and noncalcified parietal pleural plaques should be sought. For unknown reasons, calcification is extremely rare on the side of an asbestos exudate. Noncalcified plaques may be seen although their frequency is stated as less than 50 percent in most radiologic series of asbestos exudates; this is probably an understatement related to assiduity of search, lack of employment of oblique projections, tomograph[y]

and CT. The differentiation of lamellar diffuse parietal pleural thickening [from] visceral pleural thickening (interlobar fissures excluded) is not possible radiographically. *Parenchymal pulmonary fibrosis should be sought*; it may be evident on a chest radiograph except in the more severe forms or by use of oblique views. Ultrasound techniques may be helpful in locating optimal sites for diagnostic thoracentesis, since exudate volumes are usually small.[18] Thoracentesis under fluoroscopic control has been recommended when small volumes of fluid are aspirated.[19]

In addition to excluding causes of effusion unrelated to asbestos exposure, *a search must be made for bronchogenic carcinoma and mesothelioma*. In bronchogenic carcinoma, mediastinal node involvement is statistically more important than pleural involvement in the formation of an effusion. Fifty-five degree oblique tomography of the hila is useful for this assessment and is, in the author's opinion, often superior to frontal or lateral tomography although assessment of the left hilus and adjacent mediastinum is more difficult than that of the right.

Mesothelioma may simulate, be accompanied by, or be preceded by pleural effusion for many months. In addition, mesothelioma may produce bilateral effusions by involvement of the superior vena cava, mediastinal nodes, thoracic duct, and pericardium. If the azygous vein is involved, superior caval involvement will raise parietal pleural capillary pressure and so increase filtration from parietal pleura, but there is usually an accompanying element of lymphatic obstruction which, by reducing fluid and protein absorption, is of greater significance.[22] Pericardial involvement and subsequent tamponade or restrictive pericardial disease will have a similar hemodynamic effect in addition to the effect of lymphatic obstruction.

At the risk of being repetitious, the author believes that whenever the diagnosis of a "benign asbestos pleural effusion" is made, arrangements for repeated later clinical and radiographic assessment must be made to ensure that patients with mesothelioma are not missed.

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SECTION 4
PLEURAL AND PERITONEAL MESOTHELIOMATA

Mesothelial tissue, which lines the pleural, pericardial, and peritoneal spaces, may be the site of mesothelioma formation. These tumors may be benign or malignant. Benign pleural tumors include lipoma, hemangioma, benign mesothelioma, and simple cyst. Malignant primary tumors of mesothelium include malignant mesothelioma and sarcoma.

EPIDEMIOLOGY

Wagner et al.[1] in 1960 suggested that mesotheliomata were related to asbestos exposure. This initial observation has been subsequently confirmed by many sources, including surveys of workers with known occupational exposure in mining, milling, shipbuilding and repairing, insulation, cement, and textile industries, as well as those living near these industries who are not occupationally exposed but who are environmentally at risk.

The incidence of mesothelioma in the general population, using evidence from autopsy series,[2] is about 2 to 3 per million per year. An appreciation of the incidence of mesothelioma in asbestos workers is difficult to obtain, since the population at risk is undefined. Some 3.5 to 4.0 million men and women worked at one time or another in the U.S. shipyards during World War II,[3] and it is impossible, even in a developed country, to investigate such numbers. The problem in less developed areas is greater. The South African Asbestos Reference Panel totals 375 cases of mesothelioma; there is an annual work force of about 20,000 persons in the asbestos mines of South Africa, but many of these are migrant workers in the tribal tribute system, and so the total population at risk cannot be determined.[4]

The recorded incidence based on mortality studies of those known to have been engaged in asbestos industries varies. In Finnish anthophyllite mines and adjacent areas, only one death from mesothelioma has been recorded. In the chrysotile mills of northern Italy, no deaths from mesothelioma are known, while in Quebec similar workers have a 0.2 percent mesothelioma-related death rate. The Soviet Union, which produces over 2 million tons of chrysotile per year, has not released data on mortality due to mesothelioma. Selikoff et al. have surveyed the mesothelioma risk in 17,800 asbestos insulation workers in

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