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CANCER MORTALITY IN CHRYSOTILE MINING AND MILLING: EXPOSURE-RESPONSE

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Abstract—see p. 412.

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THE QUEBEC COHORT

Provenance

THE best information on exposure-response relationships in chrysotile mining comes from the Quebec cohort: this consists of all 10925 men born 1891-1920 who had worked for 1 month or more in the mines and mills in the Eastern Townships of the Province of Quebec. They have been traced to the end of 1988, by which time 1105 had been lost to view; these included well over 800 never traced after very short service before 1930. Of those traced, there were 2508 survivors into 1989, and there had been 7312 deaths, 7% more than expected on the basis of the published vital statistics of Quebec.

Reports on mortality to 1966, 1969 and 1973 were published in 1971, 1973 and 1977. McDONALD *et al.* (1980) reported on all 4463 deaths before 1976, and further analyses were described by LIDDELL *et al.* (1984) and by VACEK and McDONALD (1990). A report on subject-years analyses of mortality 1976-1988 has been published (McDONALD *et al.*, 1993), and in this paper is referred to as BJIM '93; in a section of the current review there is a brief preliminary account of case-referent analyses of lung cancer, from the earliest recorded until 1988; mesothelioma in the corresponding period has been described briefly by McDONALD *et al.* (1994).

Mortality 1976-1988

Table 1 (adapted from BJIM '93) shows that there was an excess overall of 193 deaths. The most notable excesses were of lung cancer (91), mesothelioma (25) and pneumoconiosis (48); other differences from expectation were small either numerically or relatively.

In particular, there were 18 cases of laryngeal cancer where 13.8 were expected, but this excess was concentrated in smokers, and the associations with various measures of dust exposure were negative. There were also 56 stomach cancers (47.9 expected), but the excess was confined to Thetford Mines, and there were no associations with dust exposure. The excess of 13 deaths from respiratory diseases other than pneumoconiosis was only 5% of the expected number.

TABLE 1. 2827 DEATHS, 1976-1988, BY CAUSE

Cause of death (with ICD codes)	Observed	Excess	SMR
All causes	2827	192.7	1.07
Malignant neoplasms			
abdominal: stomach (151)	56	8.1	1.17
other (150, 152-9)	146	-16.9	0.90
respiratory: larynx (161)	18	4.2	1.30
lung (162)	321	91.3	1.40
genito-urinary: prostate (185)	81	4.3	1.06
bladder (188)	20	-5.0	0.80
kidney (189)	13	0.0	1.00
lymphatic and haematopoietic tissue (200-208)	56	8.1	1.17
other (rem 140-209)	76	5.2	1.07
Mesothelioma	25	25	—
Pneumoconiosis	48	48	—
Other respiratory diseases (rem 460-519)	256	13.0	1.05
Heart disease (391, 392.0, 402, 404, 410-429)	1013	18.6	1.02
Cerebrovascular disease (430-438)	225	12.9	1.06
Chronic liver disease and cirrhosis, and alcoholism (571, 291, 303, 860)	32	-7.5	0.81
Injury and poisoning (800-999)	89	12.8	1.17
All other causes (rem 001-999) [including respiratory tuberculosis (5)]	352	-29.4	0.92

Table 2 (also adapted from BJIM '93) shows deaths from lung cancer, 1976-1988, in relation to exposure accumulated to age 55 years. There is no indication of a trend over the seven lowest categories of exposure in million particles per cubic foot (mpcf) $\times$ years. There is strong evidence that the lung cancer SMR of 1.27 for these 4145 men arose from comparatively heavy cigarette smoking.

TABLE 2. DEATHS FROM LUNG CANCER, 1976-1988, IN RELATION TO EXPOSURE ACCUMULATED TO AGE 55 YEARS

Exposure (mpcf-years)	No. of men	O	Deaths E	O/E
<3	708	36	31.4	1.14
3, <10	582	40	25.3	1.58
10, <30	712	33	31.3	1.05
30, <60	569	39	24.4	1.60
60, <100	525	30	22.8	1.32
100, <200	663	32	28.3	1.13
200, <300	386	20	17.3	1.15
<300	4145	230	180.8	1.27
300, <400	253	16	10.7	1.50
400, <1000	621	42	25.4	1.65
≥ 1000	188	22	7.2	3.04
Total	5207	310	224.1	1.38

Case-referent analyses of lung cancer

This section is a brief preliminary statement concerning the analyses presaged in BJIM '93; they will be fully reported after completion. Case-referent comparisons have been made, using conditional logistic regression, on the 548 deaths from lung cancer up to 1988 (245 before 1976 and 321 since, with certain exclusions). For each case one referent was chosen at random from among survivors to a greater age, after matching on place of employment, age of starting work, smoking habit and date of birth. For each man, and for each year of employment, we obtained the fraction of the year worked at each of six levels of intensity, assessed in mpcf, as follows: <5; 5, <15; 15, <30; 30, <40; 40, <50; and 50–140. We then calculated how many years each man spent at these various levels; the years, adjusted for the length of the working week (66 h until 1937; 48 h 1938–1949; 40 h 1950–1985), were accumulated up to 10 years before the age of death of the case.

The risk of excess lung cancer after exposure to concentrations of less than 15 mpcf was estimated as nil (i.e. the calculated Odds Ratio was less than 1). The risks of lung cancer after exposure at the four higher levels, i.e. to dust concentrations of 15–140 mpcf, appeared substantial, but exposure-response relationships were irregular, and quantification is not yet possible.

Mesothelioma

The proportional mortality from mesothelioma in the Quebec cohort, even including the factory workers many of whom are known to have been exposed to crocidolite, had reached only 0.45% (33 deaths among 7312, almost three-quarters of the cohort) by the end of 1988. This is much lower than has already been observed in cohorts exposed to commercial amphiboles at a much earlier stage of their mortality, and after markedly less severe exposure; in South African crocidolite miners, for example, the corresponding figure had reached 4.7%, when the overall mortality was still much less than one-fifth of the cohort (McDONALD *et al.*, 1994).

Discussion

No apology is made that intensity of exposure is expressed in terms of million particles per cubic foot, if only because these were the terms in which the original measurements had been made (GIBBS and LACHANCE, 1972). A further reason is explained below.

The complex relationships between dust counts and fibre counts in the Quebec mines and mills have been studied by GIBBS and LACHANCE (1974) and by DAGBERT (1976). LIDDELL *et al.* (1984) explained how a fibre/dust ratio was assessed for each job in which any of 2217 subjects had worked: these ratios ranged from 0.3 to 30 (fibres ml^{-1})/(mpcf). Nevertheless, the relationships between mortality from various causes and accumulated exposure were closely similar whether adjustment from dust terms to fibre terms was made job by job and subject by subject (involving about 10 000 adjustments) or by use of a single 'average' ratio close to 3.5 (fibres ml^{-1})/(mpcf).

The risk of lung cancer as a result of exposure at intensities of less than 15 mpcf was minimal; higher intensities, i.e. above about 50 fibres ml^{-1} , are well outside today's experience, even in the worst conditions in developing countries. Thus, risks associated with such severe exposures have become irrelevant, and it is of no practical importance that these risks cannot be quantified reliably.

It must be emphasized that all the 'new' findings are confirmation and strong reinforcement of earlier findings from the same cohort; in other words, the differences between present findings and those previously reported are of degree rather than of kind.

THE BALANGERO EXPERIENCE

Provenance

The mortality of workers at the Balangero chrysotile mine and mill in northern Italy was first reported in 1972 on men employed between 1932 and 1970. RUBINO *et al.* (1979) examined mortality from 1946 to 1975 of 952 men first employed between 1930 and 1965. An 'update' on mortality from 1946 to 1987 of 1058 men who had worked for at least 1 year between 1946 and 1987 was published by PIOLATTO *et al.* (1990). A summary of the relevant material follows.

The 427 deaths were almost 50% more than expected on the basis of national rates, an excess of 141 deaths. Most of this excess arose from causes not related to asbestos exposure, namely 'other causes' (71), hepatic cirrhosis (30), and accidents and violence (23). There were five more laryngeal cancer deaths than the 3.0 expected. There was also an excess of lung cancer, but it was tiny and not related to exposure, and there were no excesses of gastric or intestinal cancer. There were two mesotheliomas ($PMR = 2/427 = 0.47\%$), both pleural, and both after exposure for more than 20 years.

Discussion

It is apparent that the findings in relation to lung cancer, gastrointestinal cancer and mesothelioma are strongly supportive of those from the Quebec cohort. As for laryngeal cancer, the interpretation of the associations with asbestos exposure is difficult (LIDDELL, 1990), especially in a region where there is particularly heavy alcohol consumption, as at Balangero. But whatever the interpretation, the risk of laryngeal cancer as a result of chrysotile exposure of less than $100 \text{ (fibres ml}^{-1}) \times \text{years}$ must be considered minimal.

CONCLUSIONS

The following conclusions are drawn from all the evidence about cancer mortality among chrysotile miners and millers.

There is strong evidence that the risk of *lung cancer* as a result of exposure to chrysotile at concentrations of less than 15 mpcf is vanishingly small. At higher concentrations, the relative risk of lung cancer is elevated, probably less so in smokers of 20 or more cigarettes a day than in others, but the magnitude of the elevated risks cannot be evaluated with any certainty; this is of no importance, because such higher concentrations—i.e. of the orders of $50\text{--}500 \text{ fibres ml}^{-1}$ —are well outside the range of any experience nowadays.

There is no evidence that the risk of *laryngeal cancer* is increased as a result of exposures up to at least $100 \text{ (fibres ml}^{-1}) \times \text{years}$.

There is no evidence that the risk of *stomach cancer* is adversely affected by exposure to chrysotile; and there is no evidence of increased risk of *other abdominal malignancies* or of *kidney cancer* among chrysotile miners and millers.

The risk of *mesothelioma* in chrysotile miners and millers is very low compared with the risks in other asbestos-exposed populations, except those exposed only to chrysotile.

[For the discussion of the issues raised in this and the other allied papers see pp. 413-415.]

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