File Asbestos

ASBESTOS RELATED DISEASE:EPIDEMIOLOGIC & CLINICAL ASPECTS

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There are about 4 million persons alive today who have had heavy exposure to asbestos and an equal number with significant but lesser exposure (1). Among the several asbestos related disorders asbestosis, a term that should be reserved for pulmonary fibrosis (2), will remain an important but diminishing concern among the heavily exposed. The 3 pleural manifestations, hyaline plaques, benign asbestos effusion and mesothelioma, because of the lesser required exposure and long latent period, very likely will become increasing problems in all of the 8 million exposed persons. Concerning bronchogenic carcinoma, it is thought that 2 per cent of the 135,000 cases reported each year are related to asbestos exposure. Indeed, estimates of the percentage of all cancers caused by the single substance asbestos have varied from 1 to 18 per cent (1).

The radiologist's contribution in sorting out the asbestos related problems can be greatly enhanced by 1.) a strict adherence to accepted terminology and definitions, 2.) a working knowledge and use of the International Labor Organization Radiologic Classification of the Pneumoconioses, 3.)an effort to assemble old films for comparison, 4.) a detailed acquaintance with exposure history and with past history and 5.) an acquaintance with relevant epidemiology.

Asbestos: Fibrous hydrated silicates:Serpentine (chrysotile): white, curly, filamentous (90% of industrial use) and amphiboles, mainly Crocidolite (blue) and Amosite (brown). Others, including Anthophyllite and Tremolite mainly contaminants of talc.

Occupations at risk: (Incomplete list)

Process	Products (more than 3,000)	Occupations (Ex)
1. Production		
Mining, Milling	Asbestos Fiber	Mining,Crushing Transport, etc.
2. Primary use		
Spray Insulation	Fiber mixed with oil	Insulators, Construction
3. Manufacturing		
Textile	Cloth,Belts,Padding	Spinning,Card.
Cement Products	Roofing,Pipes,Gutters	Blending,cut.
"Paper" products	Felt,Electrical paper	Paper makers
Friction material	Gaskets,Clutch,Brake	Mixers,Blenders
Insulation	Pipe,Boilers,Bulkhead	Slurry,Chemical workers

Process	Products	Occupations
4. Application		
New Construction	Boards,Tile,Siding	Carpenters, Laggers,Heat.
Repair,Demolition		
Shipbuilding	Insulation:Pipes,hull	Laggers,Pipe-coverers
"Repair, Refits	"	Direct & Indirect (all)
Automotive	Undercoating,brake,etc.	Service,body shop

Epidemiology:

a.) Disease is dose-related.Exposure may have been brief and massive or lower dose for many years.
b.) "Twenty-year rule": Regardless of severity of exposure, signs and symptoms today are never seen until 10 or 15 years later and usually not until 20 years later.
c.) Asbestos manifestations correlate best with years since first exposure rather than number of years exposed. Manifestations progress despite removal from exposure.

I. Asbestosis:
This term should be reserved for a pneumoconiosis consisting of a diffuse chronic pulmonary interstitial pneumonia and fibrosis due to respirable asbestos fibers. The term should not be used for other asbestos-related manifestations or disease (2).

Asbestosis is demonstrably dose related, requires a considerable dose and therefore is not seen with out-of-plant neighborhood exposure or in relatives.

Cigarette-smoking is not a co-factor; and COPD occurs in asbestos workers with the same frequency and severity as in controls matched for age, sex and smoking history (3).

Clinical Diagnosis is based on history of exposure at least 15 and more usually 20 years earlier and at least 4 of the following 6 signs and symptoms:

1.) X-Ray: Linear-irregular markings (usually of lower lung fields) of ILO severity 1/1 or greater
2.) Dyspnea of Fletcher grade 2 or greater
3.) End inspiratory crackles (cellophane or velcro rales in 2 or more areas)
4.) Definite finger clubbing (usually late manifestation)
5.) Vital Capacity less than 80% of predicted
6.) Single breath diffusing capacity less than 80% of pred.

A clinical diagnosis is made when 4 of 6 of the above manifestations are present. "Permanent and total disability"

usually is associated with at least 2/2 radiographic profusion, an FVC of less than 50% and D_LCO of less than 40%. Lung biopsy should be required only in persons with a good exposure history but with atypical clinical or radiographic findings, or, on the contrary, when there are suggestive clinical findings but the exposure history is brief or unconvincing. The recently fashionable transbronchial biopsy may result in recovery of asbestos bodies but it is not a suitable technique for evaluating the presence or severity of interstitial pneumonia and fibrosis.

II. Parietal Pleural Hyaline Plaques:

The most recent I.L.O. classification distinguishes between diffuse pleural thickening and plaques or circumscribed pleural lesions (4). The latter, hyaline plaques, are the most common and also the most benign asbestos-related disorders.

Neither the early descriptions of the pathology of asbestosis nor the first clinical surveys in the 1930's called attention to parietal pleural lesions because at that time exposure was often severe and workers became disabled or died of asbestosis before plaques could form (5). Radiographic pleural calcifications of occupational origin were first noted in talc miners probably due to tremolite. Jacob and Bohlig (6) in their study of Dresden asbestos workers first mentioned calcifications as one of several roentgenographic features of asbestos exposure, and soon thereafter pleural plaques became established as markers of both occupational and non-occupational endemic asbestos exposure. More recent epidemiologic studies have led to the following generalizations concerning pleural plaques: (1) They are seen only following exposure to fibrous silicates. (2) Unlike asbestosis, they may result from casual, peripheral or neighborhood exposure. (3) They are rarely seen in less than 15 to 20 years after initial exposure. (4) Among asbestos workers first exposed 30 to 40 years ago, the prevalence may be as high as 35 to 60 per cent (5). (5) Only a small percentage of those present are seen radiographically. (6) They are an almost invariable finding at autopsy. (7) Plaques and calcifications occur on the parietal pleura and rarely cause pleural symphysis. The mechanism of their development is not known but probably they are due to mechanical rather than chemical irritation. (8) In the absence of asbestosis they are not harmful in that 1.) they are not associated with functional loss, 2.) they are not associated with symptoms and 3.) they do not predispose to other asbestos-related disease (CA, Fibrosis, Mesothelioma) compared to similarly exposed persons who do not have plaques. (9) Asbestos-related plaques and calcifications must be recognized and

or asbestos plants. Other types of exposure include long fiber Zeolites used for stucco and buildings. Sugar cane work, radiation and thorotrast cholangiography, as well as tuberculous empyema all have been associated with mesothelioma. McDonald and McDonald (9) have well summarized present knowledge by saying that the proportion of mesotheliomas due to occupational exposure is increasing but is certainly less than 100%, unlikely less than 50%, and probably accounts for two-thirds of all cases. They and others also have shown a gradient in mesothelioma-inducing potential from crocidolite down to chrysotile and anthophyllite.

Mesothelioma, much like the other pleural manifestations of asbestos exposure, may result from brief, slight or peripheral exposure - a finding of great concern. The latent period from initial exposure is usually very long, often 30 years or more and very rarely less than 20 years. Among asbestos workers the death rate from mesothelioma appears to be proportional to the third or fourth power of time from first exposure and is unrelated to smoking habits. The histologic diagnosis has remained difficult because the tumor arises from pleuripotential mesothelial cells and in consequence may present with widely varying histologic features. Three types are generally recognized: mesenchymal or sarcomatous, epithelial or tubolopapillary and mixed; additionally some tumors are poorly differentiated. Mesotheliomas are often diagnosed because of their typical gross appearance with spread along serosal surfaces, encasing of the lung by a continuous layer of tumor and failure to demonstrate a primary lesion in the lung. However, the same gross appearance may result from bronchogenic or metastatic tumors. These histologic problems explain why thoracenthesis or needle biopsy rarely proves diagnostic. In most of our cases a small open thoracotomy was required but thoracoscopy may be a less invasive alternative.

Mesotheliomas have not responded to any form of therapy. Pleuro-pneumonectomy or "debulking" entail high mortality and no improvement. Concerning recent chemotherapy, at Sloan-Kettering there were only 3 responses among 111 trials; and mean survival of treated and untreated cases has been the same: 9.1 vs. 9.6 months (10) and in our series it was 15.8 months for untreated vs. 12.4 months for chemotherapy.

V. Bronchogenic Carcinoma:

Case reports have accumulated since 1934 but it was not until 1955 that Doll (11) presented epidemiologic evidence

of an increased prevalence. Although acceptance came slowly it is now concluded beyond any reasonable doubt that commercial asbestos is a cause of human lung cancer, though other agents such as tobacco, may enhance its effect. The relative risk (RR), a number that represents the observed divided by the expected number od deaths from a given disease, tabulated by Backlake (2) and by McDonald (12) for 18 major cohort studies has varied from 1 (no increased risk) to 17, with the lowest values, 1 to 5, in miners and millers and the highest, 8 to 17, in pipecoverers and insulation workers. The interaction of smoking to asbestos exposure as risk factors is most important in clinical practice. Lung cancer develops only very rarely in nonsmoking asbestos workers whereas the risk from smoking and asbestos is more than additive, and more likely multiplicative. A relationship to intensity of exposure has been difficult to demonstrate because dust concentrations were rarely measured until 10 or 15 years ago. However the best available data suggest that the dose response relationship is essentially linear, but steeper for asbestos manufacture than for mining. The increased risk appears at about 20 years after first exposure and reaches a peak at 30 years, although obviously there is an interaction between age and lung cancer mortality.

The question of causal relationship or attributability is not a great problem with asbestosis or hyaline plaques which are specific for asbestos nor even for mesothelioma when there has been significant exposure. With bronchogenic carcinoma the situation is quite different in that only 1-2% of all cases can be related to asbestos exposure. The probability that a given case of lung cancer is due to asbestos exposure is based primarily on two factors: the intensity of exposure and the time since first exposure. For example, data of Enterline et al (13) indicate no increased risk (RR = 1.2) for asbestos workers who were exposed to less than 10 million particles per cubic foot (mppcf) and who were first exposed less than 20 years ago, whereas RR rose to 4.7 for those who were first exposed more than 30 years ago to more than 10 mppcf. The time since first exposure can be identified whereas in clinical practice the intensity of exposure almost invariably must be inferred from clinical and histologic evidence.

ASBESTOS RELATED DISEASE - PLEURAL ABNORMALITIES

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The pleural abnormalities following asbestos dust exposure include: (1) plaques (circumscribed or localized). (2) diffuse pleural thickening (circumferential or interlobar), (3) effusion, (4) mesothelioma. Pleural changes are more frequently found without associated pulmonary parenchymal abnormalities.

The normal pleural shadow (e.g. pleural stripe, accompanying shadow) has often been called pleural thickening. It consists mainly of internal intercostal muscle bundles and some fat. The parietal pleura is only 10 to 60 micra in thickness, as is the visceral pleura, and thus the normal pleura contributes very little to the shadow. Normally the shadow tapers from the apex and disappears usually below the fourth or fifth rib. Diffuse pleural thickening often follows a gravitational event in the pleural space (e.g. infection or trauma)and usually obliterates the costophrenic angle(casting a shadow which is wider inferiorly and tapers towards the apex).

The characteristic pleural plaque following asbestos dust exposure does not involve the pleural space or the mesothelial layer of the pleura and is subjacent to the parietal pleura. On the PA projection it is found along the costal reflection of the pleura, along the mid third of the thoracic wall. It does not involve the apical regions or the costophrenic angles until it becomes very extensive. Plaques also occur in the areas of reflection of the diaphragmatic parietal pleura (and the mediastinal pleura as well). Parietal pleural plaques occur over bony prominences and tendonous surfaces (thus involving primarily the pleura overlying the central tendon of the diaphragm). Pathologically plaques show great variation in size and shape. They are rarely thicker than 1 centimeter in cross section, until they are very far advanced.

Radiographically in the PA projection the plaques are described as shadows which are seen in "profile" with a sharply defined edge; or en face with ill defined margins. Frequently many of the plaques are projected partially in profile and partially en face. Thus the x-ray images are the result of the size, shape, and location of the plaque, but particularly the shadow will vary with the direction of the x-ray beam and the thickness of the tissue. The use of oblique projections is particularly important not only to confirm suspected questionable shadows on a PA projection but to discover additional areas of plaque formation that are not obvious on the PA projection. By rotating the patient in the oblique projection, plaques which are seen en face can be brought out in profile, and the true cross-sectional width more accurately measured.

Frequently difficulties arise as to whether certain shadows seen on the radiograph may be due to causes other than plaques. On the average it takes 20 or more years for a plaque to form and be radiographically identifiable. It usually takes three to five years for a plaque to change its size or shape. The use of comparison films for progression is helpful in the differential diagnosis. Furthermore, one must be familiar with shadows that simulate plaques.

Interdigitations of the external abdominal oblique and serratus anterior muscle slips cause shadows overlying the ribs. When they are bilateral, symmetrical and equal they are readily identifiable. They tend to disappear on the oblique view. Not infrequently, single muscle slips cause difficulties. Comparison with old films or future films for

progress is of value as one cannot always be certain that an early plaque is beginning in the area of a suspected muscle shadow. Subpleural fat casts problematical shadows. Computed tomography is helpful. Rib injuries with overlying pleural thickening, iatrogenic and postoperative pleural changes can cause localized pleural thickening. Subpleural metastatic disease, (e.g. myeloma, breast metastases, thymomas, and melanomas) is a consideration; as well as uncommonly metastatic Hodgkin's histiocytic lymphoma and other lymphomas causing localized pleural thickening (can be differentiated clinically).

Characteristically calcifications in pleural plaques occur in the center of the plaque. However, calcification is seen only in 15% of asbestos related plaques radiographically, whereas it is found in 85% of the cases pathologically. Calcifications secondary to tuberculosis empyema, hemothorax, and other etiologies which are events that occur in the pleural space, resulting in calcifications which are more medially disposed and are further away from the internal surfaces of the ribs. Tuberculosis tends to be unilateral but can be bilateral. Finding other evidence of old Tbc is helpful. With rib injuries present on the film this leads one more towards the diagnosis of the calcification being due to trauma, particularly if it is unilateral. Other rare causes of calcifications which may simulate plaques are irradiation, mineral oil aspiration, pulmonary infarction adjacent to the pleura, and even calcification of the pleura secondary to scleroderma has been described. Although calcifications in plaques are more commonly bilateral they can be unilateral and a careful history as well as seeking evidence of other disease processes helps in the differential diagnosis.

The calcifications that are seen en face radiographically are varied and can be nodular, linear, circumferential, irregular, pseudovascular, and amorphous. Occasionally when they are very extensive they appear to have a "holly leaf" or "candle wax" appearance. The use of oblique views for defining their extent and width is of great value (also in differentiating calcifications in cartilages and in granulomas). On the PA projection calcifications occur not only in the region of the leaves of the diaphragm and along the thoracic wall, but they can occasionally be found in the mediastinum and even in the pericardium. Oblique views help to show the extent of the calcification along the mediastinal area and the pericardial region. Computed tomography is a much more sensitive method of picking up plaques and calcifications in all involved areas.

The most common finding in surveys of large numbers of patients exposed to asbestos dust is a noncalcified parietal pleural plaque located along the costopleural margin or on the surface of the diaphragm. This does not mean that less frequently one can see associated diffuse pleural thickening with or without plaques; interstitial disease with or without plaques; or pleural effusions with or without plaques. Any of these events can overlap with one another. All findings appear to be dose and time related. Generally, a light exposure results in an asymptomatic patient showing isolated plaques after a long latent period. With a heavy exposure one tends to find more interstitial disease in a shorter time frame. Occasionally, however, with very heavy exposure one can find extensive diffuse plaques with calcification, with a short latent period.

Diffuse pleural thickening is non-specific but when it occurs following asbestos dust exposure, it tends to involve more of the visceral pleura rather than the parietal pleura. Radiographically one cannot differentiate

visceral or parietal pleural thickening except when one finds thickening in the interlobar fissues. Diffuse pleural thickening usually obliterates the costophrenic angle. Computed tomography is particularly helpful in outlining circumferential pleural thickening of the diffuse type which might not be recognized on the plain film. Interlobar visceral pleural thickening does occur less commonly and even interlobar calcified plaque formation can occur.

A rare type of "hyalinosis progressiva maligna" or "hyalinosis complicata" has been described. This may or may not be accompanied by pleural effusions. Diffuse pleural thickening usually occurs unilaterally, but spreads contralaterally over a short period of time. Pathologically, both visceral and parietal pleura are thickened. There is a diffuse exudative pleural "rind" and these patients have been operated on with no evidence of mesothelioma formation. They have a very poor prognosis and tend to die of infections and respiratory failure.

Benign pleural effusions are now recognized with increasing frequency (occurring from 8 to 10 years on the average after the initial exposure). They may be clear or bloody and can be unilateral or bilateral occurring with or without plaque formation. More frequently they result in diffuse pleural thickening but often they disappear with no evidence of any residual pleural changes. However, one must exclude a malignant mesothelioma by careful clinical evaluation and follow-up of the patients. Pericardial effusions and pericardial calcifications have been described.

Any patient with a history of asbestos dust exposure pleural effusion should be considered as having a mesothelioma until proven otherwise. Characteristically the pleural effusions usually do not cause a shift of the heart or mediastinum. This is usually due to the encompassing pleural tissue "rind". Computed tomography is helpful in outlining the extent of the mesothelioma particularly when used for prognosis during therapy. The incidence of mesothelioma is not related to cigarette smoking as is bronchogenic carcinoma. Mesotheliomas do metastasize both ipsilaterally and contralaterally (usually before the patient dies there are distant metastases). Clubbing is more common with mesotheliomas but mesotheliomas are much more infrequent tumors than are bronchogenic carcinomas.

Pleural plaques do not degenerate into mesotheliomas. A pleural plaque merely means that the patient has been exposed to asbestos dust and is a "marker" for asbestos dust exposure. Bronchogenic carcinomas must always be looked for on the radiograph for any patient in which plaques are found (since the plaques mean asbestos dust exposure). Cigarette smoking and asbestos dust exposure are synergistic in causing bronchogenic carcinoma.

A change which is being recognized with increasing frequency is infolding of the lung associated with plaque formation or other pleural thickening. Infolding of the lung near areas of abnormal pleura is associated with segmental and subsegmental atelectasis resulting in "pseudotumor" formation (which must be differentiated from bronchogenic carcinoma). Characteristically, a relatively wide line extending towards the costopleural margin from the shadow of the "pseudotumor" should make one suspect a possible non-neoplastic situation. Computed tomography, needle aspiration biopsy and comparison with previous films are helpful

in the differential diagnosis. The finding is non-specific. It has also been found following pneumothorax, pleural fluid with tuberculosis, and hemorrhage secondary to trauma. It should be considered in patients known to have been exposed to asbestos dust and careful study to prevent an unnecessary thoracotomy is required.

Family exposure does occur and the finding of plaques in a young adult particularly when calcified, should alert one to the fact that the occupational history should include not only the immediate family, but other relatives and also all areas in which the patient has lived. It should be emphasized that it does not take a heavy expsure to cause a pleural plaque. Exposures of only a few months have been described resulting in plaques after a very long latent period (as much as 25-30 years after a light exposure).

Bilateral pleural plaques will be discovered with increasing frequency when they are particularly looked for on every radiograph. They merely mean that the patient has had asbestos dust exposure and should be correlated particularly with a lifetime occupational and family history. The patients are usually asymptomatic and must be cautioned not to smoke. Lifetime radiographic surveillance for any progressive changes as well as the possibility of a future occurrence of a pleural or parenchymal neoplasm, is indicated.

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