Correspondence

Hepatotoxicity of organic solvents

Sir,—Edling and Tagesson (1984;41:257-9) observed increased concentrations of serum bile acids (SBA) in men exposed to styrene in the absence of ethanol abuse, drug intake, and apparent liver disease. By contrast Lundberg and Hakanasson (1985;42: 596-600) failed to observe any changes in the serum activities of liver enzymes examined in workers exposed to a mixture of organic solvents (mostly xylene).

These findings represent two examples of the controversial data reported in relation to the hepatotoxicity of organic solvents. We suggest that these findings might be reconciled in two ways; firstly, as a consequence of the different type, entity, and duration of exposure to chemicals. Secondly, it may well be that the tests (mostly serum liver enzyme activities) used to evaluate liver function are not sensitive enough to detect small changes at an early stage. Recently, it has been suggested that SBA concentrations reflect liver function better than either serum liver enzyme activities or bilirubin concentrations because they show liver impairment at an early stage.³

We examined both SBA concentrations and conventional liver function tests (alanine aminotransferase ALT, aspartate aminotransferase AST, gamma-glutamyl transferase GGT, direct bilirubin) when carrying out biological monitoring of workers occupationally exposed to organic solvent mixtures (toluene, xylene, styrene, acetone, n-butylacetate, n-butanol, n-hexane, ethylacetate, methylene chloride, methyl isobutylketone). Exposure levels ranged from

10% to 200% of the TLV-TWA adopted by the ACGIH for 1985. In 30 exposed subjects (occupational exposure for more than two years, daily ethanol consumption less than 50 ml, no history of liver disease, no drug intake for the previous three months) we observed significantly higher mean levels of SBA than in a control group of 20 subjects (table 1). As regards serum liver enzyme activities, no differences were observed between the two groups. The prevalence of subjects with abnormal levels of the parameters examined is given in table 2. Seventy three per cent of the exposed workers had SBA concentrations higher than the upper reference limit as compared with 5% of controls. The respective percentages for ALT, AST, GGT, and bilirubin were 10%, 7%, 27%, 3% in the exposed group as against 5%, 5%, 16%, 0% in controls.

We agree with Edling and Tagesson that increased SBA concentrations may represent a possible sign of hepatotoxicity in workers exposed to styrene. We suggest, however, that SBA assessment may represent a sensitive and early index of hepatic injury from exposure not only to styrene but also to other organic solvents. Hence this parameter might be adopted as an index in the biological monitoring of workers exposed to hepatotoxic risks.

G FRANCO

R FONTE

F CANDURA

Dipartimento di medicina preventiva, occupazionale e di comunità, Università di Pavia, via S Boezio 24, I-27100 Pavia, Italy.

Reference

- ¹ Anonymous. Serum bile acids in hepatobiliary disease. *Lancet* 1982;ii:1136-7.

Table 1 Mean levels $\pm$ SD of serum bile acids (SBA) and direct bilirubin, and serum liver enzyme activities (alanine aminotransferase ALT, aspartate aminotransferase AST, gamma-glutamyl transferase GGT) in the group of workers exposed to solvent mixture and in controls. (Statistical significance evaluated by Student's *t* test)

	SBA (μ mol/l)	ALT (μ kat/l)	AST (μ kat/l)	GGT (μ kat/l)	Bilirubin (μ mol/l)
Exposed group	8.0 $\pm$ 6.0	0.41 $\pm$ 0.23	0.31 $\pm$ 0.13	0.40 $\pm$ 0.24	1.9 $\pm$ 1.5
Controls	2.8 $\pm$ 1.4	0.33 $\pm$ 0.21	0.28 $\pm$ 0.15	0.45 $\pm$ 0.33	1.9 $\pm$ 0.5
<i>t</i>	3.7	0.4	1.1	0.4	0.04
<i>p</i>	<0.01	NS	NS	NS	NS

NS = Not significant.

Table 2 Prevalence of subjects with abnormal levels of the parameters examined. (Statistical significance evaluated by chi-square test)

	SBA (μ mol/l)	ALT (μ kat/l)	AST (μ kat/l)	GGT (μ kat/l)	Bilirubin (μ mol/l)
Upper limit of normal	5.6	0.65	0.65	0.50	4.2
Exposed group	22	3	2	8	1
Controls	1	1	1	3	0
Chi-square	28.4	0.34	0.17	0.29	0.64
<i>p</i>	<0.001	NS	NS	NS	NS