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Mesothelioma following exposure to crocidolite (blue asbestos). A fifty-year follow-up study

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SUMMARY

A chronological review of the pathological effects of asbestos precedes the results of a survey of 1,172 workers (mainly women) who were exclusively exposed to crocidolite when manufacturing military gas masks in Nottingham during the Second World War. During the following fifty years, 67 (or at least 6%) have died of mesothelioma of the pleura or peritoneum. Of these, the shortest exposure period was 10 days. Mineral fibre analysis on post mortem lungs reveals the lowest crocidolite concentration to be 0.4 million fibres per gram of dried lung. Comparisons are made with other workers exposed to asbestos, including those also in the gas mask industry who were exposed to chrysotile.

INTRODUCTION

Although used over the centuries since at least A.D.77, it was not until 1880 that asbestos was commercially exploited in factories in France and England. Within 20 years, health hazards in the workers were reported. Montague Murray (1906)

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described pulmonary fibrosis - later to be designated ASBESTOSIS, in a factory worker. In the 1920's increasing numbers of such cases were reported. During the 1930's and especially during and since the Second World War the asbestos industry expanded enormously, the fibres being incorporated in a widening variety of products. In the late 1940's concern was expressed about the increasing incidence of LUNG CANCER in asbestos workers. Doll (1955) confirmed this risk, particularly in those who had asbestosis. A second link with malignancy was suggested by Wagner et al in 1960 when a high incidence of the rare malignant tumour MESOTHELIOMA was found in the South African crocidolite mining communes. Of especial concern was that the asbestos exposure in these individuals was considerably less than that of the British factory workers who had developed lung cancer. Since Wagner's paper much world-wide research confirmed his findings. In order to identify the relative dangers of the different types of asbestos in commercial use (CROCIDOLITE, AMOSITE & CHRYSOTILE) searches were made to identify cohorts of workers who had been exclusively exposed to one type of asbestos only (Gilson, 1973). In 1968, Jones first reported two cases of pleural mesothelioma in women who had been exclusively exposed to crocidolite for a limited period (up to 4 years) when manufacturing "military" gas mask filter units in Nottingham during the 2nd World War. This cohort has been followed-up during the intervening years and it forms the basis of this study.

MATERIALS AND METHODS

Pathology Complete autopsies were carried out on 57 of the 67 cases of mesothelioma (48 pleura; 9 peritoneum). The remaining 10 cases were confirmed by biopsy diagnosis.

Microscopy The early cases of tumour were examined by light microscopy, using haematoxylin and eosin (H & E) stained sections, followed by diastase-PAS stains to negate the possibility of adenocarcinoma, particularly of ovarian tumours in the peritoneal malignancies. In the later cases additional confirmatory immunohistochemical techniques including CEA, cytokeratin and vimentin stains were used. Lung sections using H & E and elastic Van Gieson stains in addition to 30 micron thick unstained sections were examined by high power light microscopy to assess the presence of asbestosis.

TABLE I NUMBER OF DEATHS DUE TO MALIGNANCY IN ADDITION TO THE 67 CASES OF MESOTHELIOMA

Number of cases			
Carcinoma of:		Carcinoma of:	
Bronchus	23	Larynx	1
Breast	13	Oesophagus	1
Stomach	10	Kidney	1
Ovary	8	Uterus	1
Cervix	5	Tongue	1
Pancreas	5	Thyroid	1
Bladder	3	Fibrosarcoma	1
Vagina/Vulva	2	Ac. Leukaemia	1
Colon	2	Hodgkin's Disease	1
Carcinomatosis unknown 1°	5		
Brain Tumour	[illegible]	TOTAL 90 CASES	

Mineralogy Representative samples of lung tissue from 69 gas mask workers, including 48 with mesothelioma were examined by electron microscopic and energy dispersal x-ray techniques, using the method of Pooley and Clark (1979).

Epidemiology The tracing of the workers was derived from:-
- Company records (mainly the Wages Book)
- Medical records (local hospital, general practitioners and patients' own history.

A master index was prepared. To date the causes of death of 280 of the 1,172 workers are known, the majority of these (157) being due to malignant disease. (Table I). Further efforts to trace the remainder are in progress.

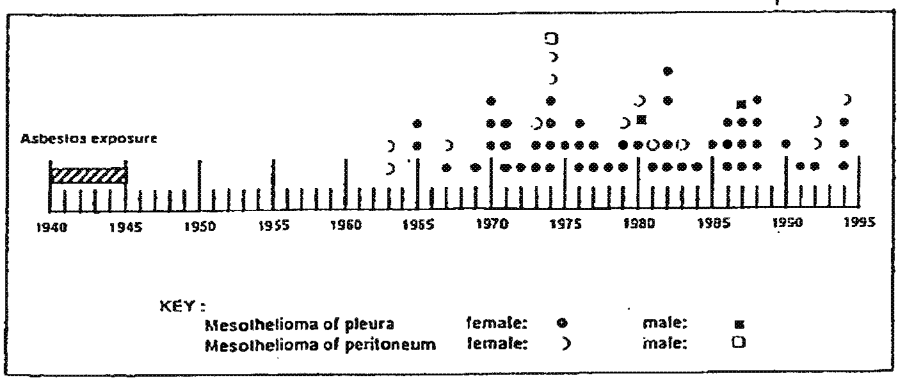
RESULTS

Of the factory workforce of over 1,000 women the causes of death are known in 280 out of an estimated total of some 500 deaths. From this group 157 deaths were due to malignant disease, including 67 cases of mesothelioma (53 pleural and 14 peritoneal). The other 90 cases of malignancy are seen in Table I.

Mesothelioma cases

The latent interval between exposure and death varied from 23 to 54 years. (Table II).

TABLE II LATENT INTERVALS BETWEEN THE PERIOD OF ASBESTOS EXPOSURE AND DEATH DUE TO MESOTHELIOMA OF PLEURA & PERITONEUM



The ages at death ranged from 42 to 84 years. The average age at death from pleural tumour was 68.5 years, and 62.8 years from peritoneal tumour.

The shortest period of exposure was 10 days. This woman had 6.5 million crocidolite fibres/gram of dry lung at autopsy 46 years later.

The lowest crocidolite count was 0.4 million fibres/gram of dry lung. The average fibre diameters in the Nottingham lungs was 0.2 microns, similar to the fibre diameters found in Wittenoom and finer than those in the South African cases.

The highest fibre counts (over 1,000 million/gram) were seen in the 4 cases of overt asbestosis. Clinical and radiological asbestosis was seldom noted in the remaining cases in this series.

DISCUSSION

The wartime manufacture of filter units for "military" gas masks in the United Kingdom was carried out in Nottingham (Jones et al, 1980; Wignall & Fox, 1982), in Leyland (Acheson et al, 1982) and in three centres in Canada (McDonald & McDonald, 1978), using the same Porton specification. This required the use of fine diameter crocidolite, derived from the mine in Wittenoom, Western Australia. Increased numbers of mesotheliomas have occurred in all these factory areas, and in the Wittenoom mining commune (Hobbs et al, 1980; Berry, 1991). By contrast, none occurred in a factory in Blackburn, U.K., where "civilian" gas masks were made which incorporated chrysotile instead of crocidolite into the filter (Acheson et al, 1982). Mesotheliomas have also followed exposure to Amosite in the U.S.A. and in a U.K. factory (Gibbs et al,.1994). There is abundant evidence that mesotheliomas follow exposure to amphibole fibres (including crocidolite and amosite), but not to chrysotile unless it is contaminated with tremolite (McDonald & McDonald, 1996).

In the Nottingham factory dust extraction precautions were taken, and some workers wore simple masks. The factory was bombed and an emergency production line had to be set up elsewhere in Nottingham. The dust levels were not known, but the fineness of the fibre diameter would have helped dispersal and respirability of the fibres. The dimensions of the fibres were within the range of carcinogenicity as defined by Stanton & Layard (1978).

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