

Chromosomal Damage in Men Occupationally Exposed to Vinyl Chloride Monomer and Other Chemicals

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INTRODUCTION

Data from various sources suggest that the biologic effects of vinyl chloride monomer (VCM) include mutagenicity as well as oncogenicity. Pertinent studies include observations concerning the mutagenic effects of VCM in bacterial test systems (Rannug *et al.*, 1974; Bartsch *et al.*, 1975), mutagenicity of VCM metabolites in mammalian cells (Huberman *et al.*, 1975), and cytogenetic studies of polyvinyl chloride (PVC) polymerization workers (Ducatman *et al.*, 1975; Funes-Cravioto, *et al.*, 1975; Kilian *et al.*, 1975; Purchase *et al.*, 1975). Also relevant may be observations suggesting increased fetal loss in families of PVC workers (Infante *et al.*, 1976). Among the several cytogenetic studies reported, three have suggested increased chromosomal breakage among polymerization workers (Ducatman *et al.*, 1975; Funes-Cravioto *et al.*, 1975; Purchase *et al.*, 1975), and one has not (Kilian *et al.*, 1975). This report concerns cytogenetic analyses conducted on workers employed at a rubber and plastics plant, some exposed to VCM and others not.

MATERIALS AND METHODS

The work described here was part of a cross-sectional study designed to provide multiphasic medical screening data on the health status of men employed at a large rubber and plastics plant. The overall study was conducted jointly by the Center for Disease Control (CDC) (National Institute for Occupational Safety and Health and Bureau of Epidemiology) and the Occupational Health Studies Group of the University of North Carolina in cooperation with the Firestone Corporation and the United Rubber Workers. Results of the entire study, together with a detailed description of the study's design and methodology, will be published separately.

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Cytogenetic analyses, primarily designed to measure frequencies of chromosomal breakage, were performed on peripheral blood lymphocytes from 35 men; specimens were obtained from 18 men in October 1974 and 19 in January 1975 (2 on both occasions). Subjects were restricted to men primarily or exclusively employed for 10 years or longer, in 3 different employment categories: 14 in PVC polymerization (presumed high exposure to VCM, intermittent or sustained), 4 in PVC processing (presumed low exposure to VCM), and 17 in rubber tire manufacture (industry controls; presumed negligible exposure to VCM). Work history details were obtained by interview and confirmed by review of company records.

Initially, the study was designed to compare breakage frequencies in workers exposed to VCM with frequencies in other workers. However, when initial analyses showed no significant differences among worker groups, a control group was selected (April 1975) consisting of four male employees at CDC not exposed directly to any laboratory chemicals. Material for cytogenetic analysis was prepared in the same manner with the same reagents as the earlier material from workers at the plant. To assess comparability in microscopic reading of slides between April 1975 and the earlier dates, previously read slides from the high VCM and industry control groups were blindly interspersed among the CDC worker slides. Breakage frequency recorded on the second reading of high VCM/industry control slides (6.0% of 150 scored metaphases) did not differ significantly from the first reading. Cytogenetic material was processed using standard procedures (Moorhead *et al.*, 1960). Cells were cultured for 72 hours in the presence of phytohemagglutinin. Giemsa staining was used without banding.

RESULTS

Frequencies of chromosomal breakage in each group are shown in Table 1. Levels of breakage in all three industry groups, whether exposed to VCM or not, were significantly increased over the CDC control level, the high VCM group at the $P < 0.01$ level, the low VCM and industry control groups at the $P < 0.05$ level. At the same time, no significant differences were noted between the three industry groups themselves. Groups were comparable in terms of age and number of months worked. Breakage frequencies for individual subjects within groups did not vary significantly one from another.

An effort was made to relate levels of breakage to duration of employment and hence extent of potential toxic exposure (Table 2). While a significant gradient was seen for industry controls, interpretation is uncertain because of small numbers and because the mean age of subjects increased with employment duration. No gradient was seen for the high VCM group, whether in terms of total employment or of employment in contact with VCM. The low VCM exposure group was too small to permit analysis by exposure duration.

Chromatid gaps comprised the majority (86%) of aberrations seen (Table 3). Similar types of aberrations were seen with similar frequencies among all four groups.

DISCUSSION

When reviewed in terms of comparisons between worker and nonworker

TABLE 1
LEVELS OF CHROMOSOMAL BREAKAGE BY EXPOSURE GROUP

Exposure	Number of subjects	Average age (range)	Average Number of months worked (range)	Metaphases		
				Number scored	Number with breakage	Percent with breakage ^a
High VCM	14	49.4 (44-65)	291.1 (215-346)	1105	74	6.7
Low VCM	4	52.5 (46-58)	315.8 (261-341)	180	14	7.8
Industry controls	17	48.5 (31-58)	305.8 (114-357)	1306	77	5.9
CDC controls	4	44.3 (37-51)	—	586	21	3.6

^a Levels of statistical significance: High VCM vs CDC control, $\chi^2 = 7.09$, $P = <0.01$; low VCM vs CDC control, $\chi^2 = 4.64$, $P = <0.05$; industry control vs CDC control, $\chi^2 = 3.95$, $P = <0.05$; high VCM vs low VCM, $\chi^2 = 0.18$, $P = >0.05$; high VCM vs industry control, $\chi^2 = 0.81$, $P = >0.05$.

TABLE 2
LEVELS OF CHROMOSOMAL BREAKAGE IN RELATION TO EXPOSURE DURATION

Exposure	Months worked	Number of subjects	Average age	Average number of months worked	Metaphases		
					Number scored	Number with breaks	Percent with breaks
High VCM (total employment)	100-199	0	—	—	—	—	—
	200-299	8	47.4	264.6	700	49	7.0
	300-399	6	52.2	326.5	405	25	6.2
$\chi^2 (1 df) = 0.16$, $P > 0.05$							
High VCM (VCM employment)	100-199	2	60.0	179.0	100	7	7.0
	200-299	9	47.7	252.3	755	53	7.0
	300-399	3	47.7	318.3	250	14	5.6
$\chi^2 (2 df) = 0.58$, $P > 0.05$							
Industry controls	100-199	2	31.0	132.5	100	0	0
	200-299	2	44.5	265.5	76	1	1.3
	300-399	13	51.8	338.6	1130	76	6.7
$\chi^2 (2 df) = 9.91$, $P < 0.01$							

groups, the present observations are not inconsistent with prior studies suggesting that industrial exposure to VCM is associated with an approximately twofold increase in levels of chromosome breakage as measured in culture of peripheral blood lymphocytes. In contrast with at least one prior report (Huberman *et al.*, 1975), however, breakage consisted mostly of simple chromatid gaps rather than more complex forms.

Chromosomes	Percent with breakage
1	6.7
2	7.8
3	5.9
4	3.6

0.01: low VCM vs
0.05: high VCM
p < 0.05.

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Percent with breaks

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3 6.7

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TABLE 3
TYPES OF CHROMOSOMAL ABERRATIONS OBSERVED

Chromosomal aberration	High VCM		Low VCM		Industry controls		CDC controls	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Chromatid gaps	59	5.3	12	6.7	74	5.7	18	3.1
Isochromatid gaps	7	0.6	0	0	6	0.5	1	0.2
Chromatid breaks	2	0.2	0	0	2	0.2	2	0.3
Isochromatid breaks	5	0.5	2	1.1	9	0.7	1	0.2
Isochromatid fragments	3	0.3	0	0	0	0	0	0
Exchange figures	1	0.1	0	0	0	0	0	0
Ring chromosomes	1	0.1	0	0	0	0	0	0
Total breakage	78	7.1	14	7.8	91	7.0	22	3.8
Total cells with breakage	74	6.7	14	7.8	77	5.9	21	3.6
Hypodiploid cells	121	11.0	33	18.3	155	11.9	61	10.4
Hyperdiploid cells	2	0.2	0	0	3	0.3	1	0.2
Total cells scored	1105	—	180	—	1306	—	586	—

The fact that overall breakage levels were similar in workers exposed heavily, lightly, or negligibly to VCM may imply, in this particular work setting at least, the presence of agents other than VCM capable of inducing chromosome breaks. Because of the wide range of chemicals to which rubber workers at this plant were exposed (primarily solvents of various kinds), it was impossible to relate any particular agents to the abnormal effects observed. No clear-cut pattern was seen to relate degree of breakage to duration of exposure.

SUMMARY

Measurements of chromosomal breakage were made in peripheral blood lymphocytes from workers exposed heavily, lightly, or negligibly to VCM at a large rubber/plastics plant. Breakage levels in all three groups were significantly increased over levels in nonindustrial controls. Breakage consisted mostly of simple chromatid gaps. The results suggest that other agents, in addition to VCM, may cause cytogenetic damage in workers employed in the rubber/plastics industry.

ACKNOWLEDGMENTS

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(One group of toxic effects of lead is the effect on the reproductive system. Agency, 1972). The Agency has suggested that the woman and fetus are more susceptible to lead than the general population. Further information is needed on the effects of lead on the reproductive system.