

PostScript

LETTERS

The correspondence by Weill *et al* (below) refers to a letter by Greenberg, which was published in February's edition of the journal. We regret the late appearance of this printed response, which arises from an administrative error. An electronic version of this text was posted on the website on 1 February 2005.

Changing trends in US mesothelioma incidence

In a letter, Greenberg,¹ commenting on our paper, "Changing trends in US mesothelioma incidence",² raises a number of points with which we disagree.

There is now a broad consensus that amphiboles are vastly more dangerous than chrysotile in their propensity to produce mesothelioma, and even a casual review of the literature indicates that where there is a continuing increase in mesothelioma rates, it is seen in countries that used large amounts of amosite and crocidolite, as we indicated in our paper.

He raises the issue of whether asbestosis must be present to attribute a lung cancer to asbestos exposure. Our paper was not about this issue, we did not say anything about necessary sequence, and the phrase he cited was the lone mention of this issue, included in the introduction before focusing on the main subject: mesothelioma. However, since Greenberg raises the subject, the Wilkinson *et al* paper³ was in no way a "consensus" by a "group of experts", rather it was the report of a study of hospitalised patients, a study which had a number of serious flaws, as we explained in our published response.⁴ Also, even if one assumes that lung cancers can be generated by high exposure to asbestos without the presence of asbestosis, it makes no sense to expect an increased lung cancer risk in the face of declining asbestos usage and increased control of exposure, exactly the factors that are driving the decreased rates of mesothelioma. Greenberg's own words clearly indicate that he is more interested in the "adversarial spectrum" than the science!

Greenberg complains about the use of national import tonnage as an indicator of potential overall worker exposures to the various asbestos fibre types. There is no other way to do this, and this approach has been used by Peto and colleagues,⁵ and in a previous publication of ours, comparing US and UK mesothelioma trends.⁶

We do not know exactly what paper Greenberg refers to in his comments about events that occur in test tubes within 4 minutes, but *in vitro* experimental data must always give way to *in vivo* experimental data, and the latter to human epidemiology. Greenberg is actually incorrect in stating that all types of fibres are equally potent causes of malignancies in animals. In fact, proper analysis of the original Wagner inhalation experiments in rats indicates that, because the asbestos was delivered on an equal mass

and not equal fibre number basis, the number of chrysotile fibres to which the animals were exposed was vastly greater than the number of amphibole fibres but the number of mesotheliomas found was about the same, thus indicating the greater potency of amphiboles in causing mesothelioma. This conclusion has been confirmed for both mesothelioma and lung carcinoma in more modern animal inhalation studies, comprehensively reviewed,⁷ and there is in fact considerable evidence that lung cancers in animals exposed to asbestos only develop when asbestosis is present.⁸

Greenberg raises a number of other issues, but the overall thrust of his letter appears to be that declining rates of (readily apparent) asbestos induced disease should not be viewed as indicating a foreseeable end to the asbestos problem. Yet if declining rates of disease do not indicate a problem that, with proper control of exposure, will slowly disappear, what will?

Finally, Greenberg closes with kudos for a conference entitled "The third wave of asbestos disease".⁹ In the view of most investigators in this field, this conference contributed little to the knowledge base on asbestos related diseases and served mainly as a political/litigation brief. One wonders if there will ever come a time when *any* good news about asbestos related health effects is welcomed by all who profess to have worker health as their primary motivation.

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Increased incidence of cutaneous malignant melanoma among longshoremen in Genoa, Italy: the role of sunlight and occupational exposure

Epidemiological evidence supports the aetiological role of natural (sunlight) and artificial (sunlamps and sunbeds) sources of ultraviolet radiation (UV-A) on the occurrence of cutaneous malignant melanoma (CMM).¹ Occupational studies have suggested increased risks for CMM among chemists, telecommunications and electronics workers,² printing industry workers,³ and harbour workers (forwarding/shipping agents, harbour masters, and ferry and harbour service assistants).⁴

To investigate the relation between occupation and cancer incidence, we retrospectively studied cancer incidence in 4993 longshoremen ever employed at the dock of Genoa, Italy, between 1933 and 1980. They were employed at two dockyard trading companies: the "Stefano Canzio" and "San Giorgio". Although men employed at the two dockyard companies loaded and unloaded the same products, employees of the former company performed their job mainly outdoors, and employees of the latter mostly inside the ships. They were categorised a priori according to their prevalent pattern of occupational sunlight exposure as indoor (2707) and outdoor workers (2286). Cancer frequency was established by record linkage with the Genoa Cancer Registry, for 1986-96 (the interval for which incidence data are available). The vital status of each man was ascertained from the demographic registry of his place of residence until 31 December 1996. Those who died (409) or emigrated (32) before 1986 (that is, the starting date of follow up), were excluded from the analysis. Thus 2451 indoor and 2101 outdoor dockyard workers were eligible for statistical analysis.

Standardised incidence ratios (SIRs) were calculated as the ratio of observed to expected site specific cancer cases (external comparison). Expected cases were calculated by applying quinquennial age specific cancer incidence for the male population of the City of Genoa (reference population) to the person-years of observation accumulated in each subgroup (24 364 and 21 087 for indoor and outdoor workers, respectively). Two sided 95% confidence intervals (CIs) for the SIRs were calculated on the assumption of a Poisson distribution of the observed cases. In addition, the site specific cancer incidence experienced by outdoor and indoor workers was contrasted by computing relative risk point estimates and their 95% CIs.⁵

Table 1 shows the results of the cohort study. All cancers incidence was similar in both subgroups and did not differ from that of the reference population. The excess incidence for larynx cancer detected in both subgroups was statistically significant only in indoor workers (24 cases, SIR = 213, 95% CI 136 to 316, p = 0.001). SIR for lung cancer was similar in the two subcohorts and did not differ from that of the reference population. Significantly increased SIRs were observed

Table 1 Cancer incidence among longshoremen, indoor and outdoor workers (1986–96)

Cancer site (ICD-9)	Indoor workers				Outdoor workers			
	Obs	Exp	SIR	(95% CI)	Obs	Exp	SIR	(95%CI)
All malignant cancers (140–208)	287	275.36	104	(93 to 117)	221	218.12	101	(88 to 116)
Digestive tract (150–157)	60	66.10	91	(69 to 117)	47	51.85	91	(67 to 121)
Larynx (161)	24	11.29	213	(136 to 316)	15	9.10	165	(92 to 272)
Lung (162)	61	62.38	98	(75 to 126)	58	49.11	118	(90 to 153)
Mesothelioma (163)	16	1.18	1362	(778 to 2211)	7	0.93	751	(302 to 1547)
Melanoma (172)	3	3.09	97	(20 to 284)	8	2.77	288	(125 to 568)
Skin (173)	19	26.86	71	(43 to 110)	14	21.36	66	(36 to 110)
Bladder (188)	25	30.84	81	(52 to 120)	33	24.54	135	(93 to 189)
Other malignant cancers	79	73.62	107	(85 to 134)	39	58.46	67	(47 to 91)

ICD-9, International Classification of Diseases, 9th revision; Obs, observed incident cases; Exp, expected incident cases based on Genova Cancer Registry; SIR, standardised incidence ratios.

Table 2 Cutaneous malignant melanoma (CMM): observed cases by age at diagnosis (age), indoor/outdoor working activity (job), ICD-9 code, and anatomical site (site)

Case	Age	Job	ICD-9	Site
1	48	Indoor	1726	Forearm
2	53	Indoor	1722	Ear
3	53	Indoor	1725	Back
4	50	Outdoor	1720	Leg
5	52	Outdoor	1720	Arm
6	52	Outdoor	1720	Scapula
7	52	Outdoor	1725	Back
8	53	Outdoor	1720	Shoulder
9	53	Outdoor	1725	Back
10	60	Outdoor	1727	Leg
11	75	Outdoor	1720	Neck

for pleural mesotheliomas in indoor (16 cases, SIR = 1362, 95% CI 778 to 2211, $p < 0.0001$) and outdoor dockyard workers (7 cases, SIR = 751, 95% CI 302 to 1547, $p = 0.0001$).

Eight cases of CMM were observed in outdoor workers (SIR = 288, 95% CI 125 to 568, $p = 0.015$), and three cases among indoor workers (SIR = 97, 95% CI 20 to 284, $p = 0.99$). Table 2 shows main anatomical site, age at diagnosis, ICD-9 code, and job type for each incident case of CMM.

SIR for skin cancer (other than CMM) was decreased (not significantly) in both indoor and outdoor longshoremen (table 1). A moderately increased SIR for bladder cancer was observed among outdoor workers (33 cases, SIR = 135, 95% CI 93 to 189, $p = 0.118$).

Internal comparison (data not shown), revealed a similar incidence for all cancers (RR = 0.97, 95% CI 0.81 to 1.16), digestive tract (RR = 0.99, 95% CI 0.67 to 1.49), and skin cancer (RR = 0.93, 95% CI 0.43 to 1.95)

in the two subgroups. A higher incidence for CMM (RR = 2.97, 95% CI 0.71 to 17.41) and bladder cancer (RR = 1.66, 95% CI 0.96 to 2.91), and lower incidence for pleural mesotheliomas (RR = 0.56, 95% CI 0.19 to 1.42) were detected in outdoor compared to indoor workers. None of the RR values were statistically significant, a finding that is due to similar exposures shared by the two subgroups and the lower statistical power achieved by internal than external comparison.

The threefold increased risk that was detected for CMM only among outdoor workers supports the causal role of exposure to sunlight, and is apparently in contrast with the previously reported evidence of a potential association with occupational exposure among chemists, telecommunications and electronics, and printing industry workers.²⁻⁴

This, together with a lower than expected incidence of skin cancer (other than CMM) observed in both indoor and outdoor workers, suggests that exposure to sunlight and to carcinogenic agents that were present in the

dockyard environment are required in the development of CMM.

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