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# Asbestos as a Carcinogenic Hazard

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Lynch & Smith (*Am. J. Cancer* 1935, **24,** 56) and Gloyne (*Tubercle, Lond.* 1935, **17,** 5) were the first to draw attention to the association between asbestosis and the risk of lung cancer. The extent of the association, as revealed in different surveys, varies between 14 and 55% of cases of asbestosis having concomitant lung cancer (Gloyne, *Lancet* 1951, **i,** 810; Isselbacher *et al. Am. J. Med.* 1953, **15,** 721; Doll, *Br. J. ind. Med.* 1955, **12,** 81; O'Donnell & Mann, *Am. J. Path.* 1957, **33,** 610; Chief Inspector of Factories, Annual Report for 1958, HMSO, London, 1959, p. 45; Williams, *Archs envir. Hlth* 1965, **10,** 44; Buchanan, *Ann. N.Y. Acad. Sci.* 1965, **132,** Art. 1, 507). It appears that the age at death from asbestosis amongst asbestos workers has been rising steadily as a result of the increasing efficiency of dust-control measures in industry (Buchanan, *loc. cit.*). As a result, more and more asbestos workers are living long enough to develop lung cancer (Table 1).

Table 1. *Incidence of lung cancer in males dying with asbestosis**

| Period | Deaths from asbestosis | % with concomitant cancer of lung† | Average age at death from uncomplicated asbestosis |
|---|---|---|---|
| 1924–40 | 79 | 16·4 | 49·3 |
| 1941–50 | 92 | 22·8 | 55·9 |
| 1951–60 | 144 | 31·3 | 58·1 |
| 1961–63 | 77 | 54·5 | 60·4 |

*After Buchanan (*loc. cit.*).
†Includes some cases of mesothelioma.

In the past some pathologists have refused to accept that mesothelioma is an entity. Now there is no room to doubt its reality. König (*Arch. Gewerbepath. Gewerbehyg.* 1960, **18,** 159) found 102 pleural and 22 peritoneal mesotheliomas in 13,307 consecutive necropsies on persons exposed to asbestos who did not develop asbestosis. Harington (in *The Prevention of Cancer*, edited by Raven & Roe, Butterworths, London, 1967, p. 207) reviews the literature with reference to the incidence of mesothelioma in persons dying with asbestosis: different surveys have revealed figures varying from 0·8% (Elwood & Cochrane, *Br. J. ind. Med.* 1964, **21,** 304) to 27% (Selikoff *et al. New Engl. J. Med.* 1965, **272,** 560). The chance that mesothelioma will be found at necropsy among asbestos workers has been estimated at between 1·0 and 2·7%, whereas among the general population the incidence is probably

between 0·01 and 0·04% (Harington *loc. cit.*). As in the case of cancer of the lung, it seems likely that the incidence of mesothelioma in asbestos workers is increasing as dust control delays death from asbestosis. According to a recent report (*Nature, Lond.* 1967, **213,** 855), there are at present in Britain the surprisingly large total of 250 registered cases of mesothelioma—once considered to be a very rare form of cancer. The evidence that exposure to asbestos increases the risk of gastro-intestinal cancer (Hammond *et al. Ann. N.Y. Acad. Sci.* 1965, **132,** 519; Mancuso & Coulter, *Archs envir. Hlth* 1963, **6,** 210) is equivocal.

The amount of asbestos used has been increasing exponentially during the past decade. It is unlikely that any person in the civilized world is not exposed to asbestos dust. Dr. I. Doniach and his colleagues at the London Hospital (Personal communication, 1967) are currently finding asbestos fibres in the lungs in more than 50% of routine necropsies on males. The qualitative finding of asbestos fibres at necropsy in a case of cancer is not therefore good evidence of a cause and effect relationship: the quantity of asbestos present must be taken into account.

The relative cancer risk for man from exposure to the main types of asbestos (crocidolite, amosite, chrysotile and anthrophyllite) is not yet known. In all cases of mesothelioma attributable to exposure to asbestos there has been a history of exposure or probable exposure to crocidolite. In experimental animals mesothelioma has been induced by amosite and chrysotile as well as by crocidolite (Wagner, in *Lung Tumours in Animals,* edited by Severi, Division of Cancer Research, Perugia, 1966, p. 589; Roe, see following paper).

For the purpose of co-ordinating experimental studies on asbestos, the UICC have organized the supply of standard samples of the main types of asbestos. These may be obtained from Dr. I. Webster, P.O. Box 1038, Johannesburg, South Africa.

The chemistry of asbestos and various theories of carcinogenesis by it have been discussed by Harington (*Ann. N.Y. Acad. Sci.* 1965, **132,** 31) and Harington & Roe (*ibid.* 1965, **132,** 439). Mineral oils present in crude asbestos or picked up as contaminants during processing or during storage in jute bags have been shown to initiate skin carcinogens in mice (Roe *et al. Int. J. Cancer* 1966, **1,** 491). Mineral oils used in the processing of jute may be strong promoters of carcinogenesis in mouse skin (Harington & Roe, *loc. cit.*) or even potent carcinogens (Roe *et al. Br. J. Cancer* 1967, **21,** 694). Extensive removal of oils from asbestos fibre possibly reduces its carcinogenicity but does not abolish it.

Further information on current research in the field of asbestos may be obtained from the Report of the Working Group on Asbestos and Cancer (*Archs envir. Hlth* 1965, **11,** 221; *Br. J. ind. Med.* 1965, **22,** 165).

## Experimental Asbestos Carcinogenesis

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After subcutaneous injection into young CBA female mice, asbestos fibre appeared to accumulate specifically in the connective tissue beneath the pleura, peritoneum and pericardium.

Table 1. *Histological changes in mice treated with subcutaneous injections of asbestos*

| Treatment | No. of survivors at 40 wk | Average length of survival after 40 wk (wk) | Injection-site sarcoma | Distant changes | | | |
|---|---|---|---|---|---|---|---|
| | | | | Macroscopic deposits of asbestos on serosal surfaces | Inflammatory changes | Non-malignant mesothelial proliferation in serosal membranes and adhesions | Mesothelioma |
| Crocidolite | 17 | 75·3 | 2 | 17 | 3 | 17 | 5 |
| Extracted crocidolite | 14 | 64·6 | 0 | 14 | 3 | 14 | 0 |
| Amosite | 13 | 96·4 | 2 | 12 | 3 | 13 | 4 |
| Extracted amosite | 15 | 79·7 | 1 | 15 | 3 | 14 | 0 |
| Chrysotile | 12 | 75·5 | 1 | 8 | 1 | 8 | 1 |
| Saline | 15 | 0 | 0 | 0 | 0 | 0 | 0 |

Five groups of 20 CBA female mice (6–10 wk old) were given six injections of 10 mg asbestos fibre suspended in 0·4 ml saline. Two injections were given on the first day of the experiment, each animal being injected subcutaneously in the inguinal region. This treatment was repeated after an interval of 2 months and again after a further interval of 1 month. In this way each mouse received a total of 60 mg asbestos fibre. The five treatment groups were injected respectively with crocidolite, 'extracted crocidolite', amosite, 'extracted amosite' and chrysotile. Twenty control animals were similarly injected with saline only. The samples of 'extracted amosite' and 'extracted crocidolite' were prepared from the crude fibre by treatment with a series of eight organic solvents of increasing polarity.

After treatment, animals were allowed to live out their life span and were only killed when sick. Six mice had to be killed because they developed sarcomas at one of the two subcutaneous injection sites. Post-mortem examination of these and other mice which survived for 40 wk or more revealed marked changes in the mesothelial and submesothelial tissues of a large proportion of the asbestos-treated mice (Table 1). These changes consisted of the deposition of asbestos fibres, thickening and oedema, inflammatory infiltration and cellular proliferation. In ten animals the changes were regarded as malignant mesotheliomas (four peritoneal, four pleural and two involving both peritoneum and pleura). These tumours which commonly presented as plaques on mesothelial surfaces were relatively homogeneous in histological appearance. Many showed a papilliferous arrangement and in all cases an origin from mesothelial cells was obvious. A feature of a number of the tumours was the presence in them of numerous lymphocytes. All the tumours appeared to be multifocal in origin. The incidence of mesothelial changes was less in response to extracted amosite and extracted crocidolite than to the corresponding crude fibres but this may have been associated with shorter average survival in the former cases.

The mechanism by which subcutaneously injected asbestos finds its way specifically to submesothelial tissues is the subject of further investigation now in progress.

## On the Distribution and Fate of the Carcinogenic Hydrocarbon Benzo[*a*]pyrene in Soil

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Benzo[*a*]pyrene can be detected by spectrofluorescent methods in soil samples, as was shown in 1959 by Shabad & Dikun (*Zagryaznenie atmosfernogo vozdukha kantserogennym veshchestvom* 3,4-*benzpirenom*. Gosudarst. Izdatel. Med. Lit., Leningrad, 1959) and later by Blumer (*Science, N.Y.* 1961, **134,** 474), Borneff & Fischer (*Arch. Hyg. Bakt.* 1962, **146,** 430), Borneff & Kunte (*ibid.* 1963, **147,** 401) and Mallet & Héros (*C.r. hebd. Séanc. Acad. Sci., Paris* 1962, **254,** 958).

Systematic laboratory studies of the pollution of soils of different districts and areas with benzo[*a*]pyrene, and its fate, have been carried out since 1964. In different districts of Moscow and its suburbs, the soil contamination with benzo[*a*]pyrene varies. In old habitation areas it is 2·5–3 times higher than in the new ones. In soil samples taken from the territory of an oil refinery, the concentration of benzo[*a*]pyrene reached about 200,000