

German Investigations on Morbidity and Mortality of Workers Exposed to Vinyl Chloride

by H. Weber,* W. Reinl,* and E. Greiser†

Two studies on mortality and morbidity of workers exposed to vinyl chloride monomer (VCM) which have been carried out on behalf of the Ministry of Labour, Health and Social Affairs on Northrhine-Westphalia are reported.

Vinyl Chloride Mortality Study

The aims of this study were to determine standardized mortality ratios (SMR) for male workers exposed to VCM, using the mortality rates of the West German male population as reference, to study the SMRs of a cohort of workers of the chemical industry comparable concerning age distribution and observation period but not exposed to VCM and to determine the SMR of a cohort of workers in PVC-processing plants.

The study was designed as a historic cohort study, covering the period from the beginning of the VCM- and PVC-production in all of the German plants till the end of 1974.

Table 1 shows the main characteristics of the three cohorts investigated. Only Germans and Austrians were included in data analysis because of insufficient mortality data on various foreign nationals employed in German factories. To determine the mortality rates of Austrians, West German rates were used. To calculate expectations of total mortality, the mortality rates of the adequate years have been used. To calculate expectations of specific causes of death for all years before 1968, the rates of 1968 have been used; for the following years the rates of the corresponding years. Following the procedure applied by Tabershaw (1),

weighting of observed cases of specific causes of death according to unknown causes of death has been done with weighting factors calculated separately for three observation periods (up to 1959, 1960-1969, 1970-1974) as well as for six age groups.

In all of the cohorts, follow-up rates have been near or above 90%. The percentage of causes of death that could not be investigated due to loss or deletion of death certificates varied from 7.3% to 13.1%. To calculate age-standardized mortality ratios of specific causes of death, weighting has been done according to the procedure used by Tabershaw and Gaffey (1) to compensate for unknown or unidentified causes of death.

Table 2 displays total mortality as well as some of the relevant specific causes of death. It can be observed that the otherwise observed "healthy worker effect" cannot be demonstrated in the German cohorts exposed to VCM or employed in PVC-processing plants.

In the VCM cohort there are significant elevations of SMR of malignancies of the lymphatic and hematopoietic tissues (ICM 200-209), and of malignancies of the GI tract (ICD 150-159). The latter is due to the paramount elevation of SMR of tumors of the liver (ICD 155).

It must be noted that there is a modest elevation of SMR of tumors of the liver also in the cohort not exposed to VCM nor employed in PVC-processing plants. No obvious explanation for this observation can be offered. In addition elevated SMRs for ischemic heart disease (ICD 410-414) can be found in all of the three cohorts. Due to methodological

*Staatlicher Gewerbearzt, Düsseldorf, W. Germany.

†Diabetes Research Institute at the University of Düsseldorf, Division of Medical Statistics and Epidemiology, Düsseldorf, W. Germany.

shortcomings of the study no assessment of cardiovascular risk factors has been made. Therefore these results are of minor interest.

When subdividing the VCM-exposed cohort according to time of exposure there is a clear-cut increase of the SMR of liver tumors with time (Table 3). This seems to be highly suggestive of a

time-response pattern. As it has been impossible to determine concentrations of VCM retrospectively due to technological and methodological problems, no dose-response pattern can be established. However time of exposure seems to be the best available guess for dose.

Subclassification according to observation period

Table 1. Characteristics of study cohorts.

	Group I, VCM/PVC production	Group II, reference group	Group III, PVC processing
Population (Germans + Austrians)	7,021	4,910	4,007
Man years	73,734	76,029	52,896
Follow-up completed till 12/31/74, % deceased	93.2	89.8	92.1
Observed	414	417	360
Expected	435	533	380
Unknown causes of death			
No.	30	47	47
%	7.3	11.3	13.1
Total mortality (SMR)	95	78	95
Foreigners (excluding Austrians)	882	711	1,454
Deceased	6	6	10

Table 2. Standardized mortality ratios.

ICD 8	Cause of death	VCM/PVC production		Reference group		PVC processing	
		Obs.	SMR	Obs.	SMR	Obs.	SMR
Total mortality		414	95	417	78	360	95
140-209	All malignant tumors	94	112	83	83	62	85
140-199	Malignant tumors of organs	79	103	77	83	60	89
200-209	Malignancies of lymphatic and hematopoietic tissues	15	214 ^b	6	77	2	34
150-159	Malignant tumors of GI tract and peritoneum	45	149 ^a	27	71	15	56
155	Malignant tumors of the liver	12	1523 ^b	4	401 ^a	3	434
191	Malignant tumors of the brain	2	162	2	184	5	535 ^a
410-414	Ischemic heart disease	91	127 ^a	115	131 ^a	96	158 ^b
410	Acute myocardial	66	114	83	120	69	143 ^b
800-949	Accidents	61	137 ^a	44	99	32	110

^aBeyond 95% confidence interval (2).

^bBeyond 99% confidence interval (2).

Table 3. Standardized mortality ratios by duration of exposure.

ICD 8	Cause of death	Duration of exposure, months							
		< 12		13-16		61-120		> 121	
		Obs.	SMR	Obs.	SMR	Obs.	SMR	Obs.	SMR
Total mortality		53	93	138	102	93	87	130	96
140-199	Malignant tumors of organs	6	74	20	88	22	116	31	115
200-209	Malignancies of lymphatic and hematopoietic tissues	1	92	4	186	5	287	5	249
150-159	Malignant tumors of GI tract and peritoneum	3	101	12	135	13	173	17	158
155	Malignant tumors of the liver	0	-	2	874 ^a	3	1525 ^b	7	2528 ^b
191	Malignant tumors of the brain	0	-	0	-	1	350	1	278

Table 4. Standardized mortality ratios by period of observation.

ICD 8	Cause of death	Observation period							
		To 1959		1960-69		1970-74		Total	
		Obs.	SMR	Obs.	SMR	Obs.	SMR	Obs.	SMR
140-199	Malignant tumors	12	160	29	84	194	103	414	95
200-209	Malignancies of lymphatic and hematopoietic tissues	1	147	9	275 ^b	5	168	15	214 ^b
150-159	Malignant tumors of GI tract and peritoneum	8	270 ^a	13	94	24	177 ^b	45	149 ^a
155	Malignant tumors of the liver	1	1282	3	834 ^a	8	2264 ^b	12	1523 ^b
191	Malignant tumors of the brain	1	557	0	-	1	223	2	162

^aBeyond 95% confidence interval.

^bBeyond 99% confidence interval.

Table 5. Standardized mortality ratios by age.

ICD 8	Cause of death	Age group													
		≤ 24		25-34		35-44		45-54		55-64		≥ 65		Total	
		Obs.	SMR	Obs.	SMR	Obs.	SMR	Obs.	SMR	Obs.	SMR	Obs.	SMR	Obs.	SMR
Total mortality		10	68	45	111	65	104	90	101	105	80	90	103	414	95
140-199	Malignant tumors of organs	0	-	4	141	13	188 ^a	19	141	22	76	21	100	79	103
200-209	Malignancies of lymphatic and hematopoietic tissues	0	-	2	194	4	303	4	264	3	162	2	197	15	214 ^b
150-159	Malignant tumors of GI tract and peritoneum	0	-	3	397	10	365 ^b	10	145	10	89	12	140	45	149 ^b
155	Malignant tumors of the liver	0	-	0	-	6	6865 ^b	0	-	3	934 ^b	3	1664 ^b	12	1523 ^b
191	Malignant tumors of the brain	0	-	0	-	0	-	1	254	1	362	0	-	2	162

^aBeyond 95% confidence interval.

^bBeyond 99% confidence interval.

Table 6. Groups for subdivision of laboratory examinations.

Group	Specification
A-I	VCM/PVC production
A-II	PVC processing
B-I	VCM/PVC production and PVC processing, work capacity loss < 20%
B-II	VCM/PVC production and PVC processing, work capacity loss ≥ 20%
C-I	Germans and Austrians
C-II	Foreigners (Excl. Austrians)
D-I	Plants with high morbidity
D-II	Plants with low morbidity

Table 7. Bromsulfalein retention.^a

	VCM/PVC Production	PVC Processing	Total
Retention normal	26	21	47
Retention abnormal	44	10	54
Total	70	31	101

^aChi square₁ = 8.09 (p < 1%).

Table 8. Bromsulfalein retention.^a

	Germans and Austrians	Foreigners	Total
Retention normal	17	30	47
Retention abnormal	33	21	55
Total	50	51	101

^aChi square₁ = 6.25 (p < 2.5%).

Table 9. Bromsulfalein retention.^a

	Work capacity loss < 20%	Work capacity loss > 20%	Total
Retention normal	41	6	47
Retention abnormal	32	22	54
Total	73	28	101

^aChi square₁ = 9.81 (p < 1%).

(Table 4) reveals a rather inconsistent pattern: malignancies of the lymphatic tissues (ICD 200-209) are significantly elevated in the sixties only, whereas SMRs for tumors of the liver increase till the end of the study period. This might be referred to different latency periods for both kinds of malignancies, but other causes might likewise have contributed to these results. However, it has to be reported that the number of angiosarcomas confirmed histologically in the Federal Republic of Germany in patients previously exposed to VCM has actually come to 17 in contrast to mere 4 at the endpoint of the mortality study (12/31/1974).

The distribution of SMRs by age (Table 5) demonstrates an obvious susceptibility of males aged 35-44 for malignancies in general as well as for malignancies of the liver.

The data base for the German morbidity study consists of all of the reports of suspected cases of occupational disease due to VCM or PVC production or PVC processing. The reference population for these reports has to be defined as the total

NORMAL \leq 120 MG/DL
 PATHOL. $>$ 120 MG/DL

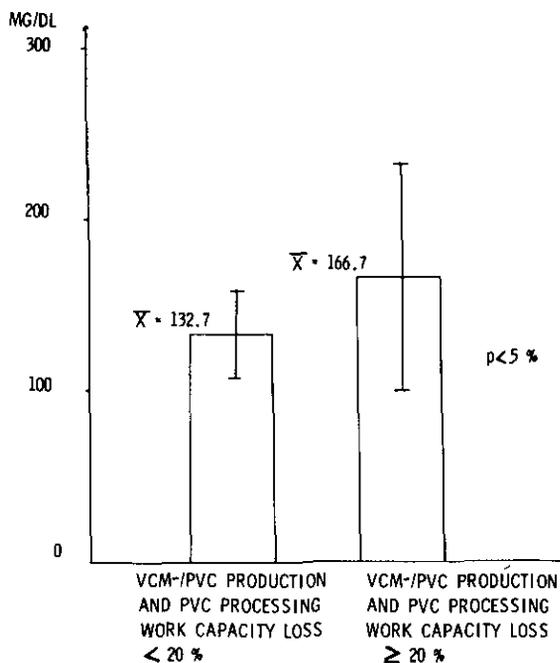


FIGURE 2. Vinyl chloride morbidity study: oral glucose tolerance test, 120 min after loading (normal 120 mg/dl).

NORMAL \leq 1.0
 PATHOL. $>$ 1.0

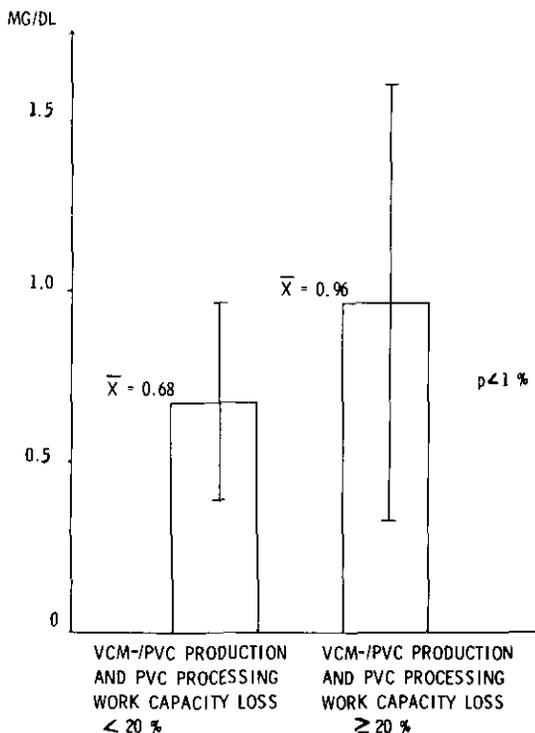


FIGURE 1. Vinyl chloride morbidity study: total bilirubin (normal 1.0).

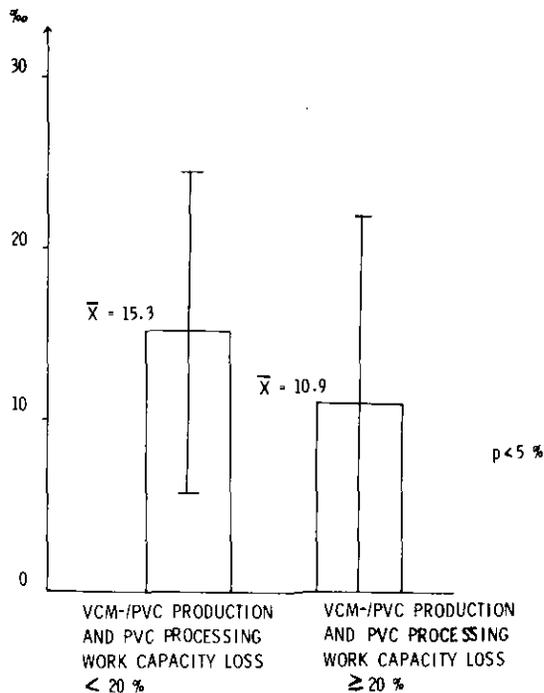


FIGURE 3. Vinyl chloride morbidity study: reticulocytes (normal 15%).

working population in 1974 in the above mentioned branches, i.e., 6,500 workers in VCM or PVC production and 42,800 workers in PVC processing (as given by the German Association of Plastic Producing Industries). Till the end of 1974, 269 reports of suspected cases of occupational disease had been received. As there has been no consistent set of examinations performed on each of the cases, numbers of observations for various variables analyzed vary according to examination method performed. Insofar as the results of this study are of much lower validity than those of the mortality study, one should regard them as hints for further investigations.

Four attempts to subclassify observation on the 269 cases have been undertaken (Table 6). Only those results showing significant differences when applying *t*-tests or chi-square tests are so classified. Amazingly none of the more sensitive lab examinations of liver functions showed a marked difference in all of the subclassifications besides bromsulfalein retention. In this instance there is a significant difference when subdividing by VCM/PVC production versus processing (Table 7), as well as by

nationality (Table 8) and most pronounced when subdividing by extent of work capacity loss (Table 9). This latter result, however, must be expected when an effect of exposure on liver function is anticipated. An impairment of the excretory liver function is suggested by elevated total bilirubin values in the subgroup with work capacity loss greater than 20% (Fig. 1). There seems to be an impaired glucose tolerance in this group, although observed in a small subsample only (Fig. 2), as well as a lower number of reticulocytes (Fig. 3). The thromocyte count in both groups was the same. These results, however, lead to no sensible interpretation, as all results attempts failed to standardize the methods applied for thrombocyte counts by various laboratories.

REFERENCES

1. Tabershaw, I. R., and Gaffey, W. R. Mortality study of workers in the manufacture of vinyl chloride and its polymers. *J. Occup. Med.* 16: 509-518 (1974).
2. Bailar, J. C. Significance factors for the ratio of a Poisson variable to its expectation. *Biometrics* 20: 639-643 (1964).