Does occupational exposure to dust prevent colorectal cancer?

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Abstract

***Objectives*—To explore the impression that occupational epidemiologists tend to focus on associations suggestive of increased risk and tend to ignore those associations in which risk is not increased. To examine the risk of colorectal cancer in cohorts exposed to dust, cohorts in which it has been suggested that occupational exposure is a cause of increased risk of stomach cancer.**

***Methods*—A review of the publications in the English language on mortality among hard rock miners, granite, and quarry workers identified from a MEDLINE search and the index of the library of the Ontario Ministry of Labour.**

***Results*—When all of the studies were combined, there were significant excesses of lung and stomach cancers, but a significant deficit of colorectal cancer (standardised mortality ratio (SMR) = 83·9; 95% confidence interval (95% CI) 76–91). Overall mortality from gastrointestinal cancer was close to expectation (SMR = 105; 95% CI 99–111). Among those cohorts with increased risk of stomach cancer, rates of colorectal cancer were significantly decreased (SMR = 80; 95% CI 72–88). Among cohorts without increased risk of stomach cancer, the SMR for colorectal cancer was not significantly different from 100 (SMR = 98; 95% CI 81–115).**

***Conclusions*—This review supports the impression that occupational epidemiologists tend to focus on associations suggestive of increased risk and tend to ignore those associations in which risk is not increased. The explanation for the inverse association between risk of stomach and colorectal cancer is uncertain and deserves further study.**

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Perusal of publications on occupational medicine suggests that epidemiologists are excited by findings that imply that an occupational exposure increases the risk of a particular disease, but that, with the exception of the healthy worker effect, they tend to pay little attention to findings of decreased risk of disease in a workforce. Work in dusty trades has often been associated with an increased risk of lung cancer and many epidemiologists have also found an increased risk of stomach cancer among these workers.[1–3] Recently, the findings were published of an investigation of increased risk of stomach cancer among gold miners from Ontario.[4] It was concluded that the excess of gastric cancer in gold miners may be the result of exposure to dust and that chromium may then be the causative agent, or closely associated with it. On reading the report of the original Ontario miners cohort study[5] I was struck by the finding that, even though mortality from stomach cancer was increased among the gold miners (60 deaths observed, 40 expected), overall mortality from digestive system cancer was less than expected (130 observed, 155 expected). This was attributable to a substantial deficit of colorectal cancers (28 observed, 65 expected). If occupational exposure to dust causes stomach cancer, could it also prevent cancer of the colon and rectum? The review of the medical literature presented here was conducted to investigate occupational associations with cancers of the intestinal tract (stomach, colon, rectum) in hard rock miners and quarry and granite workers.

Methods

Papers published in the English language on mortality among hard rock miners and granite and quarry workers were identified from a MEDLINE search of the literature from 1966 to 1994. Government reports and conference proceedings in the library collection of the Ontario Ministry of Labour provided additional data.

The significance of differences between observed and expected mortality, and 95% confidence intervals (95% CIs) were assessed with the Poisson distribution or χ^2 tests.

Results

STUDIES INCLUDED IN THE REVIEW

Table 1 shows the studies included in this overview. They have been divided into categories representing mining of various ore types, granite and quarry workers, and the Vienna study of workers in dusty trades.

Miners

Gold miners—Simonato *et al* conducted a historical cohort mortality study of employees of a French gold mining and refining company to investigate the relation between lung cancer,

Table 1 Mortality from lung and gastrointestinal cancer in cohorts exposed to dust

Cohort	Lung			Stomach			Colon		
	Obs	Exp	SMR	Obs	Exp	SMR	Obs	Exp	SMR
Gold:									
Simonato *et al*[6]	19	8·8	217	3	2·61	115	0	2·54	0
Muller *et al*[5]	196	135	145	60	40·4	148	—	—	—
Brown *et al*[7]	43	42·9	100	10	12·6	79	10	12·6	79
Armstrong *et al*[8]	59	40·8	140	4	9·8	40	—	—	—
Uranium:									
Muller *et al*[5]	119	66	181	21	16	130	—	—	—
Nair *et al* (Port Radium)[10]	83	30·6	271	7	9·4	75	7	9·2	76
Nair *et al* (Beaverlodge)[10]	112	60·9	184	18	17·9	101	18	18·3	99
Waxweiller *et al*[11]	185	38	482	9	6	150	7	10·2	69
Morrison *et al* (Fluorspar)[24]	113	21·5	525	22	16·2	135	5	8·7	76
Iron:									
Kinlen and Willows[15]	12	18·3	66	49	29·5	124	25	21·1	119
Lawler *et al*[15]	212	226	88	126	73·1	172	63	85·9	73
Muller *et al*[5]	0	2·65	0	0	0·66	0	—	—	—
Nickel or copper:									
Muller *et al*[5]	83	96	87	27	25	108	—	—	—
Other ore:									
Muller *et al*[5]	5	3·83	131	1	1·29	77	—	—	—
Battista *et al*[22]	47	35·6	131	19	18·9	100	—	—	—
Carta *et al*[23]	24	21·5	112	5	5	99	—	—	—
Mixed ore:									
Muller *et al*[5]	101	69·5	145	22	20·8	106	—	—	—
Tin:									
Fox *et al*[19]	61	52	117	33	23·4	141	—	—	—
Chen *et al*[17]	—	—	198	—	—	60	—	—	—
Granite:									
Koskela *et al*[25]	31	19·9	156	9	7·1	127	—	—	—
Mehnart *et al*[26]	27	24·7	109	13	11·2	116	3	3·8	80
Steenland and Beaumont[27]	97	81·1	119	29	29	0·99	37	33·6	110
Dusty trades:									
Neuberger and Kundi[3]	179	106	169	77	46·4	166	—	—	—
Total	1808	1202	150	564	422·3	134	175	205·9	85

ICD = International classification of diseases

mortality, and exposure to arsenic, radon, silica, and other contaminants of the working environment.[6] Muller and colleagues initiated, and are continuing, the Ontario miners study, a retrospective cohort mortality study of miners who worked in gold mines, nickel and copper mines, uranium mines, or mines for other ores.[5] Brown *et al* reported a retrospective cohort mortality study of 3328 United States gold miners who had worked full time underground for at least one year between 1940 and 1965.[7] The reason for initiating that study was the hypothesis that exposure to amphibole mineral fibres found in the ore of the mine would be associated with diseases related to asbestos, such as lung cancer and asbestosis. Armstrong *et al* studied a cohort of Australian gold miners to test the hypothesis that there was an increased incidence of lung cancer attributable to their mining experience.[8] Another study, not shown, is that of Wyndham and associates who studied a cohort of South African gold miners.[9] They reported an increased risk of lung and stomach cancers, but make no mention of any other kinds of malignancies. It is thus not possible to comment on colorectal cancers in this cohort.

Uranium miners—Uranium miners are known to be at increased risk of lung cancer, attributable to exposure to radioactive radon daughters in the mines. Nair and colleagues reported on the mortality experience of employees of Eldorado Resources employed at the Port Radium and Beaverlodge uranium mines.[10] Waxweiller *et al* studied the mortality experience of American uranium miners on the Colorado plateau.[11] There is no mention of gastrointestinal cancers in the published reports of the New Mexican[12] or Czech[13] uranium miners. It is thus not possible to comment on colorectal cancers in these cohorts.

Nickel and copper miners—Chen *et al* reported on the mortality experience of Chinese copper miners.[14] Mortality from lung, stomach, oesophagus, and liver cancers was increased. There was no specific mention of colorectal cancers, but from the data presented, one may infer that mortality from colorectal cancers was probably less than expected.

Iron miners—Kinlen and Willows studied the mortality of 1947 English iron ore miners[15] and Lawler and colleagues performed a cohort mortality study of 10 403 Minnesota iron ore miners.[16] Chen and colleagues studied the risk of mortality of iron ore miners in two mines in China.[17] There was an increased risk of lung cancer, but mortality from stomach cancer was less than expected. There was

Table 2 Lung and colorectal cancers in cohorts with and without increased mortality from stomach cancer

	Lung			Stomach			Colon		
	Obs	Exp	SMR	Obs	Exp	SMR	Obs	Exp	SMR
Cohorts with increased mortality from stomach cancer	1319	873	151	468	315	149	103	130	79
Cohorts without increased mortality from stomach cancer	484	322	150	95	105	90	72	76	94

Rectum			*Colorectal*			*Gastrointestinal (ICD:151–154)*		
Obs	*Exp*	*SMR*	*Obs*	*Exp*	*SMR*	*Obs*	*Exp*	*SMR*
1	1·4	70	1	3·89	26	4	6·5	62
—	—	—	28	65·4	43	88	105·8	83
6	5	120	16	17·6	91	26	30·2	86
—	—	—	9	11	80	13	20·8	63
—	—	—	23	28·7	80	44	44·7	98
2	4·3	47	9	13·5	67	16	22·9	70
8	8·4	95	26	26·7	99	44	44·6	99
1	3·7	27	8	13·9	58	17	19·9	85
2	4·3	47	9	13·5	67	31	29·7	104
23	17	134	48	38·1	126	97	67·6	144
45	37	123	108	112·4	96	234	185·5	126
—	—	—	2	1·15	174	2	1·81	110
—	—	—	35	42·6	82	62	67·6	92
—	—	—	0	2·13	0	1	3·42	29
—	—	—	14	7·6	183	33	26·5	124
—	—	—	4	3·9	102	9	8·9	101
—	—	—	23	34·2	69	45	55	82
—	—	—	21	37·8	56	54	61·2	88
—	—	—	68	—	68	—	—	—
—	—	—	0	3	0	9	10·1	89
12	4·6	263	15	8·33	180	28	19·53	143
13	14	90	50	48	104	79	77	103
—	—	—	34	42	81	111	88·4	126
113	100	113	483	575·4	84	1047	997·7	105

no mention of mortality from colorectal cancer. Pham *et al* reported on the mortality of French iron miners.[18] There was an increased risk of lung, stomach, bladder, and prostate cancers. Colorectal cancer was not specifically mentioned, but because mortality from cancers other than those mentioned earlier was less than expected, mortality from colorectal cancer was presumably also less than expected.

Tin miners—Fox and colleagues studied Cornish tin miners to investigate mortality among men exposed to high levels of radon in underground air[19] and Chen *et al* studied mortality among 68 000 people employed during 1972–4 at metal mines and pottery factories in China.[20] Hodgson and Jones studied the mortality patterns of United Kingdom tin miners with particular attention to lung cancer and exposure to radon.[21] They reported increased risk of lung and stomach cancers, but make no mention of colorectal cancers. It is thus not possible to comment on colorectal cancers in this cohort.

Other ores—Battista and colleagues performed a cohort mortality study of miners in Central Italy to evaluate the effects of exposure to radon,[22] and Carta *et al* studied a group of Sardinian metal miners with low level exposure to radon.[23] Morrison *et al* investigated a cohort of Newfoundland miners exposed to radon while mining fluorspar.[24]

Granite and quarry workers

Koskela and colleagues undertook a mortality study of 1026 Finnish granite workers employed in quarries and processing yards.[25] There was an increased risk of lung and stomach cancers, but no colorectal cancers were observed (expected about three). Mehnert *et al* studied mortality in a cohort of German slate quarry workers.[26] Steenland and Beaumont studied death benefit records of 1905 members of the Granite Cutters Union.[27] Proportionate mortality from lung cancer was increased. Mortality from stomach and colorectal cancer were both similar to expectation. Davis and colleagues studied the mortality pattern of 969 deceased Vermont granite workers.[28] Mortality from lung cancer was increased. Mortality from cancer of the digestive organs was slightly increased, but the authors provided no breakdown by location in the digestive tract.

Dusty trades workers

During the period 1950 to 1960, occupational and smoking histories were collected in the course of preventive medical examinations of 247 064 workers in Vienna. Of these, 1630 workers aged $\geqslant 40$ years were selected because of their occupational exposure to silica and "inert" dusts, and were matched to 1630 subjects without such exposure. Follow up to the end of 1985 found increased mortality from lung and stomach cancer, but decreased colorectal mortality among the subjects exposed to dust.[3] This paper is included here because the focus of interest of the researchers was risk of lung and stomach cancer in workers exposed to dust.

SUMMARY OF RESULTS

The summary line in table 1 shows that when all of the studies are combined, there are significant excesses of lung cancer (SMR 150) and stomach cancer (SMR = 133; 95% CI 123–145), but a significant deficit of colorectal cancer (SMR = 84; 95% CI 76–91). Combining those studies that presented details for colonic and rectal cancers separately, there was a deficit of colonic cancer (SMR = 85; 95% CI 72–98) and an excess of rectal cancer (SMR = 113; 95% CI 92–134). Overall mortality from gastrointestinal cancer was close to expectation (SMR = 105; 95% CI 99–111).

Table 2 shows the data on the question of whether or not risk of colorectal cancer varies with risk of stomach cancer. Where there is an increased risk of stomach cancer (Obs/Exp > 1) rates of lung and stomach cancer are both significantly increased and rates of colorectal cancer are significantly decreased (SMR = 80; 95% CI 72–88). Where there is no increased risk of stomach cancer (Obs/Exp < 1) risk of lung cancer is again increased, the stomach cancer SMR is 90 and the colorectal cancer SMR is 98 (95% CI 81–115), not significantly different from 100.

Rectum			*Colorectal*			*Gastrointestinal (ICD:151–154)*		
Obs	*Exp*	*SMR*	*Obs*	*Exp*	*SMR*	*Obs*	*Exp*	*SMR*
83	66	125	352	440	80	820	755	108
30	33	90	129	132	98	224	237	94

Discussion

This literature review was conducted to explore the hypothesis that occupational epidemiologists focus on positive associations and tend to ignore associations suggestive of a protective effect. Having noticed an inverse association between stomach and colorectal cancers in one cohort exposed to dust I reviewed the medical literature to find whether this was a more general finding. Is there an inverse relation between the mortalities from stomach and colorectal cancer such that the overall gastrointestinal mortality is close to expectation in cohorts exposed to dust?

In a review such as this, one has always to be concerned about bias—namely, publication bias in determining which studies are submitted and accepted for publication and selection bias in retrieving papers for review. Papers for this review were selected from a search of MEDLINE for papers in the English language on mining and quarrying, supplemented by a search of the Ministry of Labour occupational medicine database. In most of these papers the main sites of interest were lung and stomach cancers. There is thus unlikely to be any bias with respect to publication of studies with increased or decreased risk of colorectal cancer. The hypothesis that authors are primarily interested in positive findings is supported by the finding that because of the concern with lung and stomach cancers (positive sites), results for these sites were almost always presented whereas results for colorectal cancers were often omitted from the published papers.

It was found that when mortalities from stomach cancer were increased, mortalities from colorectal cancer tended to be decreased, and when mortalities from stomach cancer were not increased mortalities from colorectal cancer were similar to the expected (table 2). How might these findings be explained? The simplest explanation is that neither the increased risk of stomach cancer nor the decreased risk of colorectal cancer are caused by occupational exposures. Inappropriate reference populations have been chosen for these cohorts exposed to dust and the results for the risks of stomach and colorectal cancer are both due to confounding. The observations in table 2 would tend to support this interpretation because in those studies in which the SMR for one site was close to expectation, so was the SMR for the other site. When the SMR for one site was significantly different from expectation, so was the SMR for the other site.

The causes of colon cancer are poorly known. A recent review of the literature[29] reported that evidence from migration studies and international comparisons suggested a strong environmental component to the aetiology. Most recent studies have focused on the importance of nutritional factors. Several occupational studies have been conducted.[30 31] Associations of colorectal cancer with occupation have generally been weak and the statistical power to identify associations has been low. The main consistent finding has been the protective effect of physical exertion. Odds ratios have been in the range of 0·5 to 0·8 for active occupations in comparison to sedentary ones.[29] It has been hypothesised that physical activity stimulates peristalsis, decreasing colonic transit time and exposure to intralumenal carcinogens.

The next explanation for the association between dust exposure and risk of gastrointestinal cancer summarised in table 2 is that risk is causally related to occupation, and the same work factor caused both the increase in risk of stomach cancer and the decrease in risk of colon cancer. One might thus speculate that physical activity increases the risk of stomach cancer and decreases the risk of colon cancer, or that substances in ingested dust increase the risk of stomach cancer and that they, or modified daughters, then pass down the intestinal tract to decrease the risk of colon cancer.

The next logical combination is that separate aspects of workplace exposure are involved in modification of risk at different places in the gastrointestinal tract. Perhaps ingested dust increases the risk of stomach cancer whereas physical exertion decreases the risk of colon cancer. It is not possible to sort out all these alternatives at present, but these issues seem to be worthy of further investigation.

Conclusions

This review supports the impression that occupational epidemiologists tend to focus on associations suggestive of increased risk and tend to ignore those associations in which risk is not increased. We have found that in cohorts exposed to dust in which the risk of stomach cancer is increased, there is a concomitant decrease in the risk of colorectal cancer such that the overall risk of gastrointestinal cancer is similar to expectation. The explanation for the inverse association between the risks of stomach and colorectal cancer is uncertain and deserves further study.

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Examples of common forms of references are:

1 International Steering Committee of Medical Editors, Uniform requirements for manuscripts submitted to biomedical journals. *Br Med J* 1979;**1**:532–5.
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