

Solvent exposure, alcohol consumption and liver injury in workers manufacturing paint

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REES D, SODERLUND N, CRONJE R, SONG E, KIELKOWSKI D, MYERS J. Solvent exposure, alcohol consumption and liver injury in workers manufacturing paint. *Scand J Work Environ Health* 1993;19:236–44. Liver enzyme activity was examined in 89 South African paint makers currently exposed to a mixture of organic solvents at fairly low levels. However, the duration of exposure was substantial for many. Fifty-eight workers (65%) had at least one enzyme value above the upper reference limit. Gamma glutamyl transferase (γ GT) activity was elevated in 46% of the workers and aspartate aminotransferase (ASAT) in 52%. In a comparison between workers with high and low solvent exposure, the γ GT and ASAT values were higher in the most exposed group (eg, γ GT mean 108 versus 69 U · l⁻¹, $P > 0.05$). Adjustment for confounding by alcohol consumption and body mass index eliminated the differences due to exposure. It was concluded that the measures of liver injury used did not demonstrate solvent-induced hepatic damage but that excessive alcohol consumption was an important factor.

Key terms: alcohol, hepatotoxicity, liver enzymes, paint manufacture, organic solvent mixtures, South Africa.

Case reports of liver injury caused by occupational exposure to organic solvents are well known. Consequently the hepatotoxic potential of some organic solvents, notably aliphatic chlorinated hydrocarbons, is not in doubt. Convincing epidemiologic evidence of liver injury in workers exposed to mixtures of solvents at usual workplace levels is, however, scant. Many studies reporting liver injury in exposed workers are based on mortality data (1) or case series often without an adequate comparison group or complete exposure data (2–4). Furthermore, negative studies are well represented in the literature (5–7), although their value is limited to some extent by the small number of workers with heavy solvent exposure.

In general, it can be said that the epidemiologic evidence supporting a causal relationship between chronic exposure to mixed solvents at low levels and clinically significant liver disease is weak. This statement does not necessarily imply however that the investigation of liver function in workers using these compounds is not warranted. Nonworkplace hepatotoxins such as alcohol and medicinal drugs may increase the risk of liver injury in these workers. Also

of concern, particularly in underdeveloped countries, is the high incidence of infective liver disease (8) and the possible role of poor nutrition in increasing hepatic damage in these workers. The combined effect of occupational and nonoccupational factors on workers in developing countries may be important and was the motivation for this study of liver function in workers manufacturing paint in a South African factory.

Workers manufacturing paint are usually exposed to a mixture of aliphatic and aromatic organic solvents at relatively moderate intensity. To our knowledge no studies of the hepatic effects of this type of industrial exposure have been conducted in South Africa nor in a developing country. The major objectives of the cross-sectional study reported in this paper were (i) to determine the prevalence of abnormalities in routinely used biochemical indicators of liver injury in long-service workers making paint, (ii) to investigate the association between these indicators and solvent exposure, and (iii) to examine possible modifications in solvent effects caused by alcohol consumption and past exposure to hepatitis B virus.

Subjects and methods

Subjects

Two hundred and thirteen African men were employed at the paint factory. Limited resources prevented the inclusion of all 213. Consequently, only those workers with eight or more years of service and those with shorter service who were currently working in areas with relatively high solvent exposure (as

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identified by factory management and walkthrough inspections of the factory) were asked to participate in the study. Ninety workers satisfied the first criterion, and 12 the second. The response rates were 91% (82 workers) and 92% (11 workers), respectively — thus 93 workers participated in the study. Reasons for nonresponse were prolonged sick leave for two workers (diagnosis not established), traumatic death for one, and refusal to donate blood for the remainder.

Four of the 93 participants were excluded from the analysis either because of missing data (three subjects had blood specimens damaged in transit and were reluctant to provide a repeat specimen) or positive HB_s antigen (one subject).

The workplace

Paint manufacture started on the present site in the mid-1950s, and the production process has remained fundamentally unchanged for many years. Improved paint technology has, however, resulted in alterations in the constituents of the paints, and solvent usage has varied over the years. Recently the factory has predominantly manufactured industrial solvent-based paints, but water-based decorative paints have made up roughly a third of the 10 million liters of paint produced per year. The major intervention to decrease levels of solvents in workplace air has been the covering of paint-filled pots with plastic sheeting to reduce the surface area from which solvent vapor could be generated. Long-service employees testify to the success of this strategy, and a reduction in the air levels of solvents with time is very likely. The current levels should be treated as the minimum to which the workers have been exposed.

The general production process of the plant is as follows. Dry raw materials, such as pigments, are ball-milled in a resin vehicle (milling section). The milled material is then transferred to a mixer where it is extended with solvents and mixed (mixing section). The paint is then decanted into containers (filling section) or customized by the addition of special-function agents (special function sections 1 and 2) before the decanting. Paint is moved between sections in large pots, and these pots are cleaned with solvents in the pot cleaning section. The final steps are labeling (labeling section) and despatch (warehouse). Water-based paints are made in a separate polyvinyl acetate plant. As usual, in a paint factory, several other specialized processes are in operation. Small batches of special application paint are made in batches sections 1 and 2; solvents are decanted into small containers in the thinners section; cans of spray paint are produced in the aerosol section; paint from damaged containers is decanted into new containers in the refilling section; and special colors are mixed in the small mix section. The production process is supported by workshops, stores, quality control, transport services, and administration offices.

Exposure

After written consent was obtained, a questionnaire covering alcohol consumption, medication, previous liver disease, and full details of past and current occupational history was administered by a trained interviewer to each subject in his home language. Alcohol consumption was assessed by detailed inquiry of both the current and past peak weekly intake of beer, wine, spirits, and traditional alcoholic beverages. Total weekly intake was converted to grams per day for current and peak consumption separately.

The current exposure to solvents was determined from measurements of workplace air levels of the eight most extensively used solvents (table 1), and past exposure was assessed from data collected during routine environmental monitoring performed by the company's Occupational Health Service during 1987–1989. The current evaluation of solvent in air was conducted by an experienced industrial hygienist who divided the factory into solvent and nonsolvent sections according to walkthrough inspections and the routine monitoring data. The solvent sections were all those in which solvent exposure was likely, and they included sections directly involved in paint making, decanting, or cleaning with solvents, plus sections with historical solvent levels in excess of 5% of the threshold limit value (TLV) of the American Conference of Governmental Industrial Hygienists for solvent mixtures (9). Levels of solvent in air were determined from samples obtained from 41 solvent section workers wearing personal samplers comprised of an activated charcoal tube connected by tubing to a low-flow (20 ml · min⁻¹ calibrated orifice) Casella SP15 pump (London, United Kingdom). Vapors collected on the activated charcoal were determined with gas chromatographic analyses (10). The selection of workers to wear personal samplers was done by the industrial hygienist, who inspected each solvent section and selected workers representative of all the important procedures or jobs (tasks) performed in that section. Limited resources prevented the use of a random selection method such as that proposed by the National Institute for Occupational Safety and Health in the United States (11). The measurements took place during a period of routine production. The proportion of workers who wore samplers was 0%, 14%, 25%, 27% and 50% in aerosol, batches 1, mixing, filling and special function 1, respectively, and 100% in the remaining sections. Solvent levels were not measured in the aerosol section as workers were temporarily engaged in nonroutine activity.

The solvent levels in the air of the solvent-exposed sections are shown in table 1, along with the number of workers currently employed in each section. Eighty-three workers were currently working directly with solvents, and the solvent level in the breathing zone ranged from 50 mg · m⁻³ (special function section 2) to 434 mg · m⁻³ (pot cleaning section). The past and current levels were not always in agreement

Table 1. Mean current and past (1987–1989) levels of solvents in the solvent sections of the paint factory. Levels for the three most important solvents, the sum of all eight solvents measured (total solvent exposure), and the proportion of the threshold limit value (TLV) for the mixture of solvents (% TLV)^a are presented. (BDL = below detection limits)

Section ^b	Number of measurements		Solvent measurements (mg · m ⁻³)								Combined 1987—1990 % TLV ^a
			Toluene		Xylene		White spirit		Total solvent exposure ^c		
	Current	Past	Current	Past	Current	Past	Current	Past	Current	Past	
Milling (N = 8)											
Loader	4	11	94	72	111	35	17	24	222	171	45
Mixer	1	3	8	40	23	10	48	15	79	65	14
Mixing (N = 4)	1	3	10	67	11	10	15	10	38	106	14
Filling (N = 22)	6	3	18	73	30	34	20	35	68	188	27
Special function 1 (N = 3)	2	2	69	50	27	44	20	126	116	240	38
Special function 2 (N = 12)	2	4	12	12	20	11	15	20	50	43	7
Pot cleaning (N = 5)											
Pot cleaning	3	3	206	63	116	10	24	—	434	134	59
Drum cleaning	6	13	140	106	82	38	23	46	301	240	46
Batches 1 (N = 7)	1	—	BDL	—	BDL	—	BDL	—	—	—	—
Batches 2 (N = 2)	3	—	37	—	65	—	45	—	147	—	24
Thinners (N = 4)	4	2	16	27	14	28	26	20	56	95	19
Aerosol (N = 14)	—	5	—	39	—	41	—	81	—	177	35
Refilling (N = 3)	3	—	136	—	108	—	20	—	264	—	75
Small mix (N = 3)	5	3	36	141	27	53	20	78	83	299	42

^a TLV of mixture $(C_1/T_1) + (C_2/T_2) + (C_3/T_3) \dots$ where C_1 is the measured atmospheric concentration of a particular solvent and T_1 is the threshold limit value.

^b Number of workers currently employed in the section in parentheses.

^c Includes toluene, xylene, white spirit, ethyl acetate, methyl ethyl ketone, methyl-isobutyl ketone, N butyl acetate, and cellulose acetate.

Table 2. Duration and intensity of the low and high exposure according to exposure group. (CE = cumulative exposure, TLV = threshold limit value)

Group	Cumulative exposure		Duration of service (years)		Additional solvent exposure (years)		Current solvent exposure (TLV%)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Low exposure ^a (N = 40)	28	22	11	7	2.1	3.5	8	19
High exposure ^b (N = 49)	408	308	17	9	2.3	4.3	28	22
Low and high exposure combined (N = 89)	238	297	14	8	2.2	4	18	22

^a Low exposure = CE < 100 TLV% years.

^b High exposure = CE > 100 TLV% years.

(eg, for the pot cleaning section), probably because of the variability in daily work procedures and factors such as ambient temperature and natural ventilation. The combined 1987–1990 levels were used in the calculations of the cumulative exposure and the second exposure index.

Not shown in table 1 is that three samples were collected from three workshop workers who all had samples below the detection limits.

Thirty-four subjects reported working with solvents prior to employment at the study factory. In general this work was for short periods only, mean 2.2 (SD 4) years. The distribution of this additional service relative to the cumulative exposure at the paint factory is shown in table 2.

The hepatotoxic potential of the various solvents was considered to be equal. Therefore an additive model was used to calculate the TLV for mixtures of solvents. The TLV for the mixture of solvents was thus $(C_1/T_1) + (C_2/T_2) + (C_3/T_3) \dots$, where C was

the measured atmospheric concentration and T the threshold limit value of a particular solvent.

Cumulative exposure (CE) to solvents was calculated for each worker by multiplying the number of years spent in a section by the level of mixed-solvent exposure, as the percentage of the TLV (%TLV), and then adding these products for each section in which the worker had worked:

$$CE = (\text{years}_1 \times \%TLV_1) + (\text{years}_2 \times \%TLV_2) + \dots$$

In the calculations of the cumulative exposure, factory sections which did not use solvents but which were directly adjacent to solvent sections were arbitrarily assigned a mixed-solvent exposure level of 5% of the TLV. The remaining nonsolvent sections were assigned an exposure level of 1%.

Table 2 shows that the cumulative exposure to solvents was used to categorize workers into the two

exposure groups with the cutoff for low exposure set at <100 TLV% years. This cutoff was chosen to separate the low- and high-exposure groups into approximately equal sizes, while ensuring that the group with low cumulative exposure did not include many workers with substantial current exposure. The distribution of the cumulative exposure was positively skewed, with a median of 121 TLV% years. Using the median as the cutoff instead of 100 TLV% years altered the results shown in table 2 only minimally. As can be seen from the table, the average duration of service was substantial with a mean of 14 years. Solvent exposure at other workplaces was very similar for the groups, but the average duration of service at the paint factory was longer for the group with a high cumulative exposure (17 versus 11 years). The average cumulative exposure differed markedly, being 28 and 408 %TLV years for the low and high exposure groups, respectively. The current solvent exposure levels were fairly low. The group with low cumulative exposure was significantly younger, but the body mass index did not differ between the groups (table 3).

A second exposure index was derived as for the cumulative exposure, except that the percentage of the TLV was replaced by total solvent exposure in milligrams per cubic meter.

Liver injury

Liver function was assessed through an analysis of serum bilirubin and the activities of the serum enzymes gamma glutamyl transferase (γ GT), alkaline

phosphatase (ALP), alanine aminotransferase (ALAT), and aspartate aminotransferase (ASAT) (table 4). These analyses were performed by the South African Institute for Medical Research — which is the regional reference laboratory — using standard methods on a Boehringer Mannheim Hitachi model 704 automatic analyzer (Tokyo, Japan). Specimens were analyzed on the day of collection. The upper reference value for these determinations is shown in the legend of figure 1. Workers with any value exceeding the reference were investigated for evidence of hepatitis A (HA) and hepatitis B (HB) virus infection [A: HA immunoglobulin M antibody; B: HB core (HB_c) and HB surface (HB_s) antibody and antigen], and a liver specialist was consulted regarding further management.

The workers had not been monitored for liver injury by the Occupational Health Service prior to this study and the occupational health staff had no recall of any worker being relocated from a worksite with high solvent exposure to one with low exposure as a consequence of an abnormality in liver function.

Analysis

Multiple linear regression was done to investigate the relationships between solvent exposure (cumulative exposure, second exposure index, duration of service in paint manufacture, and current solvent exposure), Quetelet's body mass index [weight (kilograms)/height²(meters)], current alcohol consumption, age (years), and the dependent variables γ GT, ALP, ALAT, ASAT and the ALAT:ASAT ratio. An

Table 3. Body mass index, age, and alcohol use of the workers according to exposure group.

Group	Body mass index ^a		Age (years)		Alcohol use (g · d ⁻¹)			
					Current		Peak	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Low exposure (N = 40)	25	3.7	43	22	26	34	53	56
High exposure (N = 49)	25	3.7	48	15	47	45	76	64
Low and high exposure combined (N = 89)	25	3.7	45	19	37	42	66	61

^a Body mass index = weight (kg) · height⁻² (m).

Table 4. Liver enzyme activity of the workers according to exposure group. (γ GT = gamma glutamyl transferase, ALP = alkaline phosphatase, ALAT = alanine aminotransferase, ASAT = aspartate aminotransferase)

Group	γ GT ^a (U · l ⁻¹)		ALP ^b (U · l ⁻¹)		ALAT ^c (U · l ⁻¹)		ASAT ^d (U · l ⁻¹)		ALAT:ASAT (%)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Low exposure (N = 40)	69	71	95	30	26	13	33	14	79	31
High exposure (N = 49)	108	126	94	29	31	15	41	27	81	29
Low and high exposure combined (N = 89)	91	107	94	29	28	14	38	22	81	30

^a Normal value = > 50 U · l⁻¹.

^b Normal value = > 120 U · l⁻¹.

^c Normal value = > 38 U · l⁻¹.

^d Normal value = > 30 U · l⁻¹.

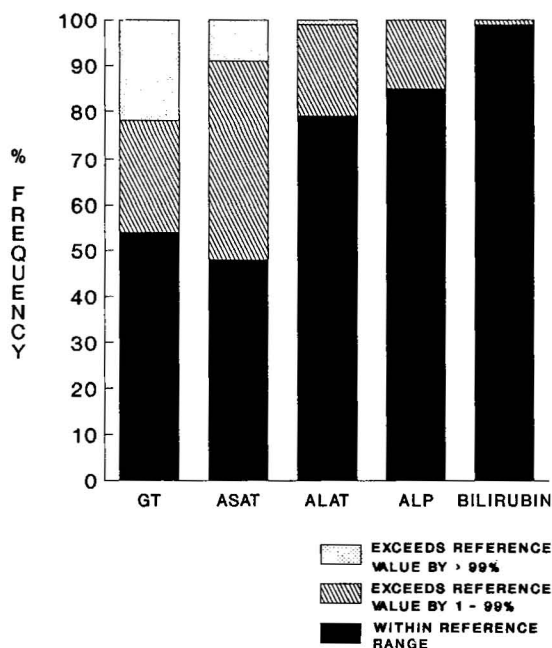


Figure 1. Biochemical indicators of liver function by the proportion of workers with values above the reference value of $50 \text{ U} \cdot \text{l}^{-1}$ for gamma-glutamyl transferase (γGT), $30 \text{ U} \cdot \text{l}^{-1}$ for aspartate aminotransferase (ASAT), $38 \text{ U} \cdot \text{l}^{-1}$ for alanine aminotransferase (ALAT), $120 \text{ U} \cdot \text{l}^{-1}$ for alkaline phosphatase (ALP), and $21 \mu\text{mol} \cdot \text{l}^{-1}$ for bilirubin.

elevated ALAT:ASAT ratio has been used to differentiate solvent-induced liver injury from alcohol damage, which can cause a disproportionate increase in ASAT activity (12).

The dependent variables were not normally distributed and were transformed ($\log_{10}$) for the regression analyses, which were done with the help of PC-SAS (statistical analysis system for a personal computer) (13).

In most instances the exposure and outcome (serum enzyme activity) data were not normally distributed, and nonparametric tests of statistical significance were used unless otherwise indicated.

Results

Fifty-eight of the 89 workers (65%) had a biochemical index of liver function above the upper reference value. Figure 1 shows the extent of liver function abnormality for each indicator tested. The γGT activity was abnormal for 41 workers (46%), as was the ASAT for 46 workers (52%), while bilirubin was mildly elevated ($22 \mu\text{mol} \cdot \text{l}^{-1}$) in one worker only.

Medication was unlikely to be an important factor in accounting for these abnormalities. Although 34 workers (38%) had used a drug within three months of the study, drug use was not associated with solvent exposure (cumulative exposure) nor with biochemical abnormalities of liver function. In addition, other than hypertension (6 workers, 7%), con-

ditions associated with the use of potentially hepatotoxic agents were not reported. For example, no worker had been exposed to an anesthetic recently or treatment for tuberculosis, epilepsy, diabetes mellitus, or a psychological condition within the past five years.

An important feature was the higher current alcohol consumption reported by the group with higher solvent exposure.

Considering the indicators of liver function, it can be seen that the mean γGT was well above the upper reference value ($50 \text{ U} \cdot \text{l}^{-1}$) for the whole group and for both exposure categories, the high-exposure group having the higher mean γGT (108 versus $69 \text{ U} \cdot \text{l}^{-1}$). The γGT values were, however, not normally distributed and the median values for the cumulative exposure groups were less different at 50.0 and $42.5 \text{ U} \cdot \text{l}^{-1}$. The ASAT pattern was similar, but the values were relatively less elevated above the reference value of $30 \text{ U} \cdot \text{l}^{-1}$. These differences were not statistically significant at the 5% level for either the untransformed or transformed data. The ALP and ALAT activity and the ALAT:ASAT% ratio were not associated with solvent use.

The group with low cumulative exposure included two workers with current exposure at 59% of the TLV for mixtures and four workers with a corresponding value of 35%. Repeating the comparisons in table 4 with these six currently exposed workers excluded from the low-exposure group left the enzyme activities essentially unaltered — no change in enzyme value exceeded $2 \text{ U} \cdot \text{l}^{-1}$. Thus the relatively high current solvent levels for a small number of subjects with low cumulative exposure did not account for the lack of significant differences between the workers with high and low cumulative exposure.

To compare enzyme activity in groups with a greater contrast in solvent exposure, we analyzed the first and fourth cumulative exposure quarters. The mean cumulative exposures for these two groups were 12.7 (range 9–18) and 707.9 (range 386–1323) TLV% years. The differences in the γGT and ASAT values were large — γGT 70.1 versus $132 \text{ U} \cdot \text{l}^{-1}$ and ASAT 31.9 versus $42.2 \text{ U} \cdot \text{l}^{-1}$ for the first and fourth quarters respectively — but did not reach statistical significance in either case ($P > 0.1$). This analysis was repeated for the first and fourth current solvent exposure quarters. The current mean solvent exposure was 1% of the TLV (below detection limits) for the first quarter and 44% of the TLV (or $196 \text{ mg} \cdot \text{m}^{-3}$) for total solvents in the fourth quarter, but the median γGT , ASAT, ALAT, and ALP values were all slightly higher for the low current exposure quarter.

To control for the effects of alcohol consumption and assess the contribution of paint manufacture to the effect on liver function, we stratified workers into low, medium, and high alcohol consumption groups so that exposure effects could be compared in groups with similar alcohol usage. Table 5 shows a strong

alcohol effect on γ GT and ASAT in both the low and high cumulative exposure groups. A possible exposure effect was present in that the high cumulative exposure workers who drank little ($0-19 \text{ g} \cdot \text{d}^{-1}$) or moderately ($20-79 \text{ g} \cdot \text{d}^{-1}$) had γ GT and ASAT values above the reference levels (50 and $30 \text{ U} \cdot \text{l}^{-1}$, respectively), and their values were also higher than the corresponding low cumulative exposure workers. This difference was unlikely to be due to obesity as the number of workers classified as obese (body mass index >29.9) was similar for the low- and high-exposure alcohol groups. The highest mean γ GT and ASAT activities were measured for workers with high alcohol consumption in the low-exposure group, probably because two were particularly heavy drinkers.

The possible exposure effect was examined through a performance of multiple linear regression analyses using cumulative exposure, age, body mass index, and current alcohol consumption ($\text{g} \cdot \text{d}^{-1}$) as explanatory variables and γ GT, ALP, ALAT, ASAT (transformed log 10) and ALAT:ASAT as the dependent variables. Table 6 presents the results of these analyses. The table does not include cumula-

tive exposure as it did not contribute significantly to the model for any of the dependent variables. Alcohol consumption was strongly associated with the activities of γ GT, ASAT, and ALAT, while body mass index was a significant factor for the γ GT and ALAT levels and the ALAT:ASAT ratio. Age was associated with the ALP levels. Possible exposure effects were sought with the use of the second exposure index, duration of service in the paint factory, duration of solvent exposure (paint factory + additional solvent exposure years), or current solvent levels in place of cumulative exposure in the model. None of these measures of exposure was significantly associated with enzyme activity.

The workers with an abnormality in liver function were investigated for viral hepatitis A and B infection. No worker was positive for HA immunoglobulin M antibody and only one worker was HB_s antigen positive. Twenty workers (48% of those tested) had immunological evidence of past exposure to hepatitis B virus (HB_c antibody and HB_s antibody positive). Table 7 shows that these 20 workers drank more alcohol than their serologically negative co-workers and they had a higher cumulative exposure.

Table 5. Liver enzyme activity for the low and high solvent-exposure groups according to current alcohol consumption. (γ GT = gamma glutamyl transferase, ALP = alkaline phosphatase, ALAT = alanine aminotransferase, ASAT = aspartate aminotransferase, TLV = threshold limit value)

Group	γ GT ($\text{U} \cdot \text{l}^{-1}$)		ALP ($\text{U} \cdot \text{l}^{-1}$)		ALAT ($\text{U} \cdot \text{l}^{-1}$)		ASAT ($\text{U} \cdot \text{l}^{-1}$)		ALAT:ASAT%	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Low cumulative exposure (< 100 TLV% years)										
0-19 g alcohol $\cdot \text{d}^{-1}$ (N = 20)	38	25	97	28	23	12	27	7	79	26
20-79 g alcohol $\cdot \text{d}^{-1}$ (N = 18)	76	57	86	30	30	14	35	11	85	32
> 79 g alcohol $\cdot \text{d}^{-1}$ (N = 2)	302	58**	110	40	25	15	69	33**	35	7
High cumulative exposure (> 100 TLV% years)										
0-19 g alcohol $\cdot \text{d}^{-1}$ (N = 16)	63	104	96	33	30	15	37	32	91	29
20-79 g alcohol $\cdot \text{d}^{-1}$ (N = 23)	105	133	88	29	28	14	37	18	80	32
> 79 g alcohol $\cdot \text{d}^{-1}$ (N = 10)	187	115**	105	24	37	16	59	32*	68	18

* $P < 0.05$, ** $P < 0.01$, Kruskal-Wallis test (trend from low to high alcohol consumption categories).

Table 6. Linear regression analyses — significant associations ($P < 0.05$) between liver enzymes (transformed) and the independent variables contributing significantly to the model (ie, age, current alcohol consumption, and body mass index). (γ GT = gamma glutamyl transferase, ASAT = aspartate aminotransferase, ALAT = alanine aminotransferase, ALP = alkaline phosphatase)

Liver enzyme	B estimate	Standard error	P-value	R-square
γGT				
Current alcohol consumption	0.014	0.002	0.0001	0.38
Body mass index	0.044	0.022	0.045	
ASAT				
Current alcohol consumption	0.006	0.001	0.0001	0.30
ALAT				
Current alcohol consumption	0.004	0.001	0.001	0.19
Body mass index	0.042	0.129	0.002	
ALP				
Age	0.007	0.003	0.044	0.06
ALAT : ASAT				
Body mass index	0.036	0.008	0.0001	0.25

Table 7. Comparison between 20 workers with and 21 workers without serological evidence of past exposure to hepatitis B virus. (TLV = threshold limit value, γ GT = gamma glutamyl transferase, ALP = alkaline phosphatase, ALAT = alanine aminotransferase, ASAT = aspartate aminotransferase)

Hepatitis B	Current alcohol use (g · d ⁻¹)		Cumulative exposure (TLV% years)		γ GT (U · l ⁻¹)		ASAT (U · l ⁻¹)		ALAT (U · l ⁻¹)		ALP (U · l ⁻¹)	
	Median	Inter-quartile range ^a (%)	Median	Inter-quartile range ^a (%)	Median	Inter-quartile range ^a (%)	Median	Inter-quartile range ^a (%)	Median	Inter-quartile range ^a (%)	Median	Inter-quartile range ^a (%)
Positive (N = 20)	66	48—102	187	59—566	110	69—261	46	34—70	30	24—46	91	71—116
Negative (N = 21)	55	13—61	60	16—297	87	36—182	34	29—46	30	25—36	98	86—136
P-value	0.03		0.06		0.13		0.11		0.47		0.35	

^a 25—75.

Although the γ GT and ASAT levels were higher in the serologically positive group, the differences were not statistically significant. Adding past exposure to hepatitis B virus to the multiple linear regression model failed to show an independent association between past viral exposure and the liver function variables tested.

Discussion

One objective of this study, the first in South Africa and probably the first reported from a developing country, was to determine the prevalence of abnormal liver function among workers with long service in paint making. Five biochemical variables were tested, and well over half of the workers (65%) had at least one variable above the local laboratory reference limit. Comparing our findings with those reported for groups of other paint industry workers is problematic, as factors such as alcohol usage, obesity, exposure intensity, and reference values can vary among the groups, but it is nevertheless interesting that this group had a much greater prevalence of values outside the reference range and far higher mean enzyme activities than has been reported in other studies of paint industry workers (4—6, 14).

Two factors should, however, be considered when these findings are interpreted. The first is that our reference values may have been inappropriate for the study population. Although they were in general use by local physicians and pathology laboratories, they were determined with the use of the 95 percentile of values obtained during a survey of predominantly white, middle-class subjects — a group clearly different from the paint workers. Appropriate reference values for purposes of monitoring specific groups of workers is important, and their selection should form part of a monitoring program (15). The second factor is that screening with multiple laboratory tests increases the probability of abnormal results arising by chance. This well-known problem in using a battery of tests to monitor workers using hepatotoxins has been discussed by other authors (15, 16). Although both of these factors are important, neither is likely

to account substantially for the high rate of abnormal γ GT and ASAT values, given the strong association shown between enzyme activities and alcohol use and the fact that many of the abnormal values were well above the reference level (figure 1).

Whatever the reason, the high prevalence of “abnormal” results found in this study are of more than passing interest. If these results are generalizable to other South African work forces, then strategies using liver enzymes to monitor workers will have to be designed to take account of large numbers of false positives (abnormal enzyme levels without chemical hepatitis).

Workers with liver function abnormality were tested for hepatitis B infection. Only one worker (2% of those tested) was positive for HB_s antigen. This number is lower than the 10% reported for black South African miners (8), but the difference may be due partly to the relatively small number of workers tested and to the urban setting.

The finding that the solvent workers apparently drank more alcohol than their co-workers is interesting and may be due to a migration of heavy drinkers to more polluted and less desirable jobs.

The major objective of this study was to determine whether long-term solvent exposure in paint manufacturing is associated with liver injury, as measured by standard biochemical indicators. No convincing evidence of such an association was found. Although the more heavily exposed workers generally had higher enzyme levels, even when the effects of alcohol were accounted for by stratification (table 3), regression analyses did not confirm an independent exposure-effect relationship. The relatively small number of subjects tested may be one explanation.

Other explanations for the absence of evidence of a causal relationship between exposure and disease are possible. First, the current solvent levels were generally not high; thus the lack of disease may be due to the fact that the workers were not sufficiently exposed. Many of the workers did have long service, however, as shown by the mean of 17 years for the high-exposure group, and it seems reasonable to assume higher solvent levels in the past. Further-

more, workplace air levels are likely to underestimate exposure, as they do not take into account skin absorption. The nature of the solvents may have played a role also, since aliphatic chlorinated hydrocarbons were not constituents of the paints and these agents are generally considered the most hepatotoxic.

Inaccurate exposure classification of workers is another important possibility. Care was taken to get to know the factory prior to the start of the study, and nonsolvent workers were confidently identified. As they were predominantly warehouse, rail yard and electrical workshop workers, office cleaners, and drivers, the low solvent classification is likely to be accurate. Significant skin absorption was not a factor for the low-exposure group.

Third, the determinations of solvents in air were limited in number and collected on relatively few workdays. Therefore the levels obtained may not be representative of usual levels. Nevertheless, their utility in grouping workers into exposure classes appears justified.

A compelling reason to accept the finding that these paint manufacturers did not have evidence of liver injury due to work is the agreement with most other studies of paint industry workers. Increased γ GT activity in the most heavily exposed of 180 paint manufacturers and sprayers was attributed to solvent exposure by the authors of a study conducted in Taiwan (17). In contrast, Kurppa & Husman (102 car painters) (5), Franco et al (30 workers producing fillers and varnishes) (14), Hane et al (52 house painters) (6), and Lundberg & Hakansson (47 paint industry workers) (7) all failed to show an association between solvents and liver injury as assessed by routine biochemical measures. Nevertheless, these negative findings should not be interpreted as an absence of a hepatotoxic effect. Serum bile acids (14) and transferrin (18) may be more sensitive measures of possible hepatotoxicity than enzyme activity. In addition, fatty liver disease, which may be present despite normal liver function tests, has been linked to solvent exposure during house painting (3) and a variety of other occupations (19). It is possible, therefore, that chronic liver damage was occurring that was not reflected by enzyme abnormalities.

The induction of enzymes and cytotoxicity due to an excessive use of alcohol appeared to be a cause for concern in this group of workers. The γ GT and ASAT activities were strongly associated with reported alcohol consumption, and strategies to reduce drinking may be the most important method of preventing liver disease. It can be concluded from this study that standard tests of "liver function" are unlikely to be a cost-efficient means of monitoring workers exposed to relatively low solvent levels unless the results are linked to a program to decrease alcohol consumption.

In conclusion, this study found that current solvent exposure during paint manufacture was generally well below the TLV for individual agents and for

solvent mixtures. This was an unexpected finding given the location in a developing country but may be explained by factors intrinsic to the production process. A high prevalence of raised serum activity of liver enzymes was detected, but an association between solvent exposure and enzyme activity was not shown when factors such as alcohol consumption and body mass were controlled for.

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