release of low concentrations of proteolytic enzymes in the skin due to the non-specific cytotoxic effects of bile salts could account for both the pigmentation and the pruritus of patients with chronic obstructive jaundice.

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CHROMOSOME ABERRATIONS IN WORKERS EXPOSED TO VINYL CHLORIDE

SIR,—Epidemiological evidence suggests that the risk of malignancy is increased in workers chronically exposed to vinyl chloride (V.C.).[1-5] The carcinogenicity of V.C. has been demonstrated in animal experiments.[6] In-vitro[7] and in-vivo[8] experiments suggest that the carcinogenicity of V.C. probably depends on the formation of an alkylating compound, presumably chloroethylene oxide. Since carcinogenic chemicals are often mutagenic,[9] we wondered if V.C. is also mutagenic. In fact V.C. has been reported as inducing mutations in *Salmonella typhimurium* in the presence of metabolically active liver homogenates.[10] If alkylation of D.N.A. by V.C. metabolites also produces chromosomal aberrations in man, chromosomal analyses could be used as an indicator of risk and also possibly be helpful in establishing a genetically meaningful maximum allowable concentration of V.C. We report an increased frequency of chromosomal aberrations in workers exposed to V.C.

Seven occupationally exposed male workers and three non-exposed control subjects, all employed in the same factory, were studied. The level of exposure to V.C. had continuously decreased during past years. In the weeks preceding the collection of blood-samples for chromosomal analysis (before the summer holidays in 1974) the air concentration in the polymerisation department was estimated to be 20–30 p.p.m. Workers had been exposed to V.C. for 9–29 years. Clinical examinations had been carried out at regular intervals. None of the workers had showed disturbed liver function, signs of acro-osteolysis or hæmatological changes, except for case A in which there was slight thrombocytopenia and an α_1-antitrypsin deficiency. Chromosomal analyses were made on cells from conventional lymphocyte-cultures incubated for 48 and 72 hours. All blood specimens and slides were coded and analysed blindly.

The result of the chromosome analysis is given in the accompanying table. The data for the control subjects were homogenous and therefore pooled. Altogether they comprised 566 cells, 11 of which (1·94%) contained chromosomal aberrations. This finding might be explained by previous diagnostic X-rays. The frequency of aberrations nevertheless accorded with that of a male population selected at random.[11]

1450 cells from the group exposed to V.C. were analysed, 800 in the 48-hour cultures and 650 in the 72-hour cultures. In none of the cases was there a statistically significant difference in the frequency of aberrations between the 48 and 72 hour cultures. Therefore these data were pooled. The frequency of abnormal cells in the group exposed to V.C. (9·52%) was significantly greater than in the controls ($P < 0·001$). This was also true for chromatid and isochromatid breaks when analysed separately, but not for the remaining types of aberrations.

The highest frequency of abnormal cells was found in those subjects who had the shortest duration of exposure (see table), and two cases (C and F) did not differ significantly from the controls. A χ^2 test of the frequencies of abnormal cells also revealed a significant deviation from homogeneity ($P < 0·001$). The negative correlation of the frequency of abnormal cells with the time of exposure was not significant. Therefore, on the basis of the present data it is not possible to discuss the biological background of this heterogeneity.

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Subjects	Duration of exposure (yr.)	No. of cells analysed	Gaps		No. of different types of aberrations							No. of abnormal cells	
			Chromatid	Isochromatid	Chromatid breaks	Chromatid exchanges	Isochromatid breaks	Dicentric chromosomes	Ring chromosomes	Other types	Total	Total	%
Controls (J)	0	566	5	4	4	1	4	2	1	0	12	11	1·94
Exposed:													
A	9	200	22	8	19	2	19	0	0	1	41	36	18·00
B	9	250	15	14	24	1	17	3	1	2	48	37	14·80
C	12	250	4	6	5	1	5	2	1	0	14	12	4·80
D	18	200	8	5	12	1	9	0	0	2	24	22	11·00
E	19	150	3	2	4	0	5	0	0	2	11	11	7·33
F	20	200	1	1	0	0	1	0	0	2	3	3	1·50
G	29	200	9	12	7	0	9	1	1	1	19	17	8·50
Total (A-G) (*J*)	..	1450	62	48	71	5	65	6	3	10	160	318	9·52*

* A test of heterogeneity gave $\chi^2 = 47·72$, 6 d.f., $P < 0·001$.