

Cancer mortality in two asbestos textile factories

Factory		Dust exposure (mpcf.y)				
		<10	10<20	20<40	40<80	>80
South Carolina ¹	E	325	44	40	25	12.5
	N	73 (31)	12 (5)	13 (8)	11 (7)	11 (8)
	P	0.22	0.27	0.32	0.44	0.88
	RR	1.0	1.22	1.45	2.0	4.0
Pennsylvania ⁴	E	505	105	104	57	48
	N	94 (21)	18 (5)	26 (10)	21 (6)	30 (11)
	P	0.19	0.17	0.25	0.37	0.63
	RR	1.0	0.89	1.34	1.99	3.38

E = Expected number of deaths of all causes, based on general population rates.

N = Number of deaths from malignant disease (respiratory neoplasms in parentheses).

P = Ratio $N \div E$.

RR = Ratio of cancer deaths relative to the lowest exposure category.

mesothelioma, it is probable that the disease would be recognised as a malignancy and that the death certificate would be coded to one of the categories of malignant disease (with the exception of ICD code 228, in which case the word mesothelioma will appear on the certificate). It is possible to use the data the authors have presented in tables 5 of their papers to assess the comparative potencies of chrysotile³ and a mixture of chrysotile and the amphiboles⁴ for the induction of asbestos associated malignancies.

From these tables one can calculate for each exposure category the number of deaths expected from all causes of death, standardised for age and calendar period. One may then calculate the ratio of observed cancer deaths (all types) to expected all cause mortality for each category of exposure. The proportion of cancers unrelated to exposure to asbestos should remain constant at roughly 20% of expected all cause mortality, whereas the incidence of asbestos associated malignancies will increase with exposure. The table presents the results of these calculations. It can be seen that the risk of death from cancer, adjusted for expected all cause mortality, was the same in both factories. These data suggest that the risk of death from asbestos associated cancer in factories manufacturing similar products is unrelated to the type of asbestos fibre used. This evidence from human populations is similar to the results of animal experiments which have found little difference in relative toxicities.¹

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² *Federal register.* Washington, 1983 Nov 4: 596-650.

³ McDonald AD, Fry JS, Woolley AJ, McDonald J. Dust exposure and mortality in an American chrysotile textile plant. *Br J Ind Med* 1983;**40**:361-7.

⁴ McDonald AD, Fry JS, Woolley AJ, McDonald JC. Dust exposure and mortality in an American factory using chrysotile, amosite, and crocidolite in mainly textile manufacture. *Br J Ind Med* 1982;**39**:368-74.

A problem in looking for relationships between concentrations of urinary components

Sir,—Falck *et al* report on an investigation between metallothionin (MT), chronic exposure to cadmium (Cd), and renal function.¹ Among other findings, they note statistically significant linear relationships between urinary concentration of MT and those of Cd, total protein, and beta-2-microglobulin, when each is expressed per unit creatinine excretion.

We write to raise a problem that arises in the interpretation of results from this and other studies that investigate relationships between concentrations of solutes in spot samples of urine. While we do not think that the major conclusions of Falck *et al* should be challenged, the problem raised is a general one which has not to our knowledge been discussed before.

If uncorrected for degree of dilution, concentrations of any two otherwise unrelated solutes of urine must inevitably be positively correlated. Urine that is concentrated overall will tend to have higher concentrations of both solutes, and conversely urine that is dilute will tend to have lower concentrations of both solutes. To aid comparability of urine concentrations, they are often expressed per unit creatinine excretion, on the grounds that creatinine excretion rate is much more constant between and within individuals than urinary dilution. While urinary concentrations thus corrected for dilution should be less subject to spurious correlations of the

type described above, they will not be entirely free from this effect. Creatinine excretion rate does vary between individuals—it is, for example, related to muscle mass—and also within an individual over time as, for example, in relation to physical activity.² Thus a urine sample from an individual who has a high excretion rate of creatinine will tend to have lower concentrations of other urinary solutes, if these are expressed per unit creatinine excretion. The low creatinine excretor will conversely tend to have apparently higher concentrations of other solutes even when rates of excretion per unit time of such solutes are equal. This effect gives rise to artificial positive correlations between urinary concentrations expressed per unit creatinine excretion. This is not to say that any such correlation observed is wholly due to this artifact, but rather that it will be difficult to disentangle a real from a spurious relationship.

In the study of Flack *et al* a statistically significant positive correlation was also found between MT in urine and cumulative exposure to Cd.¹ Individuals with “high” values of two or more of glucose, total protein, or beta-2-microglobulin in urine also had a significantly higher mean concentration of MT in serum. Since these relationships are not subject to the artificial causes described above, it seems likely that those observed between urinary concentrations are not wholly spurious either. By contrast, in a recent study of workers exposed to low levels of cadmium a statistically significant relationship was observed between urinary concentrations of cadmium and beta-2-microglobulin (expressed per unit creatinine excretion) but not between beta-2-microglobulin concentration in urine and cumulative exposure to cadmium.³ In this study it was considered more likely that the relationship between urinary concentrations was due to the effect described above.

We cannot see any wholly adequate way of avoiding this problem. Concentrations corrected by specific gravity will be subject to similar spurious correlations to those noted above. Use of specific gravity to correct one urinary concentration and expressing a second per unit creatinine excretion may possibly reduce the spurious correlation between them, since the “errors” of each method of correction may not be appreciably correlated. Alternatively it is possible to quantify the strength of the relationship that would be caused by this effect if, for example, the distribution of the rate of creatinine excretion between individuals were known. A relationship stronger than this would then be evidence for an effect additional to the spurious one. Effects of the type described will be present however relationships between urinary concentra-

tions are investigated. In particular, dichotomising one or both concentrations to give “normals” and “abnormals” does not avoid the problem.

More generally, such spurious correlations may also arise between any two independent variables in urine, each of which may be related to the functional status of the kidney, and we speculate that similar confounding may cause weak relationships between many biological variables. We should, therefore, be cautious in interpreting data exhibiting such relationships.

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Book review

Toxic Hazards of Rubber Chemicals. By AR Nutt. (Pp194 +xi, £25.) London and New York; Elsevier Applied Science Publishers, 1984.

This short book reports some risks to health that are known to be associated with rubber technology. The layout is excellent, and the scientific data appear at first sight to be exceptionally well marshalled and displayed.

Part II provides an annotated catalogue of substances used in the manufacture of rubbers, exhaustive compilations of the appropriate proprietary names, a note on their physical form, and succinct toxicity data, but there is no reference at all to the corresponding physical properties and characteristic chemical reactions, such as spot tests. Curiously, the only reference to the anils, which were mandatory ingredients of heavy duty rubbers during the second



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