An overview of how asbestos exposure affects the lung

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People exposed to asbestos often develop lung disease in later life; manifestations include benign, malignant, or diffuse interstitial lung disease. This evidence based review covers who is considered to be at risk, different ways that exposure to asbestos affect the lung, and matters relating to compensation. Because many doctors in primary and secondary care encounter patients who have been exposed to asbestos, they need to be aware of how different people can be affected.

Who is at risk of asbestos related lung disease?

All people who have worked with asbestos are at potential risk of asbestos related lung disease through inhalation of fibres. Asbestos is a mineral silicate that occurs naturally in various forms. It is resistant to heat and other means of destruction, which explains its extensive use during the 19th and 20th centuries. The fibrous nature of asbestos allows it to be woven into cloth or incorporated into cement materials, ceiling tiles, brake and clutch linings, pipe and boiler insulation, flooring, resins, polymers, and filter papers.

Historically, people with the highest exposures worked in asbestos mining, milling, and production of asbestos textiles. Countries that currently produce large amounts of asbestos include Russia, Kazakhstan, China, and Canada. In the 1920s to 1940s asbestos developed in textile workers with a latency of only a few years and progressed rapidly to death, because exposure was high. The risk to people using asbestos products was recognised in shipyard workers in the 1950s, and an association with mesothelioma was determined in the 1960s through a case-control study in South African miners. However, one of the first suggestions that exposure to asbestos can cause lung disease was in 1899 in an industrial diseases board of enquiry. Today, most people with asbestos related lung disease have a clear history of exposure, such as mixing asbestos cement or fitting insulation (builders), working with asbestos insulation materials (plumbers and electricians), or cutting asbestos cement sheet materials, although some may have been exposed without their knowledge (for example, shipyard workers or ship engineering workers). The lifetime risk of developing mesothelioma was highlighted in a recent study in which joiners, plumbers, electricians, painters, and construction workers had a greater likelihood of being diagnosed within the general population. The occurrence of asbestos related lung disease in spouses who laundered the clothing of workers exposed to asbestos is also well established.

A detailed occupational history—to determine the occupation, what it involved, dates of employment, and length of asbestos exposure—is therefore important in all patients presenting with respiratory symptoms. Because of the unregulated use of asbestos in developing countries, the incidence of asbestos related lung disease worldwide is likely to rise significantly in the years ahead.

How does asbestos affect the lung?

The shape of asbestos fibres results in their retention within the lung. Clearance from the lung occurs by the mucociliary ladder and phagocytic ingestion by macrophages or endocytosis by pneumocytes, but migration to the pleural surface can occur via the lymphatic system. The common forms of asbestos exist as serpentine curved fibres (chrysotile (white)) or amphibole straight...
fibres (crocidolite (blue), amosite (brown), and anthophyllite). Curved fibres carry a slightly lower risk of lung disease than straight fibres, although no safe threshold of exposure to asbestos of any type exists.

**What sort of lung disease can asbestos cause?**

**Benign pleural disease**

**Pleural plaques**

Pleural plaques consist of layers of hyalinised collagen fibres usually found on the parietal pleura, and they occur in 20-60% of people who have been exposed to asbestos. They most commonly appear as calcified areas adjacent to the sixth to ninth ribs and along the surface of the diaphragm, but they tend not to be evident at the lung apices or costophrenic angles. Pleural plaques can usually be identified on a chest radiograph (fig 1), although computed tomography is more sensitive and distinguishes them from solid tumours if the diagnosis is uncertain. They do not undergo malignant change or generally cause symptoms, although pleural plaques have been associated with anginal pain.

**Diffuse pleural thickening**

Diffuse thickening of the pleura is less specific to asbestos exposure than pleural plaques. It may occur after exposure to asbestos, but other causes include previous haemothorax, tuberculosis, chest surgery, radiation, infection, and exposure to drugs such as methysergide. Diffuse pleural thickening on a chest radiograph is characterised by a smooth continuous pleural density affecting at least 25% of the lateral chest wall, with or without blunting of the costophrenic angle. It has also been defined on computed tomography as a continuous sheet of pleural thickening (>5 cm wide, >8 cm in craniocaudal extent, and >3 mm thick). In extensive diffuse pleural thickening, patients may become breathless and have a restrictive ventilatory defect on lung function tests. In diffuse thickening (which is usually bilateral), the pleura will appear smooth, and the mediastinal border will be unaffected, whereas in mesothelioma, the pleura is likely to be unilaterally irregularly thickened and the mediastinal border affected. If the diagnosis is uncertain, computed tomography and biopsy are warranted.

**Benign asbestos related pleural effusion**

Benign exudative pleural effusions are often preceded by episodes of “asbestos pleurisy.” They can occur within 15 years of asbestos exposure but may also appear much later. Because of confusion with a malignant effusion, a pleural biopsy is usually needed, and this shows non-specific inflammation. Benign effusions may resolve spontaneously (often leaving an area of pleural thickening) or require drainage if large enough to cause symptoms.

**Interstitial lung disease**

**Asbestosis**

Asbestosis is caused by inhalation of asbestos fibres and is a typical pneumoconiosis (interstitial lung disease caused by inhaled inorganic dusts). The condition is directly related to the magnitude and duration of exposure to asbestos. After a latent period of 20-30 years, patients with developing asbestosis experience an insidious onset of breathlessness and reduced exercise tolerance; cough, sputum production, and wheezing are less common. As the condition progresses, fine bilateral inspiratory crackles, finger clubbing, and cor pulmonale may occur. Data from the Health and Safety Executive indicated that 111 deaths in the United Kingdom in 2006 were caused by asbestosis, and that 393 death certificates mentioned asbestosis (www.hse.gov.uk/statistics/causdis/asbestosis/index.htm).

Pulmonary function tests show reduced gas transfer, reduced lung volumes, a restrictive ventilatory defect, and exercise related hypoxaemia. Chest radiography may be normal, but usually shows bilateral lower zone interstitial changes, often with pleural plaques and thickening. High resolution computed tomography is a more sensitive tool (fig 2), and characteristic features include coarse parenchymal bands, subpleural linear densities, interstitial fibrotic change, and honeycombing in advanced disease. In contrast to idiopathic pulmonary fibrosis, confluent ground glass changes are rare in asbestosis, whereas thick band-like opacities are more common; the most discriminatory feature is concomitant pleural disease in asbestosis. Histological evidence is not necessary for the diagnosis to be made: typical clinical features along with previous asbestos exposure, consistent pulmonary function abnormalities, interstitial fibrosis...
Management strategies in mesothelioma

- Discuss at a multidisciplinary team meeting
- Skilful and empathetic communication of the diagnosis is needed, with provision of written patient-centred information
- Provide the patient with access to specialist nurses
- Liaise closely with primary care and arrange secondary care follow-up
- Discuss compensation with the patient
- Drain pleural effusions then carry out pleurodesis (talc is most effective)
- Consider an indwelling pleural catheter if pleurodesis is unsuccessful or a trapped lung is present
- Consider prophylactic or palliative radiotherapy to large biopsy or drainage sites
- Consider chemotherapy
- Consider surgery
- Consider entry into a clinical trial
- Provide the patient with access to palliative care professionals and pain clinics

(with no alternative explanation), plus other radiographic changes seen after exposure to asbestos are usually adequate. No specific treatment is available other than that for chronic obstructive pulmonary disease and cor pulmonale if present, smoking cessation, and prevention of further exposure to asbestos. The prognosis of asbestosis is highly variable and depends on the extent of lung involvement and severity of coexisting chronic obstructive pulmonary disease and presence of other comorbidities.

Malignant disease

Lung cancer

Exposure to asbestos causes lung cancer independently of cigarette smoking. In an analysis of 23 epidemiological studies, asbestos exposure increased the risk of lung cancer by a similar factor in non-smokers and smokers, with a synergistic (multiplicative) interaction seen between asbestos exposure and cigarette smoking. Even in the absence of asbestosis, very heavy asbestos exposure may cause lung cancer. Lung cancer should be considered in patients with asbestosis who have haemoptysis, worsening cough, chest pain and breathlessness, weight loss, and anorexia. Diagnostic and management strategies are the same as those for lung cancer in general (www.sign.ac.uk; www.nice.org.uk).

Mesothelioma

Mesothelioma is an aggressive pleural tumour with increasing incidence. Data from the UK mesothelioma register indicated that the annual number of deaths from mesothelioma had risen from 153 in 1968 to 1848 in 2001, and it is predicted to peak at 1950-2450 cases annually between 2011 and 2015. In 2006, the UK Health and Safety Executive gave the number of deaths from mesothelioma on death certificates as 2056 (85% male; www.hse.gov.uk/statistics/causdis/mesothelioma/). However, official mortality data may underestimate the extent by 10%. In one well conducted study of 622 patients with mesothelioma (312 men), disease was caused by occupational or domestic asbestos exposure in 86% of men and 38% of women. Around half of the men were construction workers, and only four had worked for more than five years in the manufacture of asbestos products. The lag period between initial exposure and death varies, but one retrospective analysis (1105 patients with definite mesothelioma) found a median latency of 32 years, with 96% of cases occurring after at least 20 years.

Focus on mesothelioma

The diagnosis of malignant mesothelioma is based on a combination of clinical, radiological, and histological features. However, a clear histological diagnosis removes any uncertainty and makes compensation claims more straightforward.

Clinical presentation

British Thoracic Society guidelines suggest that malignant mesothelioma should be considered in any patient with a pleural effusion or pleural thickening, especially if a history of asbestos exposure and chest pain is present. Characteristically, the pain is dull, diffuse, progressive, and occasionally pleuritic. Breathlessness may be caused by a pleural effusion or circumferential pleural thickening. Patients may also present with a palpable chest wall mass, finger clubbing (usually caused by underlying asbestosis), and features of a pericardial effusion caused by local extension in progressive disease. Ascites caused by peritoneal mesothelioma and secondary hydro pneumothorax are uncommon but recognised presentations.

Investigations

Chest radiography and computed tomography may show a pleural effusion, lobulated or nodular pleural changes, a pleural mass, rib destruction, chest wall involvement, or a small hemithorax as a result of lung entrapment (fig 3); other features of exposure to asbestos may also be present.

Pleural fluid in patients with mesothelioma is straw coloured or blood stained. Cytological analysis of pleural fluid occasionally leads to the diagnosis, although a pleural biopsy is usually needed. Percutaneous pleural biopsy has historically been performed using an Abrami’s
Compensation options according to type of lung disease

<table>
<thead>
<tr>
<th>Condition</th>
<th>Type of compensation possible</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pleural plaques</td>
<td>None</td>
<td>Existing legislation currently being reviewed*</td>
</tr>
<tr>
<td>Diffuse pleural thickening</td>
<td>IIDB and usually a lump sum under PWCA; civil claim for damages</td>
<td>For a civil claim, patients must have loss of respiratory reserve plus evidence of diffuse bilateral pleural thickening on computed tomography</td>
</tr>
<tr>
<td>Asbestos related lung cancer</td>
<td>IIDB and usually a lump sum under PWCA; civil claim for damages</td>
<td>For a civil claim, patients need to have asbestosis plus lung cancer, or a high enough degree of asbestos exposure to have doubled the risk of lung cancer</td>
</tr>
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<td>Asbestosis</td>
<td>IIDB and usually a lump sum under PWCA; civil claim for damages</td>
<td>For a civil claim, patients must have loss of respiratory reserve plus evidence of asbestosis on computed tomography</td>
</tr>
<tr>
<td>Mesothelioma with occupational asbestos exposure</td>
<td>IIDB and usually a lump sum under PWCA; civil claim for damages</td>
<td>Mesothelioma Lump Sum Payments Regulations (available from October 2008); civil claim may be possible with secondary asbestosis history (for example, spouse washing husband’s overalls)</td>
</tr>
<tr>
<td>Mesothelioma with non-occupational asbestos exposure</td>
<td>Lump sum under the Mesothelioma Lump Sum Payments Regulations; no IIDB; possible civil claim for damages</td>
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*Currently, legislation in Scotland differs from that of England and Wales.

IIIDB = Industrial Injuries Disablement Benefit; PWCA = Pneumoconiosis Workers’ Compensation Act 1979.

Treatment

Patients with mesothelioma should be discussed at a lung multidisciplinary team meeting (comprising chest physicians, surgeons, radiologists, pathologists, oncologists, and specialist nurses; see box). Although the benefits are uncertain, prophylactic radiotherapy to the pleural puncture site is often considered in patients who have had large chest wall incisions (during thoracoscopy or insertion of a large bore chest tube) to reduce the chance of tumour cells seeding along the track to the skin surface.

Palliative chemotherapy is offered to fit patients, despite a paucity of data showing any survival advantage. In one study, 448 patients were randomised to receive pemetrexed plus cisplatin or cisplatin alone. Median survival with pemetrexed and cisplatin was 12 months versus nine months with cisplatin alone (P=0.002). In another study of 250 patients, raltrexed and cisplatin significantly improved overall survival compared with cisplatin alone, although no differences in quality of life were seen, and the study had no placebo arm. The role of surgery is controversial, but recent data suggest that extrapleural pneumonectomy is not useful in the management of mesothelioma; however, the results of other trials are awaited (MesoVATS and MARS2). Lung sparing debulking procedures are now gaining popularity and should be considered for patients within the context of randomised trials.

The prognosis of malignant mesothelioma—especially in older men who are unfit and have peritoneal mesothelioma and sarcomatoid histology—is poor. The median survival in a variety of studies is between eight and 14 months from diagnosis.

Who is entitled to compensation?

Patients with asbestos related lung disease may be eligible for compensation through Industrial Injuries Disablement Benefit (IIDB) from the Department for Work and Pensions or a civil law claim for damages from the employer under whose auspices exposure occurred (table). Under the Limitation Act 1980, patients have only three years in which to make a civil claim.
from the date they became aware of a serious injury caused by an act or omission of the proposed defendant. Patients should be advised to consult their local Department for Work and Pensions benefits agency for advice on benefits that may be claimed (which may include attendance allowance and disability living allowance). Various charities can also provide help and support on compensation. Some compensation requests involve lengthy periods of investigation (especially civil claims), and patients should be made aware of this to help minimise psychological distress. Members of the armed forces who develop asbestos related diseases are unable to sue the crown for negligence that occurred before 1987 because of “crown immunity,” although they may be eligible to receive a war pension.

Thanks to Peter Montgomery for reviewing the section on compensation.

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CORRECTIONS AND CLARIFICATIONS

JAMA told to change its policy on investigating competing interests

In this News article by Janice Hopkins Tanne (BMJ 2009;339:b2936, print publication 25 Jul 2009, p 192) we mistakenly said that both Dr Jonathan Leo and Dr Jeffrey Lacasse wrote to JAMA and the New York Times claiming non-disclosure of support from a drug company for a study published in JAMA. Dr Lacasse has told us that, although he “wholeheartedly supports the actions that Dr Leo took,” his own involvement was limited to co-authoring letters to editors of medical journals. Dr Lacasse added that he had never contacted JAMA about conflicts of interest or contacted the media.

Medical Classics: Baby and Child Care By Benjamin Spock

In her review of this book (BMJ 2009;339:b2839, print publication 18 Jul 2009, p 177) Elizabeth Loder refers (in the fourth paragraph) to a review article in the journal Epidemiology. A reader has advised us that this article was in fact in the International Journal of Epidemiology (Gilbert et al, 2005;34:874-87).

Inquiry to be held into teenager’s death after radiation overdose

In this “In brief” News item (BMJ 2009;339:b3161, print publication 8 Aug, p 314) we wrongly edited the correctly written item. This resulted in the item seeming to suggest (by the phrase “given fatal radiation treatment”) that the radiation treatment had caused the girl’s death. This is not what we intended to publish. The first four words should have read: “A fatal accident inquiry is to be held into the death of a teenage patient with cancer who was given radiation treatment 58% higher than prescribed.”

Effects of statins in patients with chronic kidney disease: meta-analysis and meta-regression of randomised controlled trials

We have received a late correction to this research paper by Giovanni F M Strippoli and colleagues, published early in 2008 (BMJ 2008;336:645-51, print publication 22 Mar 2008). Although figures 1 and 2 (both forest plots) were correct at submission, when we redrew them we added the wrong labels to the x axis, and the errors were not picked up during the proof stage. To ensure correct representation of the data, we have redrawn these two figures and linked them to the article on bmj.com as “extra” material (see “Corrected figures” with the online article, doi:10.1136/bmj.39472.580984.AE). The figures were also wrong in the full (online) version of the article (where they appeared as figures 3 and 4).

Obituary: Bee Hooi Tan

The third author of this obituary (BMJ 2009;338:b1987, print publication 6 Jun, p 1390) is Dr Lee Teak Tan (not Dr Lee Tak).

Paracetamol plus ibuprofen for the treatment of fever in children (PITCH): randomised controlled trial

In this paper by Alastair D Hay and colleagues (BMJ 2008;337:a1302, print publication 27 Sep 2008, pp 729-33) a misunderstanding during editing of the first footnote to table 2 led to errors. In the final sentence of this footnote, the two sets of values (48, 65, and 71; and 65, 73, and 84) are percentages (not minutes) of time without fever over four hours and 24 hours after the first dose of study drugs respectively. The correct times are in the table.