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Job related morality risks of Hanford workers and their relation to cancer effects of measured doses of external radiation

Sir,—According to Gilbert and Peterson,¹ who disapprove of the latest attempt by Mancuso, Stewart, and Kneale (MSK) to control for job related mortality risks other than external radiation,² one of the reasons why their tests of cancer risks for radiation workers at Hanford have not confirmed the latest MSK findings for "radiosensitive cancers" is because their choice of controlling factors is more appropriate than the MSK choice. There is, how-

ever, a much stronger reason—namely, lack of conformity between the two groups of cancers which are supposed to correspond to an ICRP classification of "tissue sensitivity to cancer induction effects of radiation"³ (so called A series or radiosensitive cancers).

In the MSK analysis this group was formed from the 8th revision of the ICD list of diseases and causes of death by pooling the following code numbers: 146-9, 151, 153, 157, 162-3, 174, 193, 200-3, and 205. In the G/P analysis the group included the following code numbers: 146-159, 162-3, 174, 193, 200-9 (table). Therefore, although the total number of deaths was larger in the MSK series of 1943-79 deaths (4939) than in the G/P series of 1943-78 deaths (4635), the latter included more radiosensitive cancer (612) than the former (572). For all deaths the ratio of MSK to G/P cases (1.07) showed no signs of being dose related, but for radiosensitive cancers the ratio was much higher for the upper half of the dose scale (1.12) than the lower half (0.89).

Therefore, if Gilbert and Peterson are anxious to prove that Hanford data are not inconsistent with current estimates of radiation risks—and are not prepared to control for job related mortality risk by the MSK method—they should at least (1) show us the results of applying to their data the latest MSK groupings of radiosensitive and other cancers and (2) include the two groups of deaths from cancer in an analysis that distinguishes between craftsmen operators and other Hanford workers.

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Comparisons between two versions of Hanford data

Dose (rems)	Mancuso, Stewart, and Kneale (MSK)		Gilbert and Peterson (G/P)		Ratio of MSK to G/P cases	
	All deaths	Radiosensitive* cancers	All deaths	Radiosensitive† cancers	All deaths	Radiosensitive cancers
0.00-	1060	(105)	998	(123)	1.06	0.85
0.01-	555	(66)	522	(79)	1.06	0.84
0.08-	869	(99)	819	(117)	1.06	0.85
0.32-	647	(96)	600	(94)	1.08	1.02
0.64-	689	(77)	652	(84)	1.06	0.92
1.28-	530	(52)	491	(48)	1.08	1.08
2.56-	231	(33)	218	(31)	1.06	1.06
5.12-	150	(20)	143	(16)	1.05	1.25
10.24-	96	(17)	92	(15)	1.04	1.13
≥20.48	112	(7)	100	(5)	1.12	1.40
Total	4939	(572)	4635	(612)	1.07	0.93

*ICD Nos: 146-9, 151, 153, 157, 162-3, 174, 193, 200-23, 205.

†ICD Nos: 146-159, 162-3, 174, 193, 200-9.

Positions on the dose scale take no account of radiation doses within 10 years of death.

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Uptake of solvents from the lungs

Sir,—Any solvent, like any other drug, reaches a steady state concentration (90% of the equilibrium concentration) in any compartment in a time equal to 3.3 times the value of its half life, which may be theoretically estimated from the following formula^{1,2}:

$$T/2 = 1n 2 \times (V \times \lambda_T)/F$$

where V = volume of the tissue (compartment), λ_T = the tissue/blood partition coefficient of the solvent, and F = the blood flow to the tissue concerned.

As the enclosed table shows, methyl ethyl ketone (MEK) has a half life of 0.8 minutes, toluene a half life of 1.8 minutes, and n-hexane a half life of 3.2 minutes in the tissues of the vessel rich group. According to these values, n-hexane, which is the least soluble solvent of the three (blood/air partition coefficient = 0.8), can reach a steady state concentration in the tissues of the vessel rich group in about 10 minutes, whereas MEK, which is the most soluble solvent (blood/air partition coefficient = 202), can reach an equilibrium concentration in about three minutes in the same compartment.

If these observations are true then I find it hard to understand the sentence: "Owing to the high solu-

bility of the solvents . . . no tissue approached equilibrium with the blood during the experimental exposures. . . ." reported in the editorial: "Uptake of solvents from the lungs" (1985;42:217-8).

The tissues of the vessel rich compartment always approach equilibrium with blood within a few minutes, since its volume is small (6 litres), perfusion is large (5.2 litres/min), and the tissue/blood partition coefficient concerned is generally low (tissue solubility generally no more than 1-10 times blood solubility, apart from fat tissue).¹⁻³

Industrial jobs where exposure to solvents generally occurs do not entail a heavy work load, and, in any case, if this happens the duration of the heavy physical load is relatively short—for instance, 30-60 minutes in a seven to eight hour workshift. If this is true the considerable increase of $\dot{V}_A$ (triplication, quadruplication, or more) that follows the heavy work load can certainly modify the lung uptake, but for a time which is, in practice, only a small fraction of the work shift.

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Volume and perfusion of the four tissue groups and distribution coefficients, distribution volumes, and biological half lives of methyl ethyl ketone (MEK), toluene, and n-hexane

Parameters	Solvents	Tissue groups			
		Vessel rich	Muscle	Fat	Vessel poor
Volume in 70 kg person (V = L)		6	33	14.5	12.5
Perfusion (l/min) (F)		5.25	1.27	0.38	0.1
Percentage (%) of cardiac output		75%	18.1%	5.4%	1.5%
Tissue/blood distribution coefficient (λ_T)	MEK ³	1.0	1.2	0.88	—
	Toluene ⁴	2.3	1.6	82	1.9
	n-Hexane ⁵	4.0	5.0	130	—
	MEK	6.0	39.6	12.8	—
Distribution volume (V _D = L) (V × λ_T = V _D)	Toluene	13.8	52.8	1189	23.7
	n-Hexane	24.0	165	1885	—
	MEK	0.8 min	21.8 min	23.3 min	—
	Toluene	1.8 min	28.8 min	36.1 H	2.7 H
Biological half life (V _D /F × 0.693)	n-Hexane	3.2 min	90.0 min	57.4 H	—