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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

the United States and Canada over the period 1967–1971.[5,44] They noted 21 pleural and 26 peritoneal mesotheliomas. This reflects approximately five times the expected incidence when compared with age-matched co- ols. These people have been exposed to chrysotile and amosite but not to cr- ocid- ite. In the same survey a group of 337 amosite insulation workers h- 16 peritoneal and 4 pleural mesotheliomas. Most of the above employees were men. In a study of a factory with a large female work force employ- in spinning (crocidolite), weaving and mattress making (chrysotile and am- te gas mask filter assembly (crocidolite and amosite), brake lining (chrysotile and rubber jointing manufacture (chrysotile and crocidolite), of those w- ers followed for more than 20 years, 1.5 percent of females and 1 percent of the males died of mesothelioma.[6]

The majority of mesotheliomata are asbestos-related; in a few, no as- stos exposure can be discovered. A familial incidence has been describ- In Australia, it is estimated that only 16 percent of mesothelioma patients we- had no occupational exposure.[7] The end occupation can be misle- ng however; two-thirds of the Australian mesothelioma patients developed m- so- thelioma while they were in an unrelated occupation, although they did have prior occupational exposure to asbestos, usually in the form of crocid- lite. Australian crocidolite has very fine fibers that can penetrate pleura the- ore easily and so induce mesothelioma. Matching the Australian experienc- 15 percent of U.K. mesothelioma patients,[8] 16 percent of the South A- an patients,[9] and 11 percent of the Mayo Clinic series patients[10] have ha- no known asbestos exposure. Higher proportions of mesothelioma patients with no detectable history of asbestos exposure are recorded by Elmes, 33 perc- it," and Oels, 62 percent,[12] but occupational histories were incomplete. A- the other end of the spectrum, only 6 percent of the males and none of the fe- ales in a U.S. series developed mesotheliomata that were apparently unrelat- to asbestos exposure.[13]

An unusual group of mesothelioma patients are those who have had household contact with asbestos workers. In a group of 326 persons who lived in the same house as amosite asbestos workers, 4 have died from mesothelioma.[14]

The incidence of mesothelioma is rising rapidly, having increased about sevenfold in the last decade in the United Kingdom. More detailed mo- dity reporting, the setting up of mesothelioma registers, and a greater awaren- on the part of internists, radiologists, and pathologists, especially in urba- and shipbuilding areas, play a part in this increase, but much must be blam- on inadequate dust control in the years leading up to and including World I- I II and shortly after and the belated recognition in the 1960s of the asso- on between mesothelioma induction and asbestos. Because of the long- ent

period between first exposure and development of mesothelioma, averaging 3 to 40 years in most series, and the fact that adequate dust control has only bee achieved in the late 1960s and 1970s, the incidence of mesothelioma expected to be high until the turn of the century. The mesothelioma disea wrought by naval shipbuilding in World War II is being observed by the curre generation of physicians, much as the disease related to World War I battlesh construction was seen by previous generations, although the situation we unappreciated. The next generation of physicians will undoubtedly see mes thelioma related to naval construction during the "cold war" period, althou synthetic substitutes for asbestos are being used increasingly.

FACTORS AFFECTING THE PATHOGENESIS OF MESOTHELIOMA

The pattern of response to most toxic agents varies in large populatio samples and in general follows an S-shaped curve, but very low doses of a tox substance may preferentially affect susceptible persons.[15] Caplan's syndrom the association of pulmonary nodules and raised titers of circulating rheuma toid factor in coal miners, and drug toxicities associated with the lack of th enzyme glucose-6-phosphate dehydrogenase are two well-known example Although there are conflicting accounts of the association between raised tite of circulating antibodies (see Chapter 1) and pleural plaques, there are n published data on the relationship between pleural plaques, circulating ant bodies, and the later development of mesothelioma.

Effect of Dose

In a study of U.K. asbestos textile workers, Newhouse has shown a dose response relationship to length of exposure and degree of exposure to dust t mortality due to mesothelioma (and lung cancer).[16] The incidence of mesoth lioma more than doubles if exposure is greater than 2 years; for short exposure of less than 2 years, the ratio is about three times greater for heavy as compare to light exposure. Pipe laggers in the textile factory studied had much high rates than did asbestos textile production workers.

A dose–response relationship between amphibole asbestos exposure an induction of mesothelioma is suggested[17a,17b] by an electron microscopy stud of lung parenchyma from mesothelioma specimens compared with randor autopsy controls. Of the mesothelioma specimens, over 50 percent had sufficient amount of asbestos fibers to indicate an intermediate, short-, or lon term exposure, while only 10 percent of the controls had such an intensity

fibers. A dose–response relationship for chrysotile fibers is harder to [illegible] since these fibers fragment into smaller particles, and their detection in t[illegible] is more difficult.

Cocarcinogens are not known to be relevant in the induction of mes[illegible]oma. Although asbestos is highly adsorbent, there is no evidence th[illegible] products of combustion from smoking are additive to the risk of mesoth[illegible] formation, unlike the increased risk of bronchogenic carcinoma. Sim[illegible] trace metals in the fibers, organic substances in asbestos (paraffinlike hy[illegible] polycyclic hydrocarbons) and antioxidants incorporated in polyethylene [illegible] currently used, or oils in jute bags previously used for asbestos packin[illegible] transport are not cocarcinogenic for mesothelioma induction.[18]

Effect of Fiber Type

Fiber type is associated with a potential for mesothelioma induction[illegible] danger is greatest with crocidolite, minimal with amosite but risk is sli[illegible] greater for amosite than chrysotile, and virtually zero for anthophyllite. [illegible] main variable is fiber diameter. Of the amphiboles, this diameter is smal[illegible] with crocidolite, intermediate with amosite, and greatest for anthophyllite. [illegible] greater incidence of mesothelioma with fine-diameter fibers such as crocid[illegible] is related to less deposition in the proximal airways and easier penetrabilit[illegible] the pleura and peritoneum. The fiber shape is important; although the [illegible] curly chrysotile fiber would not be expected to reach the pleura easily, [illegible] fragmented, the short chrysotile fibers have a short arc and behave ae[illegible] dynamically like the straight amphiboles. Current belief is that asbestos fib[illegible] up to 10 μm in length and less than about 1 μm in diameter may ca[illegible] mesothelioma. A fuller account of the subject relating the problem to clin[illegible] practice is given in Chapters 1 and 2, Section 2.

PATHOLOGY AND NATURAL HISTORY

Site

Mesothelioma may arise from any mesothelial surface. Origin from p[illegible] cardium is extremely rare and denied by some. Determining the point of ori[illegible] when both the pericardium and the pleura are involved is difficult. M[illegible] thoracic mesotheliomata arise from the pleura. Figure 2-47 illustrates a tu[illegible] that probably first arose in the pericardium or adjacent pleura. No cases [illegible] reported of simultaneous origin in both pleural and peritoneal cavities. In l[illegible] phases of their natural history, a mesothelioma arising in one cavity, eith[illegible] pleural or peritoneal, may invade the diaphragm to involve the other cav[illegible]

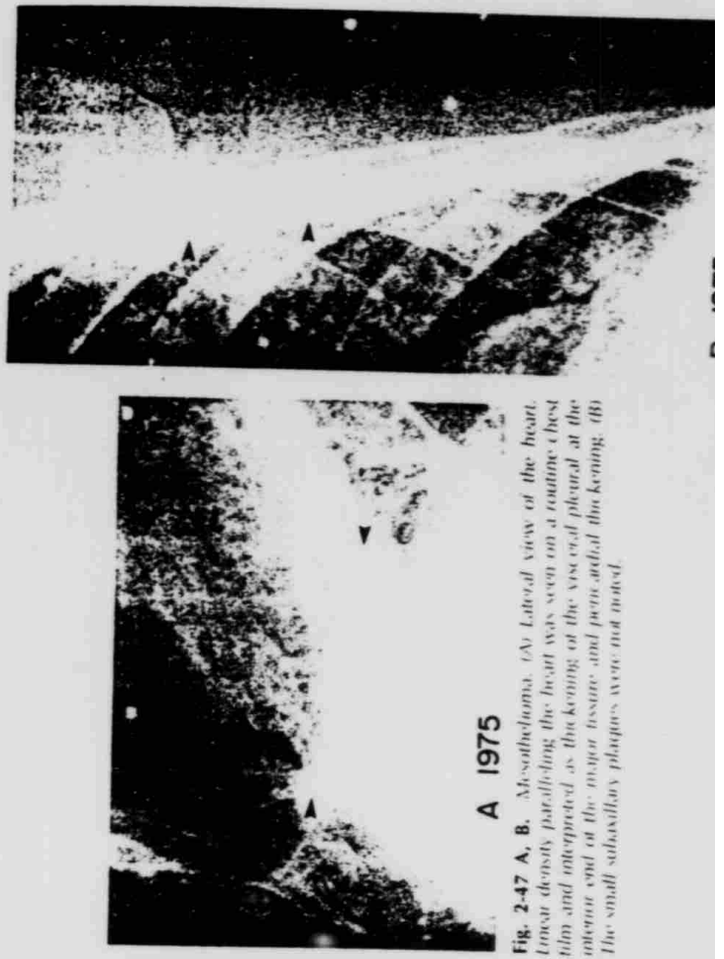


Fig. 2-47 A, B. *Mesothelioma. (A) Lateral view of the heart. Linear density paralleling the heart was seen on a routine chest film and interpreted as thickening of the visceral pleural at the anterior end of the major tissue and pericardial thickening. (B) The small subaxillary plaques were not noted.*

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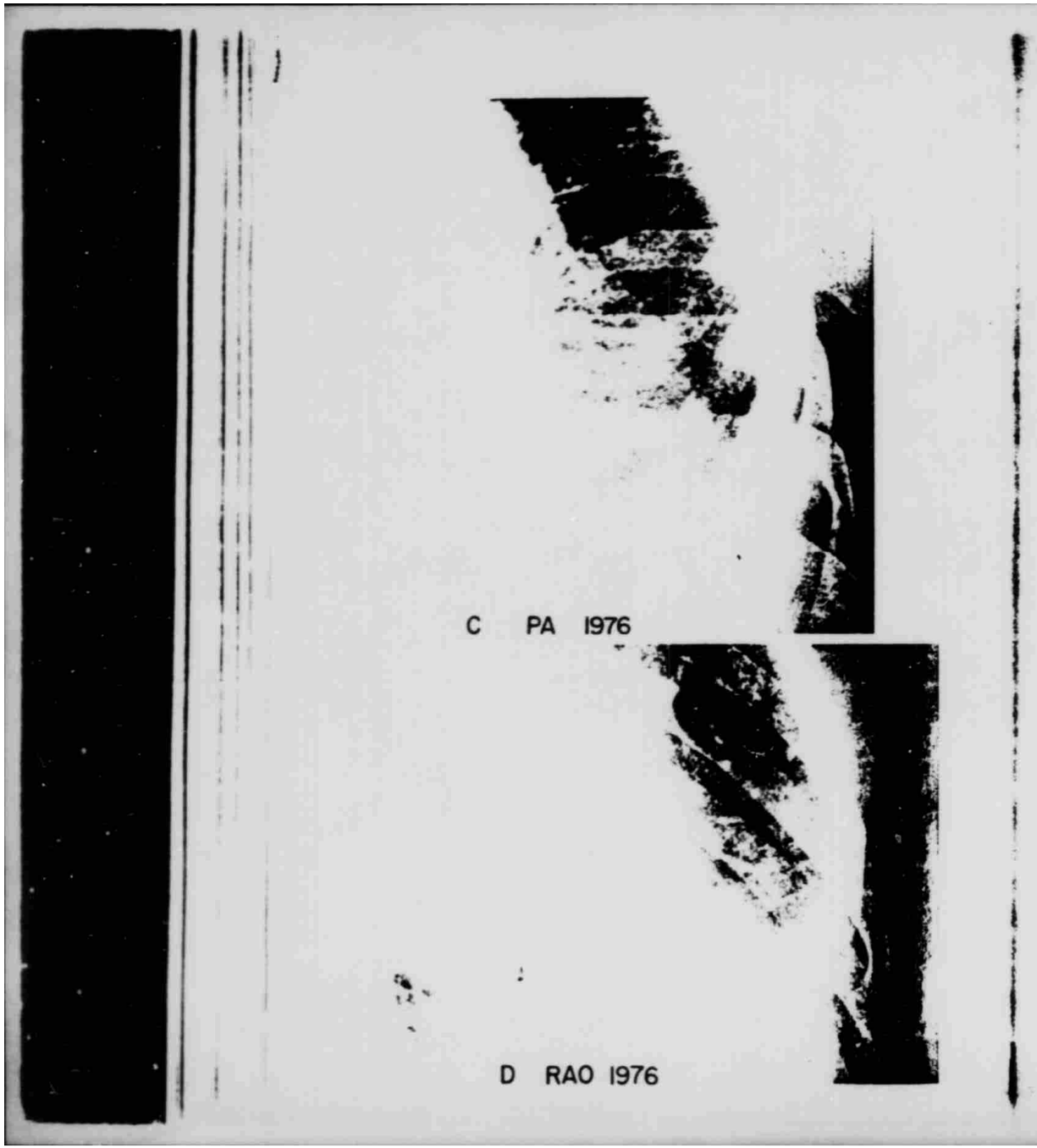


Table 2-6
Ratio of Pleural to Peritoneal Mesotheliomata

Author	Patient Sex	Ratio
Borow[10]	M and F	2:1
Greenberg[6]	M and F	26:1
Edge[19]	M	28:1
Harris[20]	M	54:1
Milne[7]	M	10:1
Elmes[40]	M and F	7:1

(Fig. 2-48). The difficulty in distinguishing a mesothelioma arising in the fem pelvis from papillary adenocarcinoma of the ovary is described on page 2 The ratio of pleural to peritoneal mesothelioma is shown in Table 2-6. In oth earlier series which included women workers, in whom there is alwavs problem of separating pelvic mesothelioma from ovarian cancer, a high proportion of peritoneal mesothelioma is recorded.[5,10,16] Borow reported on group of patients, 11 percent of whom were females, and found a ratio pleural to peritoneal mesothelioma of 2:1.[10] Most mesothelioma patients males, which is not surprising because the type of work utilizing asbestos usually physically arduous. When this is not a limiting factor, as in gas ma filter assembly using crocidolite, female mortality is high.

Pleural Mesothelioma

The tumor gradually encases part or all of the lung as a thick, yellow gray mass involving both parietal and visceral pleurae. An attempt to strip tumor from underlying parenchyma leads to tearing of the lung (Fig. 2-49 decortication is attempted during thoracotomy, air leaks may ensue. In u involved areas, parietal, pleural, and diaphragmatic plaques may be reco nized (Fig. 2-50). Their reported frequency is probably related to assiduity search (see Table 2-7).

Most authors state that mesotheliomata do not arise through malign degeneration of a pleural plaque, although there has been a report of malignant mesothelioma arising by a stalk from a pleural plaque. This is m likely coincidental.[21]

Fig. 2-47 C, D. *PA and RAO views 1 year later. The patient had severe chest p nonpleuritic in nature. Preliminary diagnosis was dissecting aneurysm of thoracic a with hemorrhagic effusion. The pleural "peel" was misinterpreted as hemorrha effusion and the widening of the aortic shadow as dissection. The "peel" did not la out on decubitus views as is usual with effusion. Pain due to mesothelioma is typic nonpleuritic in nature.*

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Fig. 2-48. *Pleural mesothelioma invading the abdomen and obstructing the small bowel. A: The erect film of the abdomen shows moderately dilated loops of small bowel in the upper abdomen and a paucity of gas in the left side of the abdomen and pelvis. A mesothelioma arising in the left lung had penetrated the diaphragm and spread along the peritoneal surfaces of the small and large bowel as well as the parietal peritoneum. Most of the tumor mass was in the left side of the abdomen. B: Barium meal study is present in the left ileum above the acetabulum (compare left and right acetabular surfaces). A post myelogram was done for suspected metastases to the midthoracic vertebrae. B and C: Barium examination shows displacement of transverse colon and displacement of the ligament of Treitz. The proximal small bowel loops are dilated from incomplete obstruction; they are slightly separated because of involvement of their peritoneal surfaces and they are displaced from the left side of the abdomen due to the bulk of the tumor mass lies.*

Table 2-7
Radiographically Visible Pleural Plaques Accompanying Mesothelioma

Author	Percent
Elmes[40]	18%
Harris[20]	34%
Edge[19]	86%

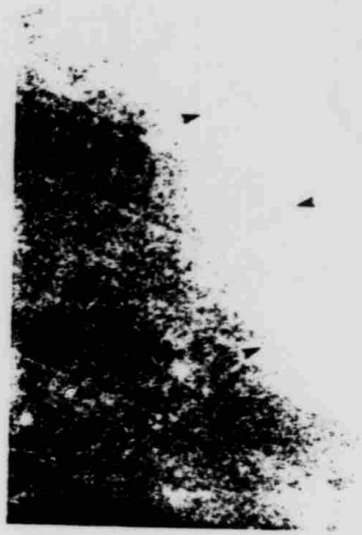


Fig. 2-49. *Mesothelioma. Iatrogenic pneumothorax (arrows) outlines irregularly thickened visceral pleura. Air escaped from the lung when decortication was attempted during thoracotomy for tissue diagnosis. If mesothelioma is suspected, decortication should not be attempted. It may lead to a troublesome pneumothorax.*

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Fig. 2-50. Mesothelioma present in contralateral pleura. There are noncalcified lateral pleural plaques (horizontal arrow) and calcified diaphragmatic plaques (vertical arrow). A search for these biological markers should be made whenever mesothelioma is a diagnostic possibility. Note the irregular destruction of the outer end of the clavicle from metastatic disease.

Since most pleural plaques are never visualized during life, there is insufficient evidence to assume that mesotheliomata do not originate from malignant degeneration of a pleural plaque. In view of the large numbers of patients with pleural plaques and the low incidence of mesothelioma, however, the possibility of malignant degeneration must be slight.

Besides spreading to encase part or all of the lung, the tumor reaches into the interlobar fissures and lung septae and invades the pericardium. Deep to the tumor there is usually some parenchymal interstitial fibrosis, even though this may not be evident radiographically. Once through the pericardium, further penetration usually involves the atria rather than the ventricles, but involvement of the interventricular septum has been known. Involvement of the pericardium may produce constrictive pericarditis with an effusion demonstrable by echocardiography (Fig. 2-51). The cardiac chambers may be compressed. If the pericardial effusion develops rapidly, cardiac tamponade may ensue. Diffuse mediastinal spread may involve the anterior, middle, and posterior mediastinal compartments. The aorta and esophagus may be encased. Primary esophageal cancer is more common in asbestos workers than in the general population, but differentiation from secondary spread of a mesothelioma is usually obvious. Spread may involve the axillary nerves or the lowest part of the brachial plexus and sympathetic ganglia and produce a Pancoast and Hornerlike syndrome. Posterior mediastinal spread may reduce the spinal cord's blood supply and result in paraplegia,[11] or this may result from

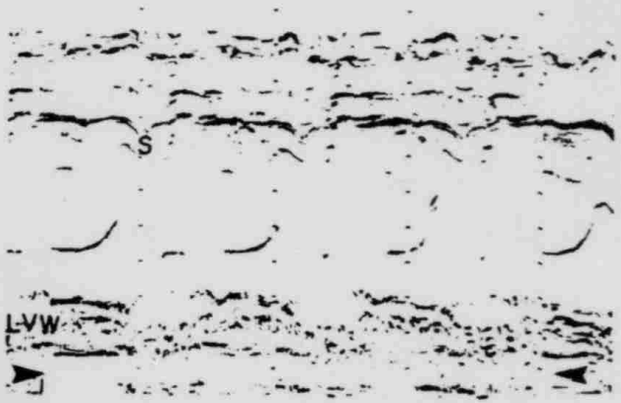


Fig. 2-51. Mesothelioma. Echocardiogram of a patient with an extensive mesothelioma encasing the pericardium. There was a diminished cardiac output. The small anterior and posterior (arrow) pericardial effusions were believed insufficient to produce cardiac tamponade as an explanation of the low cardiac output. Pericardial restrictions due to malignant invasion was postulated. The septum (s) moves paradoxically, which is seen with large effusion, and the posterior left ventricular wall (LVW) contraction pattern is abnormal. It begins with a slow and sustained contraction, but there is an abrupt relaxation at the end. The catheterization data showed elevated pressures in the right atrium (17.5 mmHg mean 12), the right ventricle, (41/10 mmHg), and the pulmonary artery (27/12 mmHg), while the pulmonary capillary wedge pressure was 12 mmHg. Two Cope needle biopsies of the pleura were productive of fibrous tissue only; a subsequent "mini-thoracotomy" and open biopsy indicated hemothorax and pleural fibrosis. A further definitive thoracotomy was needed to provide sufficient histological material for the diagnosis of mesothelioma. This sequence of events underlines the difficulty of diagnosis of mesothelioma based on small amounts of tissue obtained by biopsy techniques, whether open or closed. (Courtesy of N. Schiller, M.D., U.C.S.F.

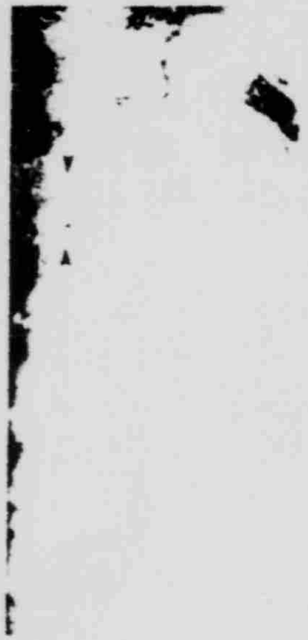


Fig. 2-52. *Mesothelioma metastatic to [illegible] vertebral body and encasing the left side of the mediastinum. A myelogram did not show a macroscopic extradural mass. The paraparesis was believed to result from [illegible] basis of the spinal cord vessels by microscopic deposits.*

direct or bloodborne [illegible] vertebral bodies with subsequent cord compression (Fig. 2-52).

Mediastinal [illegible] lymph nodes may be involved by encasement or direct spread. Axillary, cervical, and abdominal nodes are involved less frequently. In general, the sarcomatous fibrous type of mesothelioma involves the regional lymph nodes by encasement rather than by lymphatic invasion. A hilar mass is not [illegible] complicated asbestosis (pleural plaques, benign asbestos pleurisy, benign fibrosis, and probably visceral pleural thickening, unlike some [illegible] of pneumoconiosis where hilar enlargement is constituent of the [illegible] cated disease. Despite about 50 percent incidence of hilar involvement [illegible] mesothelioma, its detection by x-ray is difficult because of mediastinal pleural [illegible] vement by tumor and associated pleural thickening and fluid.

Direct spread [illegible] superior and inferior venae cavae may occur, impeding the entry [illegible] into the right atrium. Right ventricular dilation may

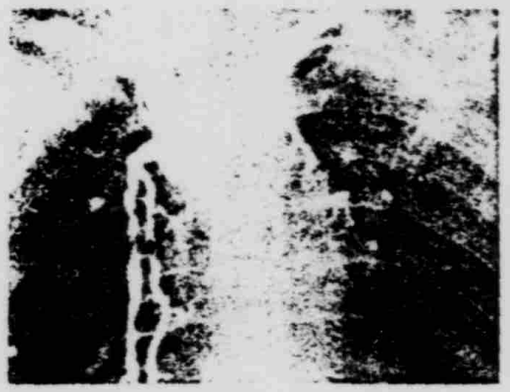


Fig. 2-53. *Localized mesothelioma arising in the superior mediastinum and causing the superior vena cava syndrome demonstrated by venography. (Courtesy of D. E. Sanders, M.D., and the editors of the Journal of the Canadian Association of Radiologists.)*

occur. Lower limb edema and ascites may result from inferior vena cava compression; rarely does a full-blown superior vena cava syndrome of facial, neck, and upper thoracic congestion with collateral vein formation develop (Fig. 2-53).

Direct spread through the chest wall occurs. In individual cases this has been preceded by percutaneous biopsy, thoracotomy, or deep x-ray or gamma ray treatment, but a causal effect is uncertain.[11] Destruction of adjacent ribs may occur. The mass may extend into the supraclavicular fossa.

Direct spread through the diaphragm and the aortic and esophageal hiatuses occurs as the disease advances but may be a relatively early complication with an appropriately sited tumor. Organs in the peritoneal cavity become encased with tumor, so that a thick peel may cover liver and spleen. Infiltration of the omentum and the visceral and parietal peritoneums occurs, so that, similar to the displacement of the esophagus that occurs in the chest, the stomach, duodenum, and small and large bowel may be displaced, adherent to each other or to the abdominal wall. Direct extension through the wall of the gastrointestinal tract develops but is usually minimal because death ensues. Spread is occasionally confined to one side of the peritoneal cavity. Direct spread into the retroperitoneal space is limited but may be sufficient to induce a severe desmoplastic reaction that may obstruct the ureters. The lumbar spine and lumbosacral plexus may be infiltrated.

There is a varying degree of pleural effusion accompanying thoracic

mesothelioma. The effusion is usually large and bloody and reaccumulates rapidly. However, in Elmes' series, 43 of 89 patients had serous effusion.[2] Loculation of fluid may result in only a small pleural aspirate. A clue may be the thickness and relative impenetrability of the involved pleura by the aspirating needle. About one-third of the patients will have a lobulated soft tissue mass and no effusion. Others may have an apparently "benign" asbestos pleural effusion for many months before a mesothelioma is discovered. A contralateral apparently benign pleural effusion may occasionally accompany a mesothelioma. In early cases, it may be possible to identify discrete nodules of mesothelioma arising from both the visceral and parietal pleurae. It is conjectural as to whether it is true early seeding or a multifocal origin.

By the time of death, as many as 50 percent of patients have distant bloodborne metastases. The sarcomatous type of mesothelioma is the most prone to such spread. The contralateral lung and occasionally the ipsilateral one, will show multiple nodules, some of which are necrotic. The liver, spleen, kidneys, adrenals, thyroid, axial and appendicular skeleton, calvarium, and meninges may be involved.

Peritoneal Mesothelioma

A mesothelioma arising in the peritoneal cavity usually appears as multiple coalescing nodules, differing from pleural mesothelioma, which usually has a more diffused sheetlike appearance. The coalescence produces large tumor masses which obliterate free spaces in the coelomic cavity, making it difficult to assign a point of origin, especially in the female pelvis where differentiation from a primary ovarian cancer is often difficult. The omentum is infiltrated early in the course of the disease and appears thickened and contracted before there is diffuse involvement of the peritoneum. As with pleural mesothelioma, the tumor tends to extend over organ surfaces, compressing them, but with only minimal invasion through their walls. The tumor mass has a glistening white color, and its cut surface has a mucinous appearance.[10] There is a varying amount of clear or bloody ascitic fluid. Bowel loops may be matted together and fixed throughout the abdomen. In other cases, the tumor may be fixed in one area, presumably at the site of origin of the tumor, and displaced by the advancing tumor mass in others. Direct spread may occur upwards through the diaphragm, its muscle being heavily infiltrated with tumor, or through the diaphragmatic hiatuses in advanced cases to infiltrate the pleura. Unlike most intra-abdominal neoplasms, there is a relative paucity of regional lymph node involvement. Bloodborne spread, especially to the liver, ensues eventually.

MICROSCOPIC FEATURES

For many years, mainly as a result of the efforts of Willis, the identity of mesothelioma as a separate tumor entity was questioned, and many thoracic mesotheliomata were considered peripheral pulmonary adenocarcinomas or metastatic. Mesotheliomata is now recognized as a specific tumor, but its cell of origin is still a question. As a result of the histological heterogeneity of mesothelioma, its histogenesis has been attributed to mesothelial cells, subpleural connective tissue, and lymphatic endothelium. Cultured mesothelial cells are capable of producing epithelial cells and fibroblasts, and this explains the heterogeneity of most mesotheliomata which contain epithelial and fibrosarcomatous elements. It may be that benign fibrous mesotheliomata differ in that there is evidence that they arise from subpleural connective tissue.[23]

A classification that is commonly used is (1) epithelial, (2) mixed epithelial and fibrous, and (3) fibrous or mesenchymal. The epithelial group includes tumors with tubulopapillary formation composed of epithelial and cuboid cells, as well as solid groups of cells without tubulopapillary formation. The fibrous group is composed of tumors made up of spindle cells arranged in bundles without much intervening hyalinized collagen. Occasionally, the fibroblasts may not follow a bundlelike pattern but may occur loosely or in solid sheets. The mixed type which is the most common is composed of epithelial cells and fibroblasts.[10,24] The tubulopapillary pattern is difficult to differentiate from metastatic adenocarcinoma, especially from prostate, lung, breast, stomach, and ovary, and Willis' earlier opinion that most mesotheliomata were actually metastatic adenocarcinomas is recalled. Even currently, tumors initially considered to be mesotheliomata are frequently thought to be otherwise when reexamined at mesothelioma registries. The initial diagnosis of mesothelioma was not confirmed in 34 percent of a Dutch series[25] and 40 percent of a British series.

The fibrous mesenchymal or sarcomatous type, when arising in the chest, needs to be differentiated from other sarcomas of the pleura, from fibrosarcoma of lung, and from metastatic fibrosarcoma. Most primary fibrosarcomas are clinically obvious. The very rare mesothelioma with osseous metaplasia may need differentiation from extraosseous osteogenic sarcoma.[26] Mesotheliomata associated with amosite exposure are unusual in that they contain large amounts of bone and cartilage.[27] Differentiation from an uncomplicated asbestos plaque may be difficult if there is an excess of collagen and very few cells. When the tumor is widely invasive, e.g., through the diaphragm into the liver, sarcomatous cellularity is usually obvious.

The mixed type may be difficult to differentiate from a primary carcino-

sarcoma of the lung, but this usually has a bronchial origin and co... squamous cells.

The epithelial polygonal cell types, if very undifferentiated, need ... differentiated from carcinoma; if differentiated they may appear rel... benign and resemble benign pleural hyperplasia such as may overlay a p... nary infarct.

Great difficulty is experienced in histological diagnosis of diffusely ... ing mesothelioma, which is most often of the epithelial type but may be ... or mixed. Purely histological criteria cannot absolutely distinguish mes... oma from certain metastatic carcinoma. Electron microscopic demonstrati... characteristic vacuoles and microvilli in the epithelial cells favors the dia... of mesothelioma.[4]

Histochemical techniques are of limited use. An effusion accompany... a mesothelioma may contain large amounts of hyaluronic acid. Secondary p... ral tumors contain this substance in only 10 percent of all cases. Effu... is accompanying squamous cell and alveolar cell malignancies may con... n hyaluronic acid.[28] Tissue may be examined for acid mucopolysacch... substances elaborated by mesothelial cells.[29] There is no histochemical ... specific for mesothelioma.

The variability of recorded plaque formation in patients with mesothe... oma, based on either x-ray or necropsy series, has been discussed. A sim... situation applies to the incidence of pulmonary fibrosis associated with me... thelioma. Although this is rarely very severe during life, either clinically ... radiographically, it is seen at autopsy examination. Oels et al.[12] reported t... 17 of 37 patients with pleural mesothelioma had necropsy-proven pulmon... fibrosis. The pulmonary fibrosis was unrelated to the histological type ... mesothelioma. Severe pulmonary fibrosis is more common with peritone... mesothelioma because this type of mesothelioma is usually associated w... severe crocidolite exposure, and this fiber is strongly fibrogenic.

CLINICAL FEATURES

Pleural Mesothelioma

The incidence in males predominates over females by approximately 4 t... 1.[30] Because of the long period needed following asbestos exposure, mo... patients are older than 50 years at death, with a mean age of about 55 to 65 ...

[4] Elis K and Wolff M: Mesotheliomas and secondary tumors of the pleura. Seminars in Roentgen... ogy 12:4, 301–311, 1977

Table 2-8
Presenting Com... aints of Pleural Mesothelioma

Onset	
Acute	4%
Insidious	96%
Pain	56%
Breathlessness	36%
Fatigue and weight loss	6%
Diagnosis in course of investigation of some other illness or prior to occurrence of symptoms	5%

Abstracted from E... es' data.[40]

most series for pleural mesothelioma and some 5 to 10 years less for peritoneal mesothelioma. Asbestos-related mesotheliomata in patients as young as 16 are known, however. Most of the patients have been cigarette smokers, but smoking has not been shown to have a multiplicative effect on the incidence of mesothelioma, unlike its effect on bronchogenic carcinoma. There is no predilection for involvement of one side of the chest in a current large series despite conflicting reports in earlier small groups. The onset of symptoms is usually insidious, but in the elderly, gradual weight loss and increasing dyspnea may go unnoticed, and only when a sudden accumulation of fluid or the development of pneumothorax is noted is an acute onset suggested. Presenting symptoms in descending order of frequency include pain, dyspnea, weight loss, fever, hemoptysis, and joint pain (see Table 2-8). Cough is often present but is rarely a presenting symptom. The pain is usually dull, gradually increasing in severity as the chest wall and nerve plexi are infiltrated, and may be located adjacent to the mass or referred to shoulder or abdomen. Sharp, severe pain may be related to a specific event, such as an acute increase in fluid or the development of pneumothorax. Pleuritic-type pain is less common, but there may be protracted episodes of pleurisy dating back many years, especially in those patients with a prior history of recurrent "benign" asbestos effusions. There may be contralateral pain if a "benign" asbestos effusion is present on the other side. The typical insidious nature of the pain is illustrated by the fact that some mesotheliomata are only diagnosed when patients seen for presumed hemothorax due to trauma or an acute pneumonia do not respond to appropriate therapy.[31] Hemoptysis is rare as a presenting symptom but may develop if there is much invasion of the lungs or if unwise attempts at decortication are made during thoracotomy before the true nature of the lesion is realized. Dyspnea may diminish temporarily if much fluid is aspirated. Dyspnea may also be related to the development of constrictive pericarditis (Fig. 2-54) or cardiac tamponade. Occasionally the patients have thrombophlebitis as a marker of a malignancy. *Painful* hypertrophic osteoarthropathy is



Fig. 2-54. *Mesothelioma invading the pericardium to produce restrictive c[ardio]pericardial disease (see Fig. 2-51).*

rare. Direct upward spread may cause a Hornerlike syndrome. Symp[toms] resulting from superior vena cava obstruction are rare. Interior spread through the diaphragm may cause gastrointestinal symptoms and complaints of abd[ominal] distention (Fig. 2-55). Distant metastases to meninges, kidney, adre[nals], thyroid, liver, opposite lung, and other organs cause appropriate symp[toms]. There is as yet no evidence that mesothelioma produces any paraendo[crine] effect, and no cases of hypoglycemia (as seen in some pleural benign s[olitary] fibromata and fibrosarcomas) have been recorded in recent large series.

The clinical findings reflect the presence of a pleural mass and eff[usion]. Extension of the tumor into the supraclavicular, chest wall, and abdo[minal] areas may be palpable. Initially, before the mediastinum is fixed, there m[ay] be displacement of the apex beat and trachea to the unInvolved side; this may eventually be reversed, and there may be physical signs of atelectasis o[f the] involved side. Clubbing of fingers and, less commonly, of toes may be p[resent].

Peritoneal Mesothelioma

Lassitude and weight loss accompanied by abdominal distention [and] ascites occur. Pain and tenderness may be dull and diffuse or localized [as a] result of ascites or of localized fluid collection. Umbilical, inguinal [and]



Fig. 2-55 A. *Mesothelioma invading the abdomen. Barium examination shows the irregular border of the lower esophagus and thickening of the mucosa of the descending duodenum. Only the latter was commented on. The patient had a prior decortication of the left lung with a tissue diagnosis of fibrothorax. Nine months later, development of a nodule in the thoracotomy scar led to diagnosis of mesothelioma. This sequence of events is not rare. The barium examination was prompted by complaints of epigastric pain.*

femoral hernias may develop secondary to ascitic distention. Physical signs relating to incomplete or complete bowel obstruction will develop.

INVESTIGATION

Although no form of treatment has been proven to be *life extending* for patients with mesothelioma, a correct tissue diagnosis is still necessary.

The accuracy of diagnostic procedures in a large series of pleural mesotheliomata is listed in Table 2-9 from Elmes[40]. The patients in this series died between 1960 and 1969. Current accuracy of cytological diagnosis is higher. Thus Butler and Berry[32] were able from appropriate aspirates to correctly diagnose by exfoliative cytological techniques 25 of 26 mesotheliomata, 28 of 30 metastatic pulmonary carcinomas, and 19 of 21 cases of mesothelial reaction.[32] Butler and Berry also examined aspirates from 6 patients believed to have "benign" and asymptomatic asbestos pleural effusion and in these found

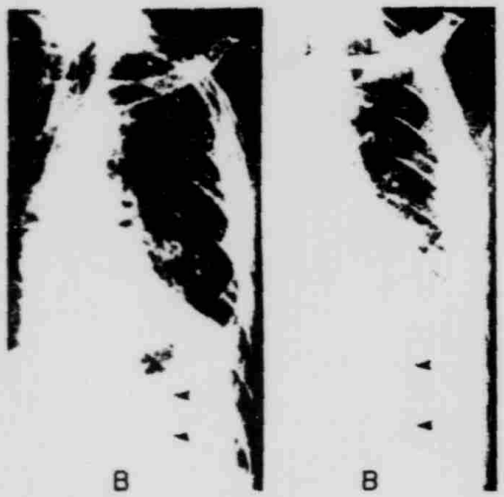


Fig. 2-55 B. *Deep x-ray therapy to the chest was given, but the oesophagus was not cleared. A contrast chest film showed widening of the space between the lesser curvature of the stomach and adjacent bowel loops (between arrows) over a period of 6 months as a result of the mesothelioma penetrating the diaphragm and infiltrating the stomach.*



Fig. 2-55 C. *Repeat examination of the oesophagus shows obvious involvement of the sides of the lower oesophagus to a greater degree than in A and displacement of its lower half to the right by extension of the mesothelioma into the mediastinum.*



Fig. 2-55 D. *Repeat examination also shows more severe involvement of the mucosal folds of the descending duodenum and widening of the space between the greater curvature of the stomach and the first loop of the jejunum. The appearance confirms the impression obtained from plain films in B. There is also an extrinsic impression in the upper part of the greater curvature which was not apparent 6 months earlier in A.*

atypical macrophages similar to those that accompany a mesothelioma effusion.[32] Two of these patients have subsequently developed clinical evidence of malignant mesothelioma, although tissue diagnosis is not yet available. Cytological diagnosis is difficult, and most pathologists need a large volume of tissue to ensure accuracy in diagnosis of mesothelioma.

Investigations other than radiographic examinations that may be of value in selective cases include computed tomography and ultrasonic examination to identify areas of fluid suitable for needle aspiration from pleural cavity and identification of solid masses in an ascitic abdomen. Echocardiography (Fig. 2-51) is helpful in identifying pericardial fluid or thickening. With constrictive

Table 2-9
Efficacy of Diagnostic Procedures

Method	Number Examined	Correct Diagnosis
Cytology of fluid	172	4%
Needle biopsy	69	26%
Open biopsy	115	38%
Excision	60	70%

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disease the posterior left ventricular endocardium, epicardium, and pariet pericardium show a reduced diastolic excursion related to restricted ventric lar filling. In addition, the anterior mitral valve may show abnormal diast closure, and septal motion may be abnormal. Pericardial effusions ma present both anteriorly and posteriorly, and with large effusions, there may swinging motion of the heart, the equivalent of electrical alternans on the E This swinging motion may simulate paradoxical septal motion. E cardiography is a simple noninvasive way of confirming cardiac tampon and avoids the need of catheterizing those patients with a short life expectar Appropriate isotope examinations are useful for detection of skeletal visceral metastases (see Figs. 2-56 to 2-60). Gray scale sonic and CT exam tions are also of use in assessing extent of tumor.

TREATMENT

Treatment is essentially supportive and palliative. Interested readers referred to a scientific but still compassionate survey of available modalities Elmes.[42]

RADIOLOGY

Pleural Mesothelioma

The radiographic diagnosis of malignant pleural mesothelioma is based the identification of appropriate radiographic findings and a compatible cli cal history. Association with a history of asbestos exposure is helpful but mandatory. The signs to be considered include pleural effusion; thickening the parietal pleura, which may be diffuse or lobulated; thickening of visceral pleura; solitary masses; hydropneumothorax; satellite lung lesio and hilar adenopathy. In addition, evidence of prior asbestos exposure sho by calcified and noncalcified pleural plaques, pulmonary fibrosis, and visc pleural thickening should be sought. A search for radiographic evidenc spread above the diaphragm to involve mediastinal structures, extrathora structures, and the diaphragm itself is made. Similarly examination of in diaphragmatic areas is made, as well as a search for distant metastases.

Pleural Effusions

Radiographically detectable pleural effusion is a frequent initial sign Table 2-10). In Ratzer's series, 15 of 16 epithelial-type mesotheliomata and 13 fibrosarcomatous type had an initial pleural effusion.[35] The difference



Fig. 2-56. *Mesothelioma. Technetium 99m polyphosphate scintigram of a man who developed a cuboidal cell mesothelioma. He had worked for 20 years as a shipfitter and boilermaker. Anterior view shows metastatic deposits in the proximal part of the right humerus and in the left seventh and eighth ribs. Bloodborne metastases were present in both lungs, which also contained much pulmonary fibrosis and many ferruginous bodies. (Courtesy of Paul Hotter, M.D., U.C.S.F.)*

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Fig. 2-57. *Mesothelioma. Technetium 99m polyphosphate scintigram of a man who had developed a mesothelioma after working for 21 years in an asbestos insulating factory. Initial histologic diagnosis was adenocarcinoma, which was later altered to mesothelioma after use of special staining techniques, such as mucin, PAS, and mucopolysaccharidase stains. Differentiation of mesothelioma from a peripheral adenocarcinoma is often difficult. Metastases are seen in the calvarium, the proximal right humerus, a right anterior rib, the thoracic and lumbar spine, and the proximal right femur. The tumor also encircled the abdomen. (Courtesy of Paul Hotter, M.D., U.C.S.F.)*



Fig. 2-58. *Mesothelioma. Technetium 99m liver scintigram showing two bloodborne metastases in a man who was a shipyard worker in World War II. The initial diagnosis based on pleural biopsy was pleural fibrosis and chronic inflammation. A decortication procedure was done, and the diagnosis was unchanged after examination of removed tissues. Development of bony metastases prompted reexamination of the material at a mesothelioma referral center, and the diagnosis was changed to mesothelioma of mixed sarcomatous and carcinomatous type. The tumor invaded the retroperitoneal tissues, setting up a desmoplastic reaction around the ureters but not blocking them. (Courtesy of Paul Hotter, M.D., U.C.S.F.)*

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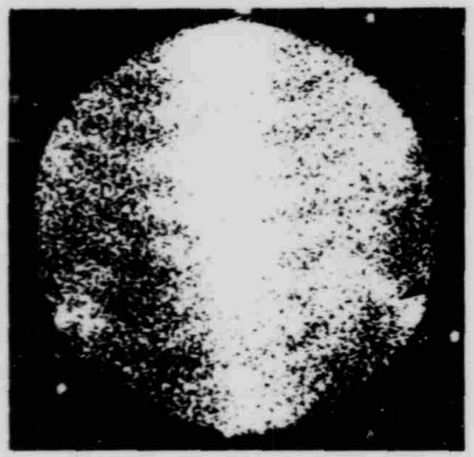


Fig. 2-59. *Mesothelioma. Technetium 99 scintigram of a rib cage. The lesion in the right upper rib is a metastases from mesothelioma. The apparent left-sided lesion is secondary to thoracotomy for a diagnosis of an underlying mesothelioma. (Courtesy of Paul Holter, M.D., U.C.S.F.)*

incidence of effusion may be related to the gross morphology. Epithelial mesotheliomata, which have a high incidence of accompanying effusion, are usually poorly demarcated areas of pleural thickening, while the fibrosarcomatous type, as elsewhere in the body, tends to more localized, discrete, and bulky. Nearly all patients will develop a pleural effusion as the disease progresses (Fig. 2-61). A frequent appearance is the irregular tumoral pleural thickening above the level of fluid (Fig. 2-62). Rarely the effusion may be large enough to produce x-ray signs of mediastinal shift; this may persist, or as the tumor enlarges and causes atelectasis or fixation, there may be shift of mediastinal structures to the affected side, as well as other signs of volume loss such as rib crowding or diaphragmatic elevation. It may be helpful for the radiologist to inquire about accompanying pain and friction rub. This is rarely typically pleuritic but more of a diffuse ache unrelated to breathing, and as the effusion increases, the pain increases. This is unlike pleurisy of an inflammatory nature in which the pain will diminish as the enlarging effusion separates inflamed parietal and visceral pleurae. Further, unlike most of the pleurisies resulting from inflammation, collagen disease, or *pulmonary infarction, a friction rub* is rarely heard, possibly because the layers of pleurae may be adherent or the effusion loculated. A certain amount of radiological caution is necessary in



Fig. 2-60. *Mesothelioma. Patchy areas of increased and reduced density proximal right humerus due to bloodborne metastases from a mesothelioma of lung. Areas of reduced bony density in the upper extremity may be due to secondary to causalgia or disuse if they are on the same side as a mesothelio brachial plexus is invaded.*

Table 2-10
Percentage of
Pleural Mesothelioma
Accompanied by
Radiographically Identifiable
Pleural Effusion

Author	Percentage
Solomon[36]	61%
Elmes[22]	63%
Heller[34]	40%
Ratzer[35]	74%



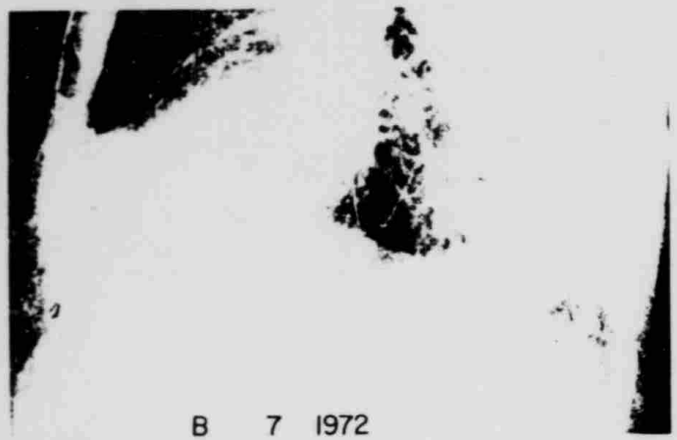


Fig. 2-61. *Mesothelioma, development. P.A and Lateral views. A and B: There is a sm pleural effusion and subpulmonic nodulated plaques in July 1972. C & D: April 197 there is extension into the mediastinum. The hilus is enveloped by tumor (arrows). A the plaques are obscured by effusion. An erroneous diagnosis of hilar carcinoma wou be suggested if the patient were first seen in this stage. D: In April 1974, there is pleural pseudosepta tions and above, a huge tumor mass and lung parenchymal invasion.*





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Fig. 2-62. *Rapid development of mesothelioma. In February 1976, the chest roentgenogram is normal, and there is some lobulation of the right hemidiaphragm. Four months later, a large pleural-based mass encases the right lung. Part of it is lobulated. There is involvement of both sides of the upper mediastinum (arrows) and a round bloodborne metastasis is seen at the base of the left lung (vertical arrow). The initial histologic diagnosis was of anaplastic carcinoma from an unknown primary site; it was later revised to mesothelioma. The patient had been a shipfitter. This sequence of events is more rapid than most mesotheliomata. Conventional bedside teaching used to state that where the clinical diagnosis was in doubt, the quickly spreading tumors were carcinoma and the more slowly spreading ones were mesothelioma.*

assessing effusion related to mesothelioma. A few patients may have a pleural effusion present for many months before clinical or cytological evidence of mesothelioma becomes apparent. An effusion may be present on the contralateral side, with no radiographic evidence of tumor spread from the side harboring the mesothelioma (Chapter 2, Section 5). Whatever the initial size of an effusion accompanying a mesothelioma, it usually reaccumulates rapidly when aspirated.

Pleural (Parietal, Visceral) Thickening

Pleural thickening may be diffuse or lobulated. Diffuse thickening is more frequent with the epithelial type (Fig. 2-63), and irregular lobular masses are more frequent with the fibrosarcomatous type. Since most tumors are mixed, this sign has its limitations. The malignant nature of diffuse pleural thickening may not be fully appreciated, because this may also occur as a nonmalignant response to asbestos exposure. Characteristically, hyaline pleural plaques, reasonably well circumscribed and either calcified or noncalcified, are



Fig. 2-63. *Mesothelioma. Thick pleural "peel" surrounds the lung from apex to base. This is a decubitus view (note gastric air bubble). The appearance in the erect view was identical with regard to the pleural peel. It is usually difficult to identify free pleural fluid accompanying a mesothelioma by conventional radiographic means, but decubitus CT sections are often helpful.*

frequent result of asbestos inhalation. Until recently, insufficient attention has been paid to the fact that diffuse thickening of the parietal pleura initially and the visceral pleura subsequently may occur.[36] Such diffuse areas of thickening of parietal and visceral pleurae do not calcify, unlike localized parietal pleural plaques. This benign thickening is progressive and has been reported up to 15 mm thick. It may therefore simulate mesothelioma, except that it is not lobulated. This benign thickening has to be differentiated from parietal and/or visceral pleural thickening residual from a prior benign asbestos effusion. The minor fissure is involved more frequently than is the major fissure in the dry type of diffuse benign pleural reaction.[36]

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Fig. 2-64. Mesothelioma: Pneumothorax accompanying mesothelioma. Mesothelio[ma] may present with pneumothorax. The mechanism is unknown. Arrows indicate tum[or] thickening of parietal and visceral pleurae.

Lobular Thickening

Lobular thickening of the pleura may be apparent initially, or it may become apparent after an invasive diagnostic procedure if sufficient air remains to separate the pleural layers. A mesothelioma may occasionally present with or develop a spontaneous pneumothorax (Fig. 2-64) which permits visualization of these lobular masses. Tomography is helpful in showing the lobular areas. Lobular areas due to tumor are more frequent with the fibrosarcomatous than with the epithelial type. Some lobular areas result from pseudotumors, which occur in both the epithelial and fibrosarcomatous type. Pseudotumor cavities within the thickened pleura filled with necrotic and fibrinous liquid material. They, too, are seen best with tomography and may sometimes appear to be within the lung parenchyma, their true site is not realized until surgical exposure or necropsy. Benign pleural tumors, especially fibrous

thelioma may arise from a stalk. Although one malignant mesothelioma on a thin pedicle has been described, this is an exception. The radiographic appearance does not differ from other lobular pleural masses; differentiation from lymphangitic spread of carcinoma, malignant lymphoma, and pleural sarcoma (Fig. 2-65) is needed.

Most malignant mesotheliomata appear to originate from the lower portion of the pleura; very few are reported as arising near the apices. This is in contradistinction to benign cellular or fibrous mesotheliomata and other benign pleural tumors, lipomas, angiomas, fibromas, and chondromas that may arise in any pleural zone (see Figs. 2-66 to 2-68). Benign pleural tumors may also develop in the interlobar fissures, which is rarely the case with the malignant type. Diffuse thickening of the interlobar fissures, however, especially the minor fissure, is a recently reported sign of benign-type asbestos exposure.[36] Malignant mesothelioma due to asbestos exposure and arising from the pericardium has not been reported, but a study of Figure 2-47 suggests that this case may be an exception.

Solitary Mass

A solitary mass is a less common x-ray finding (Fig. 2-69). This presentation occurred in 2 out of 10 of Heller's patients and is more common in the fibrosarcomatous type. It may be indistinguishable radiographically, even with tomography, from a primary peripheral bronchogenic carcinoma. When it arises in the upper pleura, radiographic diagnosis is especially difficult, since most malignant mesotheliomata have a predilection for lower zones. Some fibrosarcomatous mesotheliomata may reach large dimensions, up to 30 cm, and still be confined to one lung zone. This radiographic appearance has not been stressed, since the more common appearance of a malignant mesothelioma encasing the lung is better known.

Hydropneumothorax

This may be an occasional rare form of presentation. It permits appreciation of the diffuse or lobular malignant thickening of the pleura and assessment of any benign calcified or noncalcified pleural plaques that may be present on the parietal pleura. It is conjectured that the limited invasion of underlying lung parenchyma that occurs with mesothelioma is sufficient to allow development of a pneumothorax. Spontaneous pneumothoraxes are seen with both the epithelial and fibrosarcomatous type. Parenchymal masses or infiltrates with known association for spontaneous pneumothorax include peripheral rheumatoid nodules, cavitating pulmonary infarcts, cavitating osteogenic sarcoma and Hodgkin's disease, and pneumatoceles of varying etiology.

Fig. 2-65. *Adenogenic sarcomatoid pleural mesothelioma showing involvement of parietal and visceral pleurae. (A) There are tumoral infiltrations along the anterior mediastinal line (thick arrowheads), the posterior mediastinal line (small arrowheads), the right parahilar area (curved arrow), and the lateral margin of the right lung (thin arrowheads). (B) Enlarged collagen-lined vascular spaces (arrowheads) and adenomatous areas (arrow) are visible in the tumor. (C) Tumor cells are arranged in a glandular pattern (arrowheads) and are separated by thin bands of collagen (arrow). (Hematoxylin and eosin, original magnification ×100.)*

Fig. 2-66. *PA and lateral views of lipoma arising from parietal pleura. There is an accompanying iatrogenic pneumothorax. The elongated shape may be due to its position partly within the major fissure. (Compare Fig. 2-67.)*

Satellite Lung Lesions

This is a nonspecific term and may include metastatic deposits in the same or contralateral lung (Fig. 2-70), areas of local lung invasion, and the pseudotumors described above, which may appear on tomography to lie within the lung but are in fact areas of degeneration within the thickened pleura. Metastases to the opposite lung and/or pleura are common as a late finding, but occasionally, as in Solomon's series,[33] they may be present at first examination, making radiographic differentiation from metastatic carcinoma difficult. Although superficial invasion of the lung is common, localized deep invasion may occur to present as a satellite nodule.

Hilar Adenopathy

Hilar enlargement may be seen as a result of regional lymph node involvement. More frequently, a large mass in the region of the hilus results from the direct spread of the mesothelioma to this area (Fig. 2-71) or to primary involvement of the mediastinal pleura (Fig. 2-72).

To help substantiate the diagnosis of an asbestos-related mesothelioma, a search should be made for the other stigmata of asbestos exposure—pleural and diaphragmatic plaques and/or visceral pleural thickening and pulmonary fibrosis.

Fig. 2-67. *PA, AP, LAO, and lateral views of right lung showing localized benign fibrous mesothelioma having a broad base and attached to the visceral pleura overlying the middle lobe. The elongated shape is related to the chest position; the small, "dimple" seen on lateral view is helpful in differential diagnosis of the cysts. It is extremely rare for a localized mesothelioma to metastasize, but such instances are known. Mesotheliomas may invade the lung or chest wall. Although the cell nuclei show very little mitotic activity, absolute determination between benign and malignant mesotheliomas may not be possible histologically. The majority of benign mesotheliomas are pedunculated; the blood supply entering via the pedicle is demonstrable by arteriography or broncholipiodol, or diphragmatic vessels, according to the site of tumor origin. Over 75 percent originate in visceral pleural When the tumor is large there may be an accompanying pleural effusion, which makes radiographic identification of benign disease more difficult.*

Ellis K. and Wolff M.: Mesothelioma and secondary tumors of the pleura. Seminars in Roentgenology 12:4, 311, 1977.

Fig. 2-68. *AP view of the upper mediastinum. Above the aortic knob the round density (arrow) is a simple cyst of the pleura (arrows) containing clear fluid. (Courtesy D. Cline, M.D., U.C.S.F.)*

Fig. 2-69. *A small mesothelioma is closely applied to the posterior ribs (oblique arrows), directly anterior to an area of direct lung parenchymal invasion (white arrow*

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Fig. 2-70 A. *Mesothelioma. Tomographic section 8 cm from back shows an egg-shaped mass of metastatic mesothelioma (arrows). The main tumor lies along the lateral chest wall and is not seen well in this section. The egg-shaped mass could be construed as a primary peripheral malignancy with metastases to peripheral pleura, and a decade ago this might be the preferred diagnosis. Rib metastasis is also present.*



Fig. 2-70 B. *Tomographic cut 11 cm from back, shows typical plateau-shaped noncalcified diaphragmatic plaque (arrows). The mesothelioma lies along the lower chest wall.*

Pleural and Diaphragmatic Plaques

These should be searched for in the uninvolved areas of the pleura a diaphragm and on the contralateral side (Figs. 2-73 to 2-75). Solomon, findi only 2 of 33 mesothelioma patients to have calcified and 7 of 23 to ha noncalcified plaques, postulated that a pleura with calcified plaques is l susceptible to malignant generation.[33] This appears improbable; more lik the number of calcified plaques found reflects assiduity of search and sophis cation of radiographic techniques used. Thus, Edge found 20 of 28 mesothe oma patients to have pleural plaques, both calcified and noncalcified, on ray.[19] Since most mesotheliomata arise in lower zones, it is rare to be able identify plaques adjacent to the ipsilateral diaphragm, but these are occasio ally seen on tomograms (Fig. 2-70*B*).



A

Fig. 2-71. *Mesothelioma prior to thoracotomy. (A) There is as yet only slight invasion of underlying lung, and the mediastinum appears uninvolved. (B) Four months later, after thoracotomy. There is diffuse invasion of the mediastinum and underlying lung and encasement by sagittal and ribs (horizontal arrow). Mesotheliomata tend to infiltrate along connective tissue planes associated with bronchovascular bundles. A small localized plaque is still evident (vertical arrow).*



B

Pulmonary Fibrosis

Pulmonary fibrosis is seen histologically in about 50 percent of p with asbestos-related pleural mesothelioma but is of sufficient degree apparent radiographically in only about 20 percent (Fig. 2-76). Severe p nary fibrosis is more common in association with peritoneal mesothelio

Diffuse Parietal and Visceral Pleural Thickening

Direct extension of the tumor may be above or below the diaphragn bloodborne spread to distant organs.

Above diaphragm. Fluoroscopy identifies fixation of the diaphra a result of direct involvement or extension into the phrenic nerve. The ab of clavicular companion shadows indicates extension into supraclav nodes, but a prior scalene fat pad biopsy may produce a false-positive Enlargement of the axillary nodes is best seen by xerographic techn Extension through the chest wall may produce a soft tissue shadow obliteration of fat planes; although it has been recorded in the literatur

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Fig. 2-72. *Mesothelioma arising from mediastinal pleura. There is very little involvement of the lateral chest wall pleura. The tumor spread through the left side of the diaphragm to produce small bowel obstruction. Note the absence of bowel gas in the left upper quadrant of the abdomen and the dilated loop of small bowel.*



Fig. 2-73. *Mesothelioma in a boilermaker. In the left costophrenic angle is a pleur based shadow extending over two costal interspaces; more medially (between oblic arrows) is a less defined density that arises in the pleura but whose radiograp appearance could be that of a parenchymal lesion; more laterally there is a pathologic fracture through a rib involved in continuity. The undersurface of a midrib is destro by bloodborne spread (black and white arrows); there is a dense diaphragmatic pleu calcification (vertical arrow), and above it a small, plateaulike plaque that acts a biological marker to suggest the diagnosis of mesothelioma.*

sign appears quite rarely. More easily assessed is rib destruction. The midd and posterior mediastinal structures are encased. The esophagus may b displaced (Fig. 2-53) or circumferentially narrowed. Differentiation from primary esophageal cancer, of which there is an increased incidence asbestos workers, is usually not difficult. Mucosa of the esophagus is usual not involved when there is direct extension. Involvement of the aortic wall b mediastinal extension obliterates the radiolucent line of the mediastinal pleur periaortic reflection and may simulate a dissecting aneurysm of the descendin aorta, so that aortograms have occasionally been needed.[23] Venography ma be needed[23] if involvement of the superior vena cava or the thoracic portion the inferior vena cava occurs (Fig. 2-53). Involvement of the pericardium lea to enlargement of the cardiac silhouette, and if there is much pericardi effusion, tamponade with dilatation of the azygous vein width may occur. Th



Fig. 2-74. *Early mesothelioma. The localized pleural mass closely applied to the lower left ribs (double arrows) is a mesothelioma. Adjacent to the right ribs (3 arrows) there is a lesser degree of, but more diffuse, pleural thickening due to a noncalcified plaque. The patient died 12 months later. He also had a bowel resection some years previously for adenocarcinoma of the colon. There is evidence of approximately double the normal incidence of colon cancer in patients who have had heavy asbestos exposure.*



Fig. 2-75. *Mesothelioma. Several calcified pleural plaques are seen at the lower border of the mesothelioma mass (oblique arrows). Noncalcified plaques are usually obscured by the tumor mass. Calcified plaques may be visible, depending on their size. Note direct rib invasion (vertical arrow).*

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Fig. 2-76. *Mesothelioma. Arrows indicate an early pleural mesothelioma in a patient with severe lower lobe and lingular fibrosis. Fibrosis is more commonly associated with pleural mesothelioma.*

upper limit of the azygous vein in normal nonpregnant patients has been assessed variously as lying between 6 and 10 mm[23] on an upright 6-ft PA view. In many patients seriously ill with mesothelioma, only a supine portable film at a distance of 40 in. is available. For this group of patients, an azygous vein width greater than 15 mm is associated with a raised central venous pressure. The linear relationship between the two is (azygous vein width in millimeters − 4) − 4 = CVP millimeters of water.[23] Conventional radiography may suggest signs of pericardial effusion or thickening. These signs may be summarized as marked nonspecific cardiac enlargement, especially if lung fields are clear; encroachment of cardiac shadow on retrosternal space; asymmetric enlargement of cardiac silhouette produced by uneven distensibility of pericardial space or by loculation; sudden change in heart size, especially in absence of heart failure; and widening of the pericardial stripe.[28] In the lateral chest film, especially when coned-down and centered on the lower anterior chest wall, the thin radiolucent black line of epicardial fat is visible. Anterior to it is a radiopaque white stripe composed of the layers of the pericardium, and most anterior is the radiolucent mediastinal fat. Widening of the white pericardial



A

Fig. 2-77 A. *Mesothelioma. A 53-year-old man with decortication of right lung 3 years previously for recurrent pleural effusion. Chest film showing decreased volume of right lung, thickened pleura, and a mass at the lung apex.*

stripe is suggestive of pericardial effusion or thickening. This sign has its limitations in women, in whom breast shadows may obscure the area. The hilar overlay sign, in which an enlarging pericardial effusion obscures the origin of the pulmonary arteries, unlike an enlarging heart which displaces them, is very useful but may be difficult to assess on portable films, especially if there is a slight apical-lordotic tilt of the tube. Echocardiography[42] has replaced fluoroscopy. Positive and negative contrast examination and radioisotopic scanning in which the blood pool is labeled with ^{131}I, iodine-tagged albumin, or technetium-labeled albumin were other useful techniques prior to the advent of echocardiography.

CT has a part in the assessment of mesothelioma because of its ability to identify adjacent areas with only a slight difference in the attenuation coefficient. There may be insufficient radiographic contrast from surrounding air to visualize some mesotheliomata, peripherally located carcinomata, lymphomata, and sarcomata with conventional radiography. The transverse sections are ideally suited to the display of the circumferential or localized involvement of the lung, encasement or actual involvement of the hilar nodes, involvement of the pericardium and the myocardium of the atria and ventricles, encasement of the aorta and penetration of the intercostal muscles and the diaphragm. (Fig. 2-77). Scans at upper levels in the thorax may show spread to axillary and

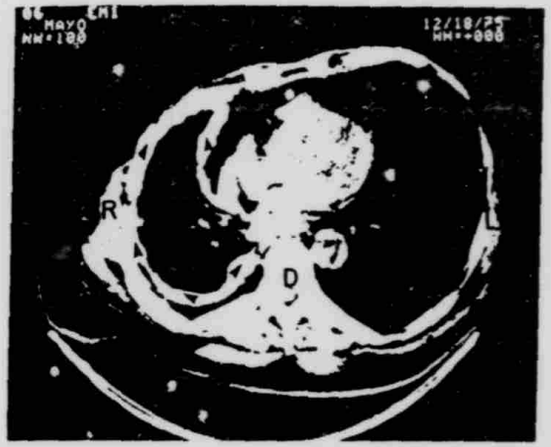
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Fig. 2-77 B. CT section through lung apices showing peripheral mesh-like ... thickening (oblique arrows) and rounded mass posteriorly. Large horizontal arrow ... innominate and left carotid arteries are seen in cross section anterior to vertebral ...



Fig. 2-77 C. CT section at lower level showing ... large oval ... thickening completely encircling the right lung (arrows). The arch of the aorta lies anterior ... vertebral body.



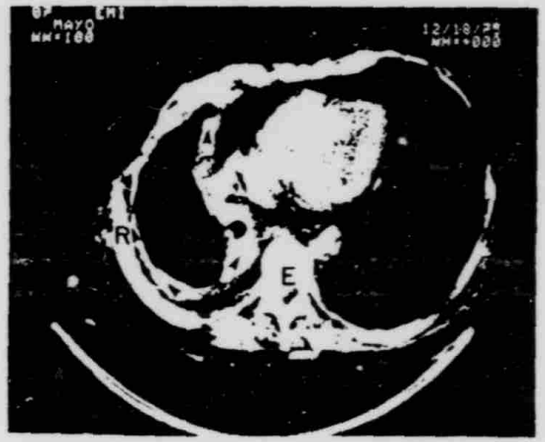


Fig. 2-77 D, E. CT sections at lower levels below the right hilus show extensive pleural ... and ... due to mesothelioma. (Courtesy of Drs. P. F. Sheedy II, D. H. Stephens, R. H. Hattery, K. Mahin, G. W. Hartman, and the publishers of the American Journal of Roentgenology.)

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retrosternal nodes. The place of CT in the differentiation of mesothelioma fr... widespread pleural involvement by anaplastic carcinoma has not yet be... determined. Use of appropriate window widths and heights will differenti... secondaries in the bony thorax, however. The thickness of a mesotheli... varies, and CT may indicate the optimal site for aspiration biopsy. Utilizing ... in the decubiti positions, an accompanying effusion may be separated f... mesothelioma tumor mass, which is an additional aid in planning percu... neous biopsy. CT in individual cases has been shown to be of value ... following reduction of mesothelioma bulk during treatment.[39]

Below diaphragm. Plain films may show signs of intestinal obstru... tion. Barium examination may be used to confirm this and show extrins... pressure on bowel. Mucosa usually shows only minimal changes. With lar... masses, it is difficult to separate intraperitoneal and extraperitoneal extensi... of the mesothelioma; both occur, although intraperitoneal extension is mo... common. Separation of bowel loops may be due to free fluid or sero... thickening. Infiltration of the omentum may displace gastric air bubble (Fig. ... 55B). Ureteric obstruction should be sought for by pyelography.

Peritoneal Mesothelioma

The radiographic findings[42] are similar to those found in thoracic mesoth... lioma extending into the abdomen and so will not be detailed. A great... amount of ascites may be present, and depending on the site of origi... distortion of the pelvic colon may be greater than when a thoracic mesothel... oma has extended interiorly. Occasionally, pleural and peritoneal mesothel... oma appear to have originated concurrently.

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