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Clinical Observations Following Asbestos Exposure

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There is a spectrum of clinical entities following occupational exposure to asbestos. Methods of evaluation for these problems are reviewed. Nonmalignant clinical conditions include asbestos warts, asbestos bodies, parenchymal fibrosis (asbestosis), pleural fibrosis and calcification, and benign asbestotic pleural effusion. Asbestosis, though a benign process, is a significant cause of death. Malignant conditions associated with asbestos exposure include lung cancer, accounting for about 20% of all deaths among insulation workers and significantly related to cigarette smoking. The lung cancers tend to occur more frequently in the lower lobes and are more peripheral. Pleural and peritoneal mesothelioma and some excesses in gastrointestinal cancers are found with asbestos exposure, although these are not related to cigarette smoking. Increased rates of malignancy first become significant after 20 years from onset of exposure and are also related to duration of exposure. Difficulties with the use of death certificate data are reviewed.

Asbestos, a generic term referring to several hydrated fibrous silicates, is found widely throughout the world and has several commercially important forms, including the serpentine form chrysotile and the amphiboles amosite, anthophyllite, crocidolite, and tremolite. All are capable of producing a spectrum of clinical diseases in man and laboratory animals.

The benign clinical conditions following asbestos exposure are as follows: asbestos warts, of little clinical importance; asbestosis, a fibrosis of the lung parenchyma, and though considered a benign condition accounts for many deaths among insulation workers; pleural fibrosis and calcification which while also benign can occasionally, if very severe, lead to death by suffocation; and benign asbestotic pleural effusion, a condition somewhat less common than the malignant condition of the pleura which often too leads to effusion, pleural mesothelioma. The finding of asbestos bodies in the sputum is not a clinical condition in and of itself and should be taken as no more than a marker of prior asbestos exposure. Finding asbestos bodies in sputum has, to date, been of little diagnostic importance. Asbestos is also commonly found in the lung and also that alone is of no diagnostic significance. Taking small samples of lung tissue from 3000 consecutive autopsies in New York City has revealed asbestos to be present in about one-half of all samples analyzed (*1*).

The malignant conditions associated with asbestos exposure are as follows. First there is the problem of bronchogenic carcinoma, with the well-known association with cigarette smoking (*2*). Next is the problem of pleural and peritoneal mesothelioma. In terms of time of onset from first exposure, the problem of lung cancer becomes important after 30 to 35 years, pleural mesothelioma after about 35 years, and peritoneal mesothelioma after about 40 years. (Table 1) It appears to require heavier exposures to produce peritoneal than pleural mesotheliomas, when one reviews the experience of many cohorts. Also, there is no relationship between cigarette smoking and either pleural or peritoneal mesothelioma.

Other malignant problems associated with asbestos exposure include an increase in gastrointestinal cancers, especially of the colon and rectum and also esophagus. There is also an increase in other forms of cancer such as laryngeal carcinoma, oropharyngeal cancers, and renal cancer.

For full evaluation of any given case where asbestos is thought to have a role in producing disease, several pieces of information are necessary. Firstly, one needs to have an adequate occupational, geo-

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Table 1. Deaths among 17,800 asbestos insulation workers in United States and Canada, January 1, 1967-December 31, 1976: analysis by duration from onset of employment.

Duration from onset, (yr.)	Number of men	Person-years of observation	Lung cancer			Pleural mesothelioma			Peritoneal mesothelioma		
			Expected[a]	Observed[b]		Number[b]		No./1000 person-years	Number[b]		No./1000 person-years
				(BE)	(DC)	(BE)	(DC)	(BE)	(BE)	(DC)	(BE)
< 10	8,190	26,393	0.7	0	0	0	0	0	0	0	0
10-14	9,063	29,003	2.7	7	5	0	0	0	0	0	0
15-19	9,948	34,066	8.5	29	27	2	2	0.06	3	0	0.09
20-24	8,887	31,268	17.0	59	57	6	4	0.19	3	2	0.10
25-29	6,596	20,657	21.0	105	96	13	5	0.63	19	3	0.92
30-34	3,547	11,598	18.4	112	103	9	3	0.78	23	6	1.98
35-39	2,020	5,403	11.5	65	57	15	4	2.78	19	5	3.52
40-44	1,108	3,160	8.1	40	31	4	3	1.27	16	3	5.06
≥45	1,448	5,305	17.8	69	53	14	4	2.64	29	5	5.47

[a]Expected deaths are based upon white male age-specific U.S. death rates of the U.S. National Center for Health Statistics, 1967-1976: *smoking habits not taken into account.*

[b](BE) = best evidence, i.e., number of deaths categorized after review of best available information (autopsy, surgical, clinical); (DC) = number of deaths as recorded from death certificate information only. Data from Selikoff et al. (*3*).

graphic and social history to ascertain any and all exposure to asbestos. As the work of Wagner (*4*) in animals and Selikoff in man (*5*) have shown, very little exposure may be needed to produce disease. Secondly, in the assessment of human disease one needs to do a complete physical examination with special attention to the findings of the chest, abdomen and extremities. As is well known, however, clinical grounds alone are insufficient in many cases to make a diagnosis, especially for the evaluation of disability. Thirdly, one needs a chest x-ray, and of value in addition to the routine posterior-anterior view one may require both oblique views. This is particularly important for the evaluation of pleural changes.

Lastly, for complete evaluation, especially for the purposes of disability, one requires pulmonary function data.

Difficulties in making a proper diagnosis are legion. For the diagnosis of asbestosis to be made, a history of exposure with consistent findings on x-ray can suffice. Clinical examination alone may not reveal changes such as rales, clubbing of fingers, etc. It may also be that the x-ray appears normal but that pulmonary function testing will reveal the existence of a restrictive process. This is uncommon but can occur. As noted, all modalities of evaluation must be employed for the assessment of disability.

Problems also exist in the evaluation of malignant disease. The diagnosis of bronchogenic carcinoma may be difficult in the presence of marked parenchymal change. Carcinomas in asbestos-exposed individuals occur more frequently in the lower lobes, and peripherally, in the same areas as the parenchymal changes. If peripheral, the differential diagnosis between carcinoma and mesothelioma may be difficult. If a solitary pulmonary lesion is noted one is required to also evaluate other sites, especially the gastrointestinal tract, to rule out the possibility of a metastasis.

Difficulty in arriving at a proper diagnosis, even when using autopsy data, are illustrated by findings of Selikoff. In a cohort, followed by Selikoff, of 17,800 insulation workers with over 166,000 man-years of exposure, 1661 deaths were expected through December 31, 1976; in contrast, 2271 deaths were seen (Table 2). As expected, lung cancer accounted for 485 deaths, but 106 were expected. There were 175 deaths from mesothelioma and 166 deaths due to asbestosis. These data are based upon ascertained deaths, which included review of tissues, including those obtained at autopsy, and assessment of additional information that may not have been present on the death certificate.

According to death certificate records, instead of the 106 lung cancer deaths expected, 429 were recorded. Upon further study, including review of tissues and other clinical records, additional cases were found. The true number was 486. For cancer of the pancreas the problem was reversed. Eighteen cases were to be expected among this cohort, while 49 cases were reported, potentially leading to the conclusion that cancer of the pancreas is markedly increased among insulation workers. In reality, upon further study, only 23 cases were found, not very different from the expected number. (Table 3).

Similarly, cases of asbestosis were underestimated by about one-half.

Table 2. Deaths among 17,800 asbestos insulation workers in the United States and Canada: January 1, 1967-December 31, 1976.[a]

Underlying cause of death	Expected[b]	Observed[c]	
		(BE)	(DC)
Total deaths, all causes	1,658.9	2,271	2,271
Total cancer, all sites	319.7	995	922
Cancer of lung	105.6	486	429
Pleural mesothelioma	[d]	63	25
Peritoneal mesothelioma	[d]	112	24
Mesothelioma, n.o.s.	[d]	0	55
Cancer of esophagus	7.1	18	18
Cancer of stomach	14.2	22	18
Cancer of colon-rectum	38.1	59	58
Cancer of larynx	4.7	11	9
Cancer of pharynx, buccal	10.1	21	16
Cancer of kidney	8.1	19	18
All other cancer	131.8	184	252
Noninfectious pulmonary diseases, total	59.0	212	188
Asbestosis	[d]	168	78
All other causes	1,280.2	1,064	1,161

[a]Number of men: 17,800; Man-years of observation: 166,853.
[b]Expected deaths are based upon white male age-specific U.S. death rates of the U.S. National Center for Health Statistics, 1967-1976.
[d]Rates are not available, but these have been rare causes of death in the general population.
[c](BE) = best evidence, i.e., number of deaths categorized after review of best available information (autopsy, surgical, clinical); (DC) = number of deaths as recorded from death certificate information only. Adapted from Selikoff et al. (*3*).

Who can be expected to develop clinical problems following asbestos exposure? At the present time, one is not able to identify specific individuals and determine if they will develop any asbestos-related disease. Epidemiologic studies do allow, however, accurate assessment of disease among various groups. It is now clear that a wide variety of exposures can lead to clinically significant disease. It is also now clear that workers directly handling asbestos, either in manufacturing or with end-product use can develop asbestosis or one of the malignant conditions. Workers without direct contact, so-called bystanders, may also develop disease. This is illustrated, to give only one such example, by the work of Harries at the Devenport Dockyard, where mesothelioma was seen among workers in many trades though few such individuals directly handled asbestos; 53 of 55 consecutive cases were in other trades

Table 3. Deaths among 17,800 asbestos insulation workers in the United States and Canada: January 1, 1967-December 31, 1976.[a]

Underlying cause of death	Expected[b]	Observed[c]	
		(BE)	(DC)
Total deaths, all causes	1,658.9	2,271	2,271
Cancer, all sites	319.7	995	922
Deaths of less common malignant neoplasms			
Pancreas	17.5	23	49
Liver, biliary passages	7.2	5	19
Bladder	9.1	9	7
Testes	1.9	2	1
Prostate	20.4	30	28
Leukemia	13.1	15	15
Lymphoma	20.1	19	16
Skin	6.6	12	8
Brain	10.4	14	17

[a]Number of men: 17,800; Man-years of observation: 166,853.
[b]Expected deaths are based upon white male age-specific U.S. death rates of the U.S. National Center for Health Statistics, 1967-1976.
[c](BE) = best evidence, i.e., number of deaths categorized after review of best available information (autopsy, surgical, clinical); (DC) = number of deaths as recorded from death certificate information only. Adapted from Selikoff et al. (*3*).

(*6*). Newhouse has reported on cases of mesothelioma among residents of a neighborhood in London in which an asbestos factory was situated (*7*). Household contact disease has been reported by Anderson (*8*), demonstrating that living in the household of an asbestos worker is sufficient to produce changes on x-ray consistent with asbestos exposure, and that mesothelioma, too, may result from such household contact.

A major public health problem today is the question of potential asbestos-related disease; particularly cancers, among members of the general population that have long-term, low-level exposure. Further investigations are still necessary to define all levels of risk.

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