Welcome to this medical grand rounds seminar on asbestos toxicity. My name is Dr. Vik Kapil and I come to you from the Centers for Disease Control and Prevention, Agency for Toxic Substances and Disease Registry in Atlanta, Georgia. I am a physician specializing in Occupational and Environmental Medicine and serve as Chief of the Surveillance and Registries branch at ATSDR.

The goal of this seminar is to increase your knowledge of asbestos toxicity and your ability to evaluate potentially exposed patients. By the end of this seminar, you will be able to:

- Describe what asbestos is
- Identify the most important route of exposure to asbestos
- Identify populations most heavily exposed to asbestos
- Describe four asbestos-associated diseases
- Identify the most common findings on medical evaluation
- Describe chest radiograph findings associated with asbestos-associated diseases
- Identify pulmonary function test findings associated with asbestosis
- Describe other tests that can assist with diagnosis
- Explain primary treatment strategies for asbestos-associated diseases
- Identify instructions that should be given to patients

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- You can receive 1.0 hours in category 1 CME credit toward the AMA Physician's Recognition Award.
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If you'd like to receive one of these types of continuing education credit for this seminar, you can go to the web page where this web cast was located and link to the online assessment questionnaire and posttest. Once you complete the process online, you will be able to print your continuing education certificate.

The course number for the Environmental Medicine Grand Rounds Asbestos Toxicity is WB/CB/CV 1115.

So what is asbestos?

Asbestos is a generic term for a group of six fibrous silicate minerals that are formed when silicate chains bond with various ions. The result is long, thin, separable fibers, often arranged in parallel or matted masses.

Asbestos occurs naturally, but much of its presence in the environment stems from mining and commercial uses. In the past, asbestos was widely used commercially because of it's:

- high tensile strength
- flexibility, and
- resistance to break down by acid, alkali, water, heat, and flame.

Although these properties make asbestos commercially useful, the fact that asbestos is also non-biodegradable causes problems. Once released into the environment, it tends to persist.

Asbestos fibers are classified as either serpentine or amphibole depending on their shape. As you can see here, serpentine fibers are very long, snake-like fibers. Amphibole fibers, on the other hand, are straight and rod-like. Both serpentine and amphibole fibers can cause disease, but their toxicity may differ in some respects.

For example tremolite asbestos may be more carcinogenic than chrysotile asbestos. However, both types of asbestos are carcinogenic. Chrysotile is the only member of the serpentine family. It accounts for 93 percent of the world's commercial, purposeful use of asbestos.

The amphiboles include:

- actinolite
- amosite
- anthophyllite
- crocidolite and
- tremolite

These types of fibers account for 7 percent of the world's commercial, purposeful use of asbestos or are encountered as contaminants.

Asbestos exists pretty much everywhere in the environment due to its past uses and occurrence in nature. Background levels of asbestos are very low, though, and not likely to pose a significant health risk.

Health concerns in the United States during the 1970s led to voluntary phase-outs and partial bans on asbestos. Before that, asbestos had been widely used commercially in the automobile, home and commercial building construction and shipbuilding industries. Some specific products that were used in these industries prior to 1975 include clutch, brake, and transmission components; electric motor components, and cement pipes.

Asbestos can also be a contaminant in commercial products made with vermiculite. Vermiculite ore from Libby, Montana, was contaminated with tremolite asbestos. Until 1990, this ore was mined at Libby and processed at more than 200 sites around the country.

The contaminated vermiculite was used in potting soil, home insulation, fireproofing and a variety of other applications. These products were distributed nationally, and the insulation remains in some homes today.

Although all the vermiculite used in today's products is generally amphibole free, old contaminated vermiculite insulation is a particular concern because it is a loose material that can easily be disturbed, causing asbestos fibers to be released into the air.

Almost every city in the United States contains a number of homes and buildings that were built before the use of asbestos was significantly reduced during the mid 1970's. In fact when we speak of old homes and buildings a structure that was built just over 30 years ago is often not even considered "old." Yet many of these pre-1970's buildings may contain asbestos in many different areas.

The biggest problem is with asbestos in friable (easily pulverized or crumbled) materials. Again, because these materials are easily disturbed, asbestos fibers can be released into the air. Asbestos embedded in solid materials (such as wallboards) is less easily disturbed, so it is less likely to be released into the air. Even solid materials can be problematic, though, if they are cracked or otherwise disturbed—during home repairs and renovations, for example.

Any work involving asbestos-containing materials should be performed by trained and certified professionals who know how to encapsulate or remove these materials properly. People who try to do this work on their own often make the problem worse by disrupting the materials in a way that releases large quantities of asbestos fibers into the air.

Although we may not realize it, many of us may frequently come in contact with and use home, office and building materials that were manufactured before 1975, before the use of asbestos decreased.

A few examples of these types of products include:
- duct and home insulation,
- fireplace artificial logs or ashes, and
- underlayment for sheet flooring, carpet underlays, and floor tiles.

Although its use has been significantly reduced, asbestos is still used in a limited number of products that are produced and sold today.

Some examples include:
- Car and truck brakes pads and clutches,
- roofing material,
- vinyl tiles, and
- some cement pipes

In nature, asbestos exists mainly in underground rock formations. In most areas, the rock is too deep to be disturbed easily, so fibers are not released into the air. In some areas, asbestos-bearing rock is close to the surface. This is the case in parts of California and in some other areas of the world. When asbestos-bearing rock lies close to the surface, construction and other human activities can disturb the rock, releasing asbestos fibers into the air. These fibers can also be released through the natural weathering of the rock by the forces of nature.

Given the wide range of uses of asbestos in the past, you can imagine that many people were exposed to asbestos as part of their work. Mining and milling of asbestos and product manufacture using asbestos all entailed heavy exposures. These heavy exposures peaked in the United States during the 1960s and 1970s, and have declined since then for two reasons:

- asbestos has been phased out of most products in the United States, and
- OSHA was created, and instituted workplace regulations for asbestos including Personal Protective Equipment (PPE) and worker education on health risks involved with hazardous substances in the workplace.

Because asbestos related disease may take several decades to develop, aging workers from that era are now showing the latent effects of exposure and are presenting with an array of asbestos-associated diseases. Those diseases will likely peak in the next decade or so, and may then start to decline. For the moment, we are still seeing many people who were heavily exposed to asbestos in the United States in the 1960s and 1970s during their work as:

- mechanics,
- construction workers,
- shipyard workers, and
- military personnel

Even people who didn't work in these occupations were sometimes exposed if they shared the same workspace with people who handled asbestos. These secondary exposures are something to look for if you see a patient with signs of asbestos-associated disease but without an occupational history suggestive of exposure.

Paraoccupational exposures are also important to keep in mind. In the past, due to lack of proper industrial hygiene, many workers carried asbestos dust home on their skin, hair, and clothing. So, household contacts were sometimes exposed to significant levels of asbestos by breathing in this dust during close contact with the worker or his or her clothing.

People living around asbestos facilities such as mines, factories handling asbestos, etc., could be exposed, too, if asbestos dust was released to the air and soil around the facility. That's another exposure scenario to keep in mind.

Asbestos is still used in brake pads, roofing materials, vinyl tile, and imported cement pipe and sheeting. Today, the workers with the greatest occupational risk for asbestos exposure are those in the construction trades, including workers in building and equipment maintenance. These workers are mainly at risk because their occupation makes them likely to disturb asbestos fibers in old asbestos-containing materials.

Again, when these materials are deteriorating or disturbed, they can release significant quantities of asbestos fibers into the air. Indeed, given the right conditions, asbestos release can be a problem in the home as well.

People can receive significant asbestos exposures in the home if they have loose tremolite-contaminated vermiculite insulation or cracked or crumbling asbestos-containing materials. They can also be exposed if previously intact solid materials are disrupted during home repairs or renovations.

People need to be cautioned not to work with home asbestos materials themselves. If they want to encapsulate or remove the materials, or if they want to undertake renovations that might disturb asbestos-containing materials, they should find a qualified and licensed contractor specializing in asbestos abatement. For information on where to find certified asbestos contractors in your state, contact your local department of health or environment.

In the past few decades, some people have been worried about children being exposed to asbestos in schools that have asbestos tiles, pipe coverings, insulation, etc. Studies tell us that asbestos levels in schools are usually extremely low. Again, if the material is solid and intact, it might not need abatement, or encapsulation may be sufficient. Improper disposal and removal can make the problem worse.

Lastly, some people might be worried about environmental exposure to asbestos, because it is a naturally occurring mineral. In most areas, background levels of asbestos are extremely low. In those areas that I mentioned before, where asbestos-bearing rock is close enough to the surface to be disturbed by construction, release of asbestos can be quite heavy locally.

So far, I've given you an overview of where people run into asbestos and who tends to be exposed to asbestos. Now I'll get into the details of exposure pathways, biologic fate, disease pathogenesis, and what we see clinically.

All along, I've been referring to the release of asbestos fibers into the air when asbestos-containing materials are loose, crumbling, or disturbed. You won't be surprised to hear, then, that inhalation of contaminated air and dust is the most important pathway of exposure to asbestos. Inhalation is the most important pathway for two reasons: it is the most common pathway, and it is the pathway most likely to result in illness. Historically, people commonly inhaled asbestos fibers:

- during work with asbestos,
- during work in the same space as others working with asbestos,
- from workers' skin, hair, and clothing, and
- in areas surrounding mining operations.

Today, it is more common for people to inhale asbestos fibers:

- during work in homes and buildings where renovations or demolitions disturb asbestos-containing building materials, especially loose or crumbling materials.
- during work with other asbestos-containing products, such as brake pads, and
- less commonly, in areas where construction is disturbing asbestos-bearing rock.

Ingestion is a minor exposure pathway. People can swallow asbestos fibers in material removed from the lungs via mucociliary clearance. They might also ingest asbestos fibers in drinking water, though drinking water levels are usually extremely low.

In the past, when people didn't wear adequate personal protective equipment, handling asbestos could result in heavy dermal exposures. This could lead to the development of corns forming from asbestos fibers penetrating the skin.

I've stated that the most important pathway for exposure to asbestos is inhalation. What happens to those asbestos fibers after they've been inhaled? Some of the fibers are exhaled and some are deposited in the respiratory tract and removed by mucociliary transport and swallowing. Wide fibers, those with a diameter of 2 to 5 microns, are especially likely to be deposited and cleared in this fashion. Many fibers, especially long thin fibers, penetrate the lungs. In fact, they typically reach the lower airways and alveoli.

In the respiratory tract and lungs, the asbestos fibers are subject to several defenses:

- Initially, some fibers are cleared via mucociliary transport, followed by ingestion. Fibers that are ingested in this way, and indeed those ingested in drinking water, are typically eliminated in the feces unchanged.
- Some fibers are subject to attempted phagocytosis. Due to the fibrous nature of asbestos, phagocytosis is usually not successful in eliminating asbestos fibers. Instead, the fibers are fragmented and split.
- Finally, some asbestos fibers are encapsulated by proteins and deposited in ferrous material in a drumstick configuration called a ferruginous body, or an asbestos body. This image shows a typical asbestos body.

Despite all these defenses, deposited asbestos fibers are retained in lung tissue for many years. How long they are retained depends on the size, shape, and type of fiber. Wider fibers have a diameter greater than 2 to 5 microns and tend to be deposited in the upper respiratory tract and cleared. Long thin asbestos fibers reach the lower airways and alveoli and tend to be retained in the lungs. However, it is important to remember that asbestos fibers of all lengths can induce pathological changes and cannot be excluded as contributors to asbestos-related diseases.

From the lungs, some of the shorter, fragmented fibers migrate to pleural and peritoneal spaces, especially following patterns of lymphatic drainage. The presence of asbestos fibers in the lungs sets off a variety of responses leading to cell injury, fibrosis, and possibly cancer.

Three processes are believed to account for asbestos' pathogenicity. The first process is the direct interaction of asbestos fibers with cellular macromolecules. Asbestos fibers carry a surface charge, which enables them to adsorb to cellular macromolecules (proteins, DNA, RNA). This columbic binding induces changes in macromolecular conformation thereby affecting protein function and this process can lead to structural changes in chromosomes.

The second pathogenic process caused by asbestos is the secondary generation of reactive oxygen species, or ROS. The presence of asbestos fibers in the lungs results in the formation and release of ROS by alveolar macrophages, mainly hydrogen peroxide (H2O2) and the superoxide radical anion (O2-). These ROS can react with each other to produce hydroxyl radicals, which are even more potent oxidizers.

The third includes other cell-mediated mechanisms. The presence of asbestos fibers in the lungs also causes macrophages, other lung cells, and pleural cells to release cellular factors that lead to:

- inflammation
- macrophage recruitment
- cell and DNA damage
- cell proliferation, and
- apoptosis (or cell death)

The exact role of all these cellular processes in the formation of fibrosis, which is the hallmark of asbestosis, is still being defined. All of these mechanisms can result in disease and some of them in cancer. Asbestos is both genotoxic and carcinogenic.

Both the International Agency for Research on Cancer and the U.S. Environmental Protection Agency classify asbestos as a known human carcinogen as do OSHA and NIOSH. Some experts believe that the amphibole type of asbestos is a more potent carcinogen than the serpentine type (chrysotile), but that's still a matter for research and discussion.

Asbestos fibers mainly enter the body via inhalation, and are mostly retained in the lungs where they induce a range of pathogenic responses that most commonly affect the respiratory system. Four respiratory conditions are associated with asbestos exposure:

- parenchymal asbestosis
- asbestos-related pleural abnormalities
- lung carcinoma, and
- pleural mesothelioma.

Asbestos exposure can also affect other organ systems. Non-respiratory syndromes associated with asbestos exposure include:

- peritoneal mesothelioma
- possibly other extrathoracic cancers, and
- rarely, cor pulmonale or constrictive pericarditis.

Any combination of these asbestos-related conditions can be present in a single patient. Clinically, it is important to distinguish non-malignant conditions from malignant diseases, and asbestos-associated conditions from other, more treatable diseases. I'll talk about differential diagnosis in a moment.

First, I'll talk a bit more about each of the asbestos-associated diseases.

I'll start with parenchymal asbestosis. This is the disease most people think about as an asbestos-associated disease. Parenchymal asbestosis is a diffuse or patchy pneumoconiosis caused by inhalation of asbestos fibers. Fibers lodged in lung tissue produce diffuse alveolar and interstitial fibrosis, leading to reduced lung volumes, decreased compliance, and impaired gas exchange.

Parenchymal asbestosis is associated with a restrictive pattern of disease as evidenced by pulmonary function testing, with obstructive features due to small airway disease. The main symptom is exertional dyspnea, which has an insidious onset and becomes progressively worse as the disease progresses.

Radiographic changes are usually seen about 20 years after first exposure to asbestos. Symptoms appear later, usually 20 to 40 years after exposure. Parenchymal asbestosis has no unique signs or symptoms, but the results from constellation of sufficient exposure history and latency, dyspnea on exertion, bibasilar end-inspiratory crackles, restrictive lung function, and characteristic x-ray appearance are highly suggestive. The disease tends to be more advanced in smokers due to smoking-related decreases in the clearance of asbestos fibers from the lungs.

People with parenchymal asbestosis are at increased risk of lung carcinoma and mesothelioma. Both of these malignancies can occur in an asbestos-exposed person even in the absence of asbestosis, but asbestosis tends to be a marker of the types of high-level asbestos exposures that result in an increased risk for lung cancer. The combination of asbestos exposure and smoking increases the risk of lung cancer even more. Parenchymal asbestosis is not treatable; we treat the symptoms rather than the disease itself. So it's important to distinguish this disease from other, more treatable diseases.

About half of people with asbestosis die within 10 years of diagnosis. According to one study, 20% of these deaths are from the pneumoconiosis itself, 39% are from asbestos-associated lung cancer, 9% are from mesothelioma, and 32% are from other causes. You probably noticed that I referred to asbestosis as parenchymal asbestosis. This is to distinguish it from what some call pleural asbestosis.

Today we more often use the term asbestos-related pleural abnormalities." These are a group of four types of pleural changes. They are relatively benign conditions compared to other asbestos associated diseases.

Pleural plaques are well-circumscribed areas of thickening, usually located bilaterally on the parietal pleura. Patients are usually asymptomatic, though there can be small reductions in lung function. Pleural plaques are the most common manifestations of asbestos exposure. They are so common that they are considered to be a biomarker of asbestos exposure. Most typically, they form following short-term high-level exposures or chronic low-level exposures to asbestos and their appearance depends on length of time from the first exposure rather than a threshold dose like asbestosis.

Pleural plaques can result from exposures to other types of materials, however, including talc, silica, and refractory ceramic fibers. Pleural plaques are not themselves premalignant, but are associated with an increased risk for lung cancer and mesothelioma.

Benign asbestos pleural effusions are small, unilateral effusions, often occurring as blood-stained exudates. They are usually asymptomatic, but can rarely cause pain, fever, and dyspnea. These effusions typically last for months, and can recur.

Diffuse pleural thickening is a noncircumscribed fibrous thickening of the pleura. The fibrotic areas are ill-defined, involving costophrenic angles, apices, lung bases, and interlobar fissures. Patients with this condition are often asymptomatic, but the fibrosis can cause mild or rarely severe restrictive deficits, resulting in progressive dyspnea and chest pain. Diffuse pleural thickening is most typically associated with moderate- to high-level exposures and have been reported to occur in 10% of patients with asbestosis.

Rounded atelectasis (or folded lung) occurs when blebs of lung tissue are caught in bands of fibrous pleural tissue with an in-drawing of the bronchi and vessels. This produces a distinctive x-ray appearance: a rounded pleural mass with bands of lung tissue radiating outwards. Patients with rounded atelectasis are usually asymptomatic, though again some patients develop dyspnea or dry cough.

Exposure to asbestos is associated with all major histological types of lung carcinoma. Although most lung cancers are associated with exposure to tobacco smoke, it is estimated that 4-12% of lung cancers are related to occupational exposure to asbestos.

An individual's risk of developing lung cancer depends on:

- the level, frequency, and duration of asbestos exposure
- the time elapsed since the first exposure occurred
- the age of the individual when the exposure occurred
- the individual's smoking history, and
- the type and size of the asbestos fibers involved

Asbestos-associated lung cancer is usually associated with large cumulative exposures, and typically occurs 20 to 30 years after exposure. If the person was heavily exposed to asbestos and also smokes, the risk is much greater.

It is estimated that 20-25% of heavily exposed asbestos workers will develop bronchogenic carcinomas.

Most asbestos-related lung cancers reflect the dual influence of asbestos exposure and smoking. Smoking and asbestos exposure have a synergistic effect on the risk of lung cancer. Since there may be multifactorial contributors toward the development of lung cancer including individual susceptibility factors, the issue of causality is tricky.

Asbestos-associated lung cancer does tend to occur in the lower lung fields, but that doesn't exclude other causes. The presence of parenchymal asbestosis is an indicator of high-level asbestos exposure, but again asbestos-associated lung cancer can occur even in the absence of asbestosis. In any case, diagnosis and treatment of the cancer is essentially the same, regardless of etiology. The chest x-ray of a person with asbestos-associated lung cancer looks pretty much the same as one you'd see with another etiology.

Diffuse malignant mesothelioma is a tumor arising from the thin serosal membrane surrounding the body cavities, arising from the pleura, peritoneum, tunica vaginalis testis, and ovaries.

Pleural mesothelioma affects the pleura, while peritoneal mesothelioma affects the peritoneum. In either case, the disease is rapidly invasive locally.

I'll talk about pleural mesothelioma first.

Pleural mesothelioma frequently presents with sudden onset of pleural effusion or thickening, dyspnea, and chest pain. By the time these symptoms appear, the disease is often rapidly fatal. The average survival time is 8 to 14 months following diagnosis. The one-year survival rate is less than 30%. When we see patients with a history of asbestos exposure, we usually have many years to be on the alert for mesothelioma. This disease usually has a long latency period, anywhere from 10 to 60 years; 30 to 40 years is typical. So it's important to monitor patients to increase the chance of early detection. This is especially important because, though the disease is rare compared to lung cancer, it is on the rise. In the year 2000, about 3,000 people in the U.S. died of mesothelioma. The incidence of mesothelioma is increasing as people exposed during the peak asbestos exposure years—1940 to 1970— develop the disease.

Pleural mesothelioma is a sentinel tumor for asbestos exposure. All asbestos types can cause mesotheliomas, but the amphibole form is thought by some to be more likely to induce this tumor than the serpentine form. Typically, patients who develop pleural mesothelioma have a history of short-term high-level exposure or chronic low-level exposure to asbestos. Mesothelioma incidence has likely started to decline in the United States, although it may still be increasing in Europe and Australia due to more abundant and prolonged used of asbestos in these areas.

Peritoneal mesothelioma is similar to pleural mesothelioma, except that it arises in the peritoneal membranes. Like pleural mesothelioma, this tumor is rapidly locally invasive and often quickly fatal by the time it is diagnosed. A "doughy" feeling may be noted on abdominal palpation. Peritoneal mesothelioma is quite rare, though. Pleural mesothelioma is much more common in males, at a 5:1 ratio, while peritoneal mesothelioma is only slightly more common in males, at a 1.5:1 ratio.

Some studies suggest that other extrathoracic cancers might also be associated with asbestos exposure. The cancer most commonly mentioned is colon cancer. Certain researchers suggest that some cases of cancer of the larynx, stomach, kidney, and esophagus could also be linked to asbestos exposure. Except for cancer of the larynx, these cancers are presumed to be due to ingestion of asbestos.

The idea that ingested asbestos could cause cancer is controversial. Nevertheless, ATSDR and the National Toxicology Program agree that it is prudent to consider increased risk of gastrointestinal cancer, especially colon cancer, in persons exposed to asbestos. Colon cancer screening for people over 50 years of age who have been exposed to asbestos in the past is recommended. The same is recommended for everyone over the age of 50. Screening for other extrathoracic cancers in people exposed to asbestos is not currently recommended.

As with all severe lung diseases, the pulmonary fibrosis of asbestosis can lead to increased resistance to blood flow through the pulmonary capillary bed, eventually resulting in pulmonary hypertension, leading to right ventricular dilatation or cor pulmonale. Cor pulmonale is most commonly seen in patients with severe parenchymal asbestosis, though it can occur with less severe fibrotic disease—especially if obstructive lung disease is simultaneously present, as is often seen in smokers.

Constrictive pericarditis is very rare, but can also occur secondary to asbestos-associated disease. The pericarditis results from severe fibrosis or calcification of the pericardium.

As we have seen, exposure to asbestos can lead to a variety of diseases, mainly lung diseases and their sequelae. Obviously, not everyone who is exposed to asbestos develops all, or even any, of these diseases. So who is most likely to develop an asbestos-associated disease?

The two main risk factors are the nature and extent of exposure to asbestos and exposure to other carcinogens. I'll talk first about the nature and extent of exposure. In general, the higher the total dose of asbestos, the greater the pathogenic response and the greater the risk of disease. This means the risk of disease depends in part on:

- the concentration of asbestos fibers involved in the exposure
- the duration of exposure, and
- the frequency of exposure.

Brief high-level exposures and chronic lower-level exposures tend to increase the risk of disease. But very low-level and brief exposures can also cause disease. Pleural mesothelioma, for example, can occur with brief and very low-level exposures.

In summary, the more asbestos fibers that are retained in the lungs, and the longer they are retained, the greater the risk of disease.

It won't surprise you to hear that smoking increases the risk of asbestos-associated lung cancer. In fact, smoking greatly increases the risk—up to 50 times, according to some research. Smoking can also worsen the result of asbestos exposure in patients who develop parenchymal asbestosis. This is because smoking results in lung damage. These increases in risk are believed to diminish after a person quits smoking. Smoking does not appear to increase the risk of mesothelioma.

Now that I've talked about what asbestos is, who is at risk for exposure, and the diseases that are associated with asbestos, I'm going to talk about what happens in the clinical setting. As you know, asbestos toxicity is irreversible. However, an early and accurate diagnosis can greatly improve the patient's prognosis. Whether a patient has been exposed to asbestos but is asymptomatic, or the patient is already exhibiting symptoms that may be related to a past exposure, it is important to perform a thorough medical evaluation.

This should include:

- an assessment of the clinical presentation
- an exposure history
- a medical history
- a physical examination, and
- a chest radiograph and pulmonary function tests.

In some cases, the patient may need more specialized radiologic and laboratory testing such as a high resolution CT (HRCT) or, very rarely, bronchoalveolar lavage (BAL) or a lung biopsy, if deemed necessary by a pulmonologist.

I'll talk about each of these aspects of medical evaluation in some detail, and then I'll move on to discuss management strategies.

When a patient presents, he or she may be completely asymptomatic, but may be concerned about a past or present exposure to asbestos. In other cases, the patient will present with signs or symptoms of an asbestos-associated disease.

If the patient has parenchymal asbestosis, the most typical clinical presentation includes an insidious onset of dyspnea on exertion. This might be accompanied by fatigue and possibly weight loss. In more advanced stages of disease, there may be clubbing of the fingers or cor pulmonale.

A patient with asbestos-related pleural abnormalities will generally have an unremarkable presentation, and will often be asymptomatic.

On the other hand, some patients with diffuse pleural thickening may present with progressive dyspnea and intermittent chest pain. And, patients with rounded atelectasis may present with dyspnea and dry cough.

Asbestos-associated lung cancer looks very much the same as lung cancer of other etiologies. The patient is often asymptomatic, though as the disease advances the patient may present with:

- fatigue
- weight loss
- dry cough
- hemoptysis,
- dyspnea, or
- chest pain.

The same is true for pleural and peritoneal mesotheliomas. Patients are often asymptomatic while the tumors are developing. These tumors are rapidly invasive locally, though and some patients with advanced disease may present with a sudden onset of symptoms:

- dyspnea
- severe and progressive chest pain
- pleuritic chest pain, or
- systemic signs of cancer such as weight loss and fatigue.

As you talk with and examine the patient, it is important to keep in mind the possibility of other diseases with overlapping findings. It is especially important to distinguish between other treatable conditions and asbestos-associated diseases…and between non-malignant asbestos-associated conditions and malignant asbestos-associated diseases.

Some respiratory conditions with findings similar to those of asbestos-associated diseases are:

- idiopathic pulmonary fibrosis
- other pneumoconioses related to non-asbestos exposures such as talc and silica
- hypersensitivity pneumonitis
- sarcoidosis, and
- chronic obstructive pulmonary disease.

A non-respiratory condition with similar findings is left ventricular failure.

It is important to note that if the patient's asbestos exposure was recent, this exposure is probably not the cause of the patient's symptoms. Asbestos-associated diseases have latency periods, so sufficient time must have elapsed to attribute symptoms to asbestos toxicity. So, it is clearly important to have a good understanding of the patient's exposure and medical history in order to make an accurate diagnosis. Even if the patient is currently asymptomatic, knowing the patient's exposure history is vital to understanding his or her risk for future disease.

Many asbestos exposures are work-related. That means it is important to find out about the patient's work history when taking an exposure history. What jobs has the patient held during his or her lifetime? Did any of these jobs involve working with asbestos? Did the patient work near asbestos or close to others who were handling asbestos?

Whether or not the patient was exposed in the workplace, other sources of exposure should be investigated. You'll need to explore the possibility of para occupational exposures from family members or other household contacts, or from living near vermiculite or asbestos processing plants.

You might also ask about other possible exposures stemming from hobbies or other recreational activities possibly involving asbestos. Once you establish the probability that an exposure took place, you'll want to get a better feel for the source, intensity, and duration of exposure. The more detailed the information you can get from the patient, the easier it will be to assess risk of disease.

You might see if they can provide workplace dust measurements or a cumulative fiber dose, for example, or a description of exposure scenarios so you can get a feel for the extent to which they have been exposed. And you'll need to ask about use of any personal protective equipment such as respirators in the workplace during work with asbestos-containing materials.

Remember that asbestos-associated diseases have long latency periods. Patients who have been exposed, even those who have been significantly exposed, can be asymptomatic for decades. The medical history is just as important as the exposure history in making a diagnosis. The patient may have a history of smoking, which can increase the risk of lung cancer or add to the lung damaging effects of asbestosis.

The patient may also have or have had other treatable respiratory conditions or non-respiratory conditions with overlapping findings that could confound the diagnosis of asbestos-associated disease. In any case, you should conduct a detailed review of the patient's medical history, including the clinical status of all organ systems.

Once you have taken the patient's exposure and medical history, you'll have a sense of the patient's risk for asbestos-associated diseases and the likelihood that these diseases could reasonably account for the patient's current symptoms.

The next step is the physical examination.

The physical examination will include all the usual elements with a focus on the lungs, heart, digits, and extremities. Particularly if the patient has parenchymal asbestosis, on pulmonary auscultation you may hear fine, bibasilar end-inspiratory crackles; these are typically described as sounding like Velcro separating.

Bibasilar rales occur in a bilateral basilar distribution at the base of the lungs, with pan-inspiratory or end-inspiratory accentuation. They start at the mid-axillary lines and spread to the posterior bases. As disease progresses, they spread to levels higher up from the bases.

Be aware that they can be difficult to distinguish from rales due to congestive heart failure. In addition to rales, you will of course also check for other signs of respiratory disease, such as clubbing of the fingers and cyanosis.

You'll also want to keep an eye out for possible signs of other neoplasms:

- hoarseness
- blood in urine or stool
- "doughy" feeling in the abdomen associated with peritoneal mesothelioma.

Regardless of the patient's clinical presentation and your findings on physical examination, if the patient has a history of asbestos exposure you should also consider ordering a chest x-ray and pulmonary function tests. Pulmonary function tests are particularly useful in detecting parenchymal asbestosis, though asbestos-related pleural abnormalities may also occasionally be associated with pulmonary function defecits. If a patient has parenchymal asbestosis, abnormal pulmonary function tests will typically reveal restrictive defects. Findings may typically include a reduction in forced vital capacity (FVC) with a normal FEV1/FVC ratio.

If a patient has asbestos-related pleural abnormalities, lung function tests will typically indicate either normal results or reduced FVC associated with diffuse pleural thickening.

In some cases of asbestosis, combined patterns of restrictive and obstructive disease may be seen. Consider consulting a pulmonologist if the diagnosis is unclear, there is a rapid decline in pulmonary function, or if there is a need for a tissue biopsy or BAL (such as cases where lung cancer or mesothelioma or an infectious etiology is suspected).

The chest radiograph is also useful in diagnosing asbestos-associated diseases. It can identify structural parenchymal changes associated with asbestosis or assess asbestos-related pleural disease such as pleural plaques and mesothelioma.

Asbestosis can occur in the absence of radiographic changes, however, so diagnosis should be based on an overall clinical evaluation. Diagnosis of asbestosis should emphasize but should not be based totally on radiographic findings per the diagnostic criteria of the American Thoracic Society.

Interpreting chest x-rays of patients with asbestos-associated diseases can be somewhat complex in that early or subtle changes are easy to miss. The International Labor Organization has developed a classification system for these radiographic changes. Physicians certified to read chest x-rays using this classification system are termed B readers; we strongly recommend using B readers or other standard measures to interpret chest x-rays when you suspect asbestos-associated disease.

That said, I'll briefly review typical radiographic changes seen with the major asbestos-associated diseases.

In patients with parenchymal asbestosis, the chest x-ray typically shows small, parenchymal opacities with a pattern of irregular linear opacities. With advanced disease, the X-ray may also show an appearance that blurs the heart border and diaphragm. This is caused by combined interstitial and pleural involvement, and is often referred to as the "shaggy heart sign." You might also see honeycombing and upper lobe involvement, which have been known to develop in advanced stages of asbestosis. This image shows typical changes that may not be seen with milder disease. Asbestosis is usually associated with high-level exposures, but lesser fibrosis, with fewer or no radiographic changes, can occur with lower-level exposures.

With asbestos-related pleural abnormalities, radiographic findings depend on which type of abnormality is present.

Pleural plaques typically appear as multiple bilateral well-circumscribed areas of thickening found on the parietal and visceral pleura, sometimes with calcification. Pleural effusions are seen as blunting of the costophrenic angle, or a density in the pleural space. Diffuse pleural thickening is usually marked by thickening of the pleura, which appears as a lobulated prominence of the pleura, adjacent to the thoracic margin. Rounded atelectasis (also known as folded lung syndrome) appears as a rounded pleural mass with bands of lung tissue radiating outwards.

The radiologic appearance of asbestos-associated lung cancer is the same as that of lung cancer of other etiologies. Pleural mesothelioma typically appears as pleural effusions, a pleural mass or a diffuse pleural thickening.

Asbestos-associated malignancies mainly involve the lower portions of the lungs, but they can occur in other areas of the lungs as well. Suspected asbestos-associated malignancies require pathology confirmation.

If the chest x-ray is inconclusive, it can sometimes be useful to perform a CT or a high resolution CT (HRCT) scan of the chest. These scans are more sensitive, and can be used to detect early changes that do not appear in the chest radiograph. They are especially useful in detecting and assessing:

- early parenchymal changes of asbestosis
- subtle pleural disease, such as plaques and rounded atelectasis
- the difference between asbestos-associated pleural plaques and soft tissue densities, and
- mesothelioma.

However, these tests do have their drawbacks. They are associated with higher doses of radiation, and their cost effectiveness and efficiency as screening tools have not yet been established. Other tests that may be useful include:

- Bronchoalveolar lavage (or BAL) may be useful for the detection of asbestos exposure and is performed by pulmonary specialists or thoracic surgeons. BAL can help assess exposure to asbestos by looking for the presence of asbestos bodies in BAL fluid.

Asbestos bodies are inhaled asbestos fibers that have been coated by hemosiderin by alveolar macrophages. BAL is used by specialists to detect possible asbestos exposure in order to facilitate histopathological confirmation of asbestos-associated diseases, and facilitate differential diagnosis. BAL is preferable to the use of open lung biopsies in the detection of asbestos fibers.

- Lung biopsies are rarely necessary in the diagnosis of asbestosis and pleural plaques. Appropriate referral to a specialist is indicated if lung cancer or mesothelioma is suspected since a lung biopsy may be indicated under those conditions.
- ABG and pulse oximetry may be helpful to measure decreases in oxygen in the blood associated with respiratory changes associated with asbestos-related disease.
- Exposure to asbestos may increase a patient's risk for colon cancer. Routine colon cancer screening is recommended in all adults over the age of 50.

Once you make a diagnosis of asbestos-associated disease, what do you do?

Asbestos-associated diseases such as asbestosis and pleural plaques are not readily treated. Treatment is largely symptomatic, except of course for chemotherapy and the like for malignant disease. So, prevention and prompt attention to symptoms are key.

First, it is important that the patient avoid further exposure to asbestos to the extent possible. They should be using proper personal protective equipment. OSHA standards provide for the use of respiratory protection above the action level. In practice, individuals should be able to maintain their employment while being protected from exposure.

Symptomatic patients may also need documentation of impairments caused by asbestos-associated disease for work-related claims. This may require the assistance of a specialist. There is a list of resources in the Asbestos Case Studies in Environmental Medicine, which is located on the ATSDR web site. All patients, whether symptomatic or not, should be monitored for the onset or progression of disease. Regular exposure and medical histories should be taken, along with routine physical examinations.

These should be followed by periodic chest x-rays and pulmonary function tests to help identify early signs of disease. Smoking cessation and patient education are also important aspects of managing asbestos-associated diseases in all patients.
I'll talk a bit about each of the major diseases.

Parenchymal asbestosis is irreversible and the rate of disease progression varies. Corticosteroids or immuno-suppressants have not been effective.

Researchers are working on new treatments, but we've seen little advancement thus far. So, in addition to the interventions that I just mentioned, management of parenchymal asbestosis includes:

- stopping further exposure

- careful monitoring to facilitate early diagnosis
- smoking cessation
- regular influenza and pneumococcal vaccines, and
- pulmonary rehabilitation when needed
- disability assessment, and
- aggressive treatment of respiratory infections.

Patients with advanced disease and hypoxemia at rest, during exercise, or during sleep will benefit from continuous home oxygen therapy, which may help in prevention of cor pulmonale. These patients should be informed that pleural plaques are evidence of asbestos exposure.

Although the plaques are benign in most cases, they can result in pulmonary impairment in some cases. Patients with pleural plaques are also more likely to have or develop parenchymal asbestosis or asbestos-related cancers, so they should be monitored every 1 to 3 years depending on age, years since first exposure, or level of change.

Lung cancer is the most frequent cause of asbestos-related deaths. Treatment of asbestos-associated lung cancer is, once again, the same as that of lung cancer of other etiologies. It should include appropriate combinations of surgery, chemotherapy, and radiation.

For the rare patient with diffuse malignant mesothelioma, prognosis is generally poor and patients seldom live longer than 8 to 14 months following diagnosis.

Now, what to tell your patients. Patients who visit your office may present differently. Some will be asymptomatic and will remain so for many years. Some will just be beginning to show signs of illness, and some will have well established disease. I've talked already about clinical management of the various asbestos-associated conditions. In addition to explaining whatever tests and interventions you recommend, you'll need to give your patients some basic guidance about self care and when to call you.

The Agency for Toxic Substances and Disease Registry has developed a patient education sheet on asbestos toxicity that can help you explain all this to patients. This patient education fact sheet is located on the ATSDR web site and gives some basic information about asbestos and asbestos-associated diseases, as well as provides checklists for self care and instructions.

I'll go over the basic advice now, and you can use the checklist as needed in your practice.

For self care, you should tell your patients to:

- Provide you with contact information for their employer.
  Employers are required by the Occupational Safety and Health Administration (OSHA) to provide personal protective equipment and medical surveillance, as well as health information on asbestos.

- Stop smoking and avoid exposure to second-hand smoke. This one is obvious: smoking increases the risk of lung cancer, decreases lung defenses, and worsens the effects of asbestosis.
- Removal from further asbestos exposure (if possible) or provision of personal protective equipment up to OSHA standards.

Patients also need to understand when and why they should call you for further medical attention. In particular, they should call you if they develop signs or symptoms of health changes, so you can evaluate the changes and their significance with regard to any asbestos-associated disease they have or may be developing.

Again, take a look at the patient education sheet. The instruction's checklists can help you explain these things to your patients.

Now I'd like to review some of what I talked about in today's presentation.

Asbestos was widely used in industries throughout the United States until the 1970s and is still present in materials today. Because of the long latency periods seen with asbestos-associated diseases, patients who were exposed during the peak occupational exposure years are now beginning to exhibit signs of disease.

Exposures to asbestos continue to occur in the workplace, mainly in the construction trades. Many of today's occupational exposures occur during repair, renovation, removal, and maintenance of asbestos that was installed years ago. People living in homes where asbestos materials are loose, crumbling, or disturbed can also be exposed. It is very important to remember that renovations and abatements involving asbestos should be carried out by trained and certified asbestos contractors.

They know how to encapsulate or remove asbestos properly to avoid further release of asbestos into the air.

When asbestos fibers enter the lungs, a series of responses occur that produce pathogenic changes and ultimately disease.

Asbestos-associated diseases include parenchymal asbestosis, asbestos-related pleural abnormalities, lung carcinoma, and mesothelioma. Asbestos exposure may increase the risk of colon cancer.

When a patient presents, he or she may be asymptomatic or may have signs of asbestos-associated disease. In either case, medical evaluation begins with an assessment of the patient's clinical presentation, a complete exposure and medical history, and physical examination.

If the patient has been exposed to asbestos, even if he or she displays no signs or symptoms of asbestos-associated disease, it is prudent to proceed with a chest radiograph and pulmonary function tests.

Early detection is very important in managing asbestos-associated diseases, so you'll want to repeat these tests regularly. And, of course, order other tests as needed based on the patient's clinical status. Smoking cessation and patient education should be emphasized as well.

Management of asbestos-associated diseases focuses on:
- preventing further exposure to asbestos and other respiratory irritants
- impairment assessment
- aggressive treatment of respiratory infections
- annual influenza and regular pneumococcal vaccines at intervals recommended by the CDC, and
- respiratory therapies and pulmonary rehabilitation when needed.

Today I've given you an overview of asbestos and diseases associated with asbestos exposure.

For more information on asbestos and asbestos-associated diseases, you may contact ATSDR directly using the information provided on this slide. You may also refer to Where can I find more information? in the Case Study in Environmental Medicine: Asbestos Toxicity, for a list of Web resources and suggested readings.

As a reminder, if you'd like to receive continuing education credit for this seminar, please go to the web page where this web cast was located and link to the online assessment questionnaire and posttest. Once you complete the process online, you will be able to print your continuing education certificate.

This concludes the seminar, thank you.