Asbestos-Related Pleuropulmonary Disease

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Educational Objectives:
1. Identify risk factors for asbestos exposure
2. Define the various subtypes of asbestos related lung disease
3. Discuss the components of an appropriate evaluation and follow up for patients with known or suspected asbestos related lung disease

Scenario 1:
A 65-year-old male with a history of tobacco use (45 pack-years, current smoker), undocumented COPD (has recent breathing problems, started on inhalers by primary care physician, no spirometry has been done), and hypertension presented to your office for evaluation of an abnormal chest CT scan. His primary care physician performed chest imaging as a part of a lung cancer screening program. He was told to follow up with a pulmonologist for this CT abnormality to discuss next steps in management. He may have had chest x-rays in the past but doesn’t remember the details. He recently retired after working as a subcontractor for the last 45 years. He mostly did welding and cut concrete without respirator use. His CT is shown below in Figure 1.

Figure 1. Representative slice of patients CT chest.
Question 1: What is asbestos?

“Asbestos” is a broad term referring to a group of fiber containing hydrated magnesium silicates. They naturally occur as rocks throughout the world and are still mined heavily in Russia and China with well over 700,00 million metric tons mined per year in 2022. Asbestos minerals form long fibers that are woven and have extremely desirable properties in heat, fire, acid, and electrical resistance. However, when these fibers are disturbed and separated into microscopic fibrils, there are risks of inhalation. The most common form of asbestos (~95% of US consumption) is called Chrysotile (chemical formula Mg₃(Si₂O₅)(OH)₄), with fibrils in a serpentine form. About a third of the world’s countries have completely banned the use of any asbestos products, although they are still permitted for certain applications in the US.

<table>
<thead>
<tr>
<th>Mineral: Group and Form</th>
<th>Location of Major Deposits, Commercial or Other</th>
<th>Main Commercial Uses and/or Other Sources of Human Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASBESTOS MINERALS</td>
<td></td>
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<tr>
<td>Serpentine</td>
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<td></td>
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<tr>
<td>Chrysotile (white asbestos)</td>
<td>Canada (Quebec, British Columbia, Yukon, Newfoundland, Russia, China (Szechwan), Brazil, Mediterranean countries (Cyprus, Corsica, Greece, Italy), southern Africa (South Africa, Zimbabwe, Swaziland)</td>
<td>Brake lining, shipbuilding and repair, polishing of precious stones, stone cutting, whetstone cutting, foundry operations (mainly for insulation) Asbestos cement products (pipes, gutters, tiles, roofing); insulation, fireproofing, reinforced plastics (fan blades, electric switchgear); textiles; friction materials; paper products; filters, spray-on products</td>
</tr>
<tr>
<td>Amphibole</td>
<td></td>
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<tr>
<td>Crocidolite (blue asbestos)</td>
<td>South Africa (Northwest Cape, western Australia)</td>
<td>Used in combination, mostly in cement but also in some of the products listed above</td>
</tr>
<tr>
<td>Amosite (brown asbestos)</td>
<td>South Africa (Northern Province, former Transvaal Finland)</td>
<td></td>
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<tr>
<td>Anthophyllite</td>
<td></td>
<td>Fillers in rubber and plastics</td>
</tr>
<tr>
<td>Tremolite</td>
<td>Contaminates ore in certain asbestos, talc, iron, and vermiculite mines; also found in some agricultural soils</td>
<td>May or may not be removed in processing; has rural domestic uses (e.g., stucco)</td>
</tr>
<tr>
<td>Cummington-grunerite</td>
<td>Contaminates ore in certain iron mines (often not fibrous)</td>
<td>No commercial use</td>
</tr>
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</table>

*Table 1. Types of asbestos. (adapted from Murray and Nadel’s Textbook of Respiratory Medicine)*
Question 2: What aspects of the occupational history would make you suspicious for possible asbestos-related lung disease?

Asbestos exposure may occur via occupational exposure, in asbestos mining, or outside of work (such as para-occupational exposure via handling soiled work clothes, living near a geological source where asbestos is disturbed, or living near a facility that processes asbestos). Occupations involving maintenance or demolition of structures containing asbestos materials are at risk as well (see Table 2). In the United States, asbestos use has been very restricted since the 1970s-1980s by federal and state regulation, though its use is still permitted in some products such as brake pads. Of note, there is no significant health risk associated with occupying a building containing asbestos that is adequately maintained and undisturbed (i.e. not respirable). Internationally, bans on the commercial use of asbestos exist in numerous other countries. However, mining of asbestos continues to occur in countries including Russia, China, Brazil, and Kazakhstan.

The following occupations and industries may raise concerns for asbestos exposures.

<table>
<thead>
<tr>
<th>Occupations</th>
<th>Industries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plumbers</td>
<td>Construction</td>
</tr>
<tr>
<td>Pipefitters</td>
<td>Shipbuilding and repairing</td>
</tr>
<tr>
<td>Steamfitters</td>
<td>Chemicals and other manufacturing</td>
</tr>
<tr>
<td>Electricians</td>
<td>Nonmetallic mineral stone products</td>
</tr>
<tr>
<td>Insulation workers</td>
<td>Railways</td>
</tr>
<tr>
<td>Carpenters</td>
<td>Yarn, thread, and fabric mills</td>
</tr>
<tr>
<td>Laborers</td>
<td>Trucking</td>
</tr>
<tr>
<td>Boilermakers</td>
<td>Plastic and rubber manufacturing</td>
</tr>
<tr>
<td>Welders and cutters</td>
<td></td>
</tr>
<tr>
<td>Janitors</td>
<td></td>
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</tbody>
</table>

Table 2. Professions at risk of asbestos exposure. (Adapted from Wagner GR, Lancet 1997)

There is also a significant environmental risk for people living close to facilities where asbestos is mined and used. For example, the vermiculite mine in Libby, Montana was contaminated with the Tremolite form of asbestos, and between the 1970s and 2000s more than 200 people (about 10% of the town’s population) died from asbestos related lung disease.

There is a long latency time from asbestos exposure to detection of asbestosis or mesothelioma, with an estimated range of about 10-40 years. Epidemiological studies have also demonstrated a dose response.

In the US, current OSHA standards specify that employers should ensure no employee is exposed to an airborne concentration of asbestos greater than 0.1 fiber per cubic centimeter of air in an 8-hour time-weighted average. They also specify that medical surveillance should occur in employees exposed to asbestos above the permissible exposure limit, including at least annual
medical and work histories and questionnaires, physical examination, CXR, pulmonary function tests, and any other evaluation deemed necessary by the examining physician.

Question 3: What are the subtypes of asbestos-related lung disease?

**Pleural Plaques**
- Pleural plaques are benign consequences and the most common manifestations of prior asbestos exposure. These occur in more than half of patients and are virtually pathognomonic for asbestos exposure. They are radiographic/histologic finding only and do not cause any pulmonary symptoms. These usually arise from the parietal pleura, and when originating from the visceral pleura they are more often associated with other asbestos-related lung disease. There is a significant lag time between asbestos exposure and the development of plaques, as long as 20-30 years from first exposure. It is believed that sub-pleural lymphatics carry the inhaled microscopic asbestos fibers to the pleura where these remain. Then, these were internalized by mesothelial cells, which leads to fibrosis and hyaline membrane production. Under histologic examination, there may or may not be asbestos fibers present in the plaques. Curiously, for patients with an equivalent asbestos exposure, presence or absence of plaques does not correlate with risk of developing malignancy.

**Diffuse Pleural Thickening (DPT)**
- Although DPT and pleural plaques share similar names and a benign nature, they are distinct disease processes with different causes. DPT is a broader disease not limited to asbestos exposure, arising from the visceral pleura, and often manifesting a few years after exposure to asbestos. Unlike pleural plaques, DPT is believed to result from fibrosis due to chronic pleural irritation rather than direct fiber internalization. In cases related to asbestos, it may follow the development of benign pleural effusion or respond to reactive oxygen and nitrogen species and inflammatory cytokines triggered by asbestos fibers. DPT is diagnosed radiographically when the pleura is measured to be >3 mm thick for 8 cm in the craniocaudal dimension and 5 cm in the lateral or anterior/posterior dimension. While DPT can lead to restrictive physiology and severe symptoms, the overall prognosis is generally favorable. Decortication may be considered in severe cases, but mortality from DPT alone is rare, typically occurring only in isolated cases without associated asbestosis or malignancy.

** Rounded Atelectasis**
- In cases of significant parietal pleural scarring, such as in pleural plaques and DPT, adjacent alveoli are prone to collapse in a pattern extending from the pleura. Unlike typical plate-like atelectasis, rounded atelectasis is, by definition, always adjacent to the pleura, and vessels and bronchi entering the area of collapse appear bent, forming a “comet tail” motif that is typical for rounded atelectasis. The collapse itself is rarely symptomatic, and when accompanied by other evidence of pleural disease should not be cause for alarm. However, if detected as a solitary lesion, further investigation is warranted to rule out an underlying peri-pleural malignancy.

**Benign Asbestos Pleural Effusion (BAPE)**
- Approximately 3-7% of asbestos-exposed workers develop BAPE, a potentially underestimated condition due to its asymptomatic nature and found incidentally on imaging. These effusions often spontaneously resolve in a few months, but some cases may persist or recur over several years. While predominantly unilateral, BAPE can manifest bilaterally or switch sides during resolution and recurrence. It may manifest earlier than other asbestos-related findings, such as within 10 years of asbestos
exposure. The effusion is typically exudative, blood-tinged, and may be eosinophilic. Asbestos fibers are uncommonly found in the effusion but may be present in the underlying lung parenchyma. Diagnosis is based on consistent occupational history and exclusion of other causes including malignancy.

**Asbestosis (Fibrosis, ILD)**

- Not all asbestos-related pleuropulmonary disease is asbestosis. Asbestosis refers to interstitial lung disease and pulmonary fibrosis caused by inhalation of asbestos fibers. Fibrosis can be mild or can progress to diffuse pulmonary fibrosis. Radiologically, asbestosis presents with a HRCT pattern of UIP. Histologically, the fibrosis typically starts with a predominantly subpleural distribution similar to UIP but differs in that fibroblastic foci are less common in asbestosis. Asbestosis often demonstrates mild fibrosis of the visceral pleura, which is not seen in UIP. Asbestos fibers (also called ferruginous bodies) may be present on histological examination if iron staining is used, and their presence support the diagnosis of asbestosis.

**What about cancer?**

- Asbestos exposure is linked to increased risk of lung cancer and mesothelioma. The risk of malignancy is dose-dependent and synergistic with smoking: compared to nonsmokers without asbestos exposure, smokers with asbestos exposure have 8-fold higher odds of developing lung cancer while nonsmokers with asbestos exposure have 1.7-fold higher odds.
- While mesothelioma is famously associated with asbestos exposure, the most common cancer associated with asbestos exposure is lung cancer (i.e. bronchogenic carcinoma). The subtypes of lung cancer associated with asbestos exposure are similar to the overall distribution of lung cancer subtypes.

**Question 4: What are the characteristic imaging findings of each type of asbestos-related process?**

**Pleural Plaques:**

![Image of pleural plaques](image)
Figure 2. Pleural plaques may be more difficult to visualize on plain chest films [A], with one study quoting a sensitivity a little over 50%, whereas chest CT [B] has a 95-100% sensitivity for detecting them. Approximately 15-20% of plaques are calcified, increasing their visibility on XR. As plaques grow, they form a characteristic "table-top mesa" appearance [C].
Diffuse Pleural Thickening:

Figure 3. Diffuse pleural thickening is diagnosed radiographically when the pleura is measured to be >3mm thick for 8 cm in the craniocaudal dimension and 5 cm in the lateral or anterior/posterior dimension. It usually involves the costophrenic angles and can therefore be mistaken for pleural fluid on plain film images.

Rounded Atelectasis:
Figure 4. Rounded atelectasis seen in the Lingula with additionally noted pleural plaque along the diaphragm [A], seen with typical comet tailing [B, source: Radiopaedia], named after the light distortion that follows telescopic images of celestial bodies. [C, source: European Space Agency]

BAPE:
Asbestosis:

![Figure 5. A. High-resolution CT scan (HRCT) of 65-year-old man with asbestosis. B. HRCT of 54-year-old man with asbestosis. (Source: Akira et al)](image)

**Question 5: What are the typical clinical presentations of patients with asbestos-related disease?**

Certain asbestos-related pleuropulmonary disease such as pleural plaque, pleural thickening, and BAPE are often asymptomatic. In contrast, asbestosis often presents with nonspecific respiratory symptoms including progressive dyspnea on exertion, chest pain, and nonproductive cough. Sputum production and wheezing are less common and may be associated with concomitant COPD or a history of tobacco use. Physical exam may reveal bibasilar crackles and digital clubbing. Severe cases may be associated with hypoxemia or pulmonary hypertension and right heart failure. Evaluation should include full PFTs, which characteristically show a restrictive pattern with decreased TLC and FVC, decreased DLCO, and no obstruction (though there is some controversy about whether a mixed obstructive-restrictive pattern may sometimes be seen even in never smokers).

**Question 6: What diagnostic studies should be considered in someone being evaluated for asbestos-related lung disease?**

For patients incidentally diagnosed with pleural plaques, there are no specific tests that need to be obtained. The imaging findings are pathognomonic with an appropriate clinical history. The plaques do not cause symptoms. Although patients with either more concerning or non-diagnostic plain films (as may be seen in milder disease) should be referred for CT imaging to further evaluate the pleura and lung parenchyma. In patients with asbestos-related lung disease, baseline PFTs are recommended as significant restrictive physiology may warrant referral for decortication or other pleural procedures.

Patients with BAPE often undergo thoracentesis as effusions precede other lung findings. Other etiologies of effusions should be ruled out, regardless of a convincing occupational history. It is rare to find asbestos fibers in the pleural fluid, although they may be present.
While asbestos fibers are rarely found in pleural fluid, increased eosinophils, combined with an appropriate history, is usually adequate for diagnosing asbestos-related disease.

During bronchoscopy with bronchoalveolar lavage or thoracentesis, asbestos fibers may be seen in the pleural fluid or BAL aspirate. In parenchymal lung biopsy, asbestos bodies (fibers encased in collagen and iron-rich material) may be present in patients with asbestosis; however these bodies are absent in pleural plaques.

![Figure 6. An asbestos body as may be seen on histopathology.](image)

**Question 7: What other pulmonary processes are in the differential for patients who may have asbestos-related pulmonary disease?**

Pleural plaques are pathognomonic for asbestos exposure, and BAPE will likely be diagnosed relatively confidently based on history and pleural fluid analysis.

However, asbestosis, especially if not accompanied by pleural plaques, can be challenging to differentiate from other conditions, with IPF being a primary radiologic mimic, as both will display a UIP pattern on CT scan. The main differentiator will likely be the clinical history of exposure, and the presence of other asbestos-specific findings, such as pleural plaques or effusion.

Silicosis may also be an asbestosis mimic. As noted previously, the main motif in asbestos fibers is the silicate molecule. Both conditions share similar pathophysiology involving phagocytosis of particles by alveolar macrophages, leading to inflammation, collagen synthesis, and fibrosis upon macrophage apoptosis. The overlap in occupational exposure to asbestos and silica dust further complicates diagnosis. Silicosis will be more likely to involve hilar nodes, have upper lung zone predominance on HRCT, exhibit less pleural involvement, and may exhibit egg-shell calcification. Ultimately, treatment (or prevention of further progression) is effectively the same.

Other interstitial diseases such as hypersensitivity pneumonitis, sarcoidosis, and radiation pneumonitis may be confused with asbestosis on imaging. Table 3 outlines specific radiographic characteristics aiding differentiation, complementing a comprehensive patient history for a conclusive diagnosis.
Table 3. A subset of interstitial lung disease that may be similar radiographically. (adapted from Tzilas et al)

**Question 8: How would you manage a patient that you have diagnosed with asbestosis?**

Asbestosis lacks a disease-specific treatment. Table 4 shows 2004 ATS recommendations for management after a diagnosis of asbestosis. Patients with asbestosis should be counseled about its occupational nature, expectations for progression, and their cancer risk in the context of asbestos exposure history and other risk factors. For progressive fibrosis, treatment with nintedanib and referral for lung transplantation can be discussed. Routine preventive care such as vaccinations and supportive care such as pulmonary rehabilitation and oxygen therapy for those with hypoxemia should be recommended.

At this time, there are no USPSTF guidelines regarding lung cancer screening related to asbestos exposure, however some feel that asbestos exposure should warrant regular lung cancer screening. Patients should be counseled to stop smoking.

When a diagnosis of asbestosis is established, patients should be counseled about potential legal avenues for compensation and may be advised to seek legal counsel.
Recommendations for Management after Diagnosis of Asbestosis

1. Patient notification
   - Inform patient of work-related illness
   - Report to appropriate authority as occupational disease, as required by law
   - Inform patient that there are options for compensation

2. Impairment assessment
   - Conduct an assessment of functional impairment
   - Rate impairment in accordance with ATS criteria, which are incorporated into the AMA Guides

3. Tertiary prevention
   - Smoking cessation (primary prevention for smoking-related disorders)
   - Withdrawal from further excessive exposure
   - Immunization (pneumococcal pneumonia, influenza)
   - Management of concurrent respiratory and other diseases

4. Monitoring
   - Chest film and pulmonary function testing should be conducted every 3 to 5 years
   - Active monitoring (periodic screening for colon cancer)
   - Observation and elevated index of suspicion but not screening for lung cancer, mesothelioma, gastrointestinal cancers (other than colon)

5. Development of a patient-specific management plan for symptomatic disease

Table 4. Adapted from ATS 2004 guidelines.

References: