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A mail-out questionnaire examined symptoms previously associated with vinyl chloride exposure. Assessment of exposure levels was made by analytical measurement and observation. The resulting statistical analysis revealed a dose-response type of relationship between exposure and certain morbidity symptoms.

The association of vinyl chloride exposures with morbidity symptoms

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VCM
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Introduction

Before its recent implication in the etiology of angiosarcoma, vinyl chloride (VC) had been given a relatively clean bill of health. First synthesized in 1833, VC has come into increased use since World War II in the production of polyvinyl chloride (PVC) resins. Until 1960, no industrial fatalities associated with VC use had been reported. However, two fatalities then occurred in a PVC polymerization plant—one worker died cleaning out a polymerization vessel, and the other while working in a pit.[1] These two deaths underscored the potential seriousness of the acute effects of VC upon the central nervous system.

Relatively few effects have been reported as a result of acute exposure to VC. Lehmann and Flury[2] reported that VC was highly narcotic, but had a wide margin between its narcotic and lethal concentrations. Its local irritating effect, however, was described as very slight. It was estimated that VC concentrations of 7-10 percent in air (70,000-100,000 ppm) would be narcotic to humans in a short time.

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Dr. Van Ert is currently serving as an industrial hygienist and laboratory director for the Occupational Health Studies Group in Chapel Hill. Dr. Van Ert did his graduate work at the University of North Carolina at Chapel Hill and holds a Master of Science in environmental chemistry and biology and a Ph.D. in industrial hygiene and toxicology.

Two cases of VC gassing were reported in Great Britain.[3] A process worker, standing outside a polymerization vessel and washing it with a water stream, suddenly collapsed across the open manhole. Subsequently, he experienced tightness of the chest, nausea, abdominal pain and headache. The second case, a maintenance worker, was overcome while repairing a VC leak.

A study of clinical manifestations of 186 male PVC workers identified the presence of the "narcotic syndrome", asthenic nervous symptoms, Raynaud's syndrome and hepatomegaly.[4] However, the absence of a control (unexposed) population, or of comparisons between PVC workers experiencing different exposures, hampered the interpretation of these findings.

On studies of VC as a possible anesthetic agent, using dogs as subjects, incoordinated muscular activity of the extremities and serious cardiac arrythmias were observed.[5] Angioneurosis (spasm of peripheral blood vessels) in PVC polymerization workers has also been reported.[6] The association of vascular spasms (manifested as Raynaud's phemonenon) with acroosteolysis has been reported by several investigators.[7,8] The pathogenesis of these peripheral vascular manifestations has been variously interpreted as disordered vasomotor control via the hypothalamus,[4] as a general central nervous system dysfunction,[9] or by localized physico-chemical action in conjunction with specific individual susceptibility.[7]

Overall, the literature of the recent decades has suggested that most of the toxic effects of exposure to VC act via the central nervous system occurring most obviously at very high exposure concentration, and that both acute and chronic toxic effects occur.

A recent cross-sectional health survey of 354 VC workers related the proportion of workers who had experienced acute central nervous system symptoms at work (headache, light-headedness, dizziness and loss of consciousness) with their duration of employment.[10] Although a dose-response relationship was implied in the report, this relationship could be partly or wholly explained by differences between the several employment-duration categories either in age or in duration of opportunity to experience these acute symptoms.

Methods

In 1974, a mail questionnaire survey was conducted on a population of VC polymerization workers, seeking information about the frequency of occurrence of job-related symptoms. These self-reported symptoms were related, by the respondent, to the specific type of job he was engaged in within the polymerization plant, and to the calendar year of their occurrence. (See Appendix 1.) Further, equivalent information was collected, in identical fashion, from a sample of rubber workers in the adjoining plant. (See Appendix 2.) These two aspects of the study allowed internal comparisons between polymerization workers in different jobs and at different time-periods (i.e., different exposure situations), and also an external (in the sense of vinyl chloride exposure) comparison of polymerization workers with rubber workers. In this way, the frequency of self-reported symptoms could be more meaningfully interpreted. The validity of self-reported work history information has been tested in another study being done on the workers in this plant and found to be acceptable. In the previous study, a sample of workers were asked to indicate the dates and job titles for all jobs held. This information was compared with company work histories. The results showed that workers were able to recall most jobs they had had and that their memory as to dates was fairly reliable within the last ten year period, but worsened in trying to go back further than ten years.

Information was sought on the frequency of eight symptoms. The first four (dizziness or light-headedness, passing out, nausea or "sick feeling" and headache) were symptoms of central nervous system disturbance, similar to those examined in the study of Lilis, et al.[10] The next two sought symptom information for peripheral neurovascular and neuromuscular disturbance ("pins and needles" and muscle weakness). The seventh symptom referred to local irritation (of eyes, nose and throat), and the eighth symptom referred to the generalized asthenia ("run-down" feeling) originally reported by Suciu et al.[4]

Questionnaires were mailed to all workers involved in the vinyl chloride plant, and to a sample of the workers in the adjoining rubber plant. The latter population consisted predominantly of rubber workers, with a small minority (five percent) of polyvinyl chloride (PVC) fabrication workers. The statistical sampling

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1. Clock Card

2. List the m

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SUPPLEMENTARY QUESTIONNAIRE: CHEMICALS (RESIN) DIVISION

Appendix 1

The company has provided the university with the names of all persons who have worked in the chemicals division (i.e. depts. 093, 836 or 733). Recent evidence suggests that some chemicals involved in PVC manufacture may be health hazards. We would therefore like to ask you about your health experiences during your employment in that area.

1. Clock Card Number . . . . . [| | | |]

2. List the main types of job that you have done in the chemicals division:

	Dept. No. (Example: 093	Type of job e.g. Dryer operator	Time period e.g. 1954-59)
a.	093	6. Service + Utility	1965
b.	093	7. Dryer Operator	1965
c.	093	7. Centrifuge Bagger	1966
d.	093	7. Centrifuge #10 Line	1967-68
e.	093	5. Relief in #1 + #2 Build	1967-68

3. If you experienced any illness or adverse health effects that might have been related to working in any of these above jobs, please describe the symptoms. For each symptom that you experienced, record an answer in Columns A and B.

Symptom	A. In which one of the above jobs did this symptom occur most? (Circle one letter to identify the job, as listed by you in Question 2.)					B. How often did the symptom occur? Once	Occasionally	Often
Dizziness, light-headedness	(a)	b	c	(d)	e	1	(2)	3
Passing out	a	b	c	d	e	1	2	3
Nausea, "sick" feeling	(a)	b	c	(d)	e	1	(2)	3
Headache	(a)	(b)	(c)	(d)	e	1	2	(3)
"Pins and needles" in arms or legs	a	b	c	d	e	1	2	3
Muscle weakness	a	b	c	d	e	1	2	3
Irritation of eyes, nose or throat	a	b	(c)	(d)	e	1	2	(3)
General fatigue, "run-down" feeling	a	(b)	(c)	(d)	e	1	2	(3)
Other symptom: Weight loss (1-7)	a	(b)	c	d	e	1	2	(3)
. . . . .	a	b	c	d	e	1	2	3

4. If you underwent medical examination for any of these symptoms, please describe, on the reverse side of this page, the following: medical tests carried out, diagnosis or explanation given to you, type of treatment, any known or suspected relationship of symptoms to factors in your work environment.

PLEASE BE SURE TO ENCLOSE THIS PAGE ALSO, WHEN RETURNING THE MAIN QUESTIONNAIRE.

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SUPPLEMENTARY QUESTIONNAIRE: OTHER TYPES OF SYMPTOMS

Appendix 2

Recent evidence within the PVC-manufacturing industry has emphasized the potential health hazards of exposure to chemicals in the work environment. In order to conduct an initial survey of adverse health effects due to chemical exposure, we are asking a sample of workers to answer these extra questions, in addition to the main questionnaire.

1. Clock Card Number . . . . . | | | | | |

2. List the main types of jobs that you have done while employed in the work areas that you recorded on page 5 of the main questionnaire:

	Dept. No.	Type of job	Time period
(Example:	115	e.g. Warm-up millman	e.g. 1954-59)
a.	112	Banbury Operator	1966-68
b.	112	Compounder	68-70
c.	131	Tire Builder	71-74
d.			
e.			

3. If you experienced any illness or adverse health effects that might have been related to working in any of these above jobs, please describe the symptoms. For each symptom that you experienced, record an anwer in Columns A and B.

Symptom	A. In which one of the above jobs did this symptom occur most? (Circle one letter to identify the job, as listed by you in Question 2.)					B. How often did the symptom occur?		
						Once	Occasionally	Often
Dizziness, light-headedness	a	b	(c)	d	e	1	(2)	3
Passing out	a	b	c	d	e	1	2	3
Nausea, "sick" feeling	a	b	(c)	d	e	(1)	2	3
Headache	(a)	(b)	c	d	e	1	2	(3)
"Pins and needles" in arms and legs	a	b	c	d	e	1	2	3
Muscle weakness	a	b	(c)	d	e	1	(2)	3
Irritation of eyes, nose or throat	(a)	(b)	c	d	e	1	2	(3)
General fatigue, "run-down" feeling	a	b	(c)	d	e	1	(2)	3
Other symptom:								
. . . . .	a	b	c	d	e	1	2	3
. . . . .	a	b	c	d	e	1	2	3

4. If you underwent medical examination for any of these symptoms, please describe, on the reverse side of this page, the following: medical tests carried out, diagnosis or explanation given to you, type of treatment, any known or suspected relationship of symptoms to factors in your work environment.

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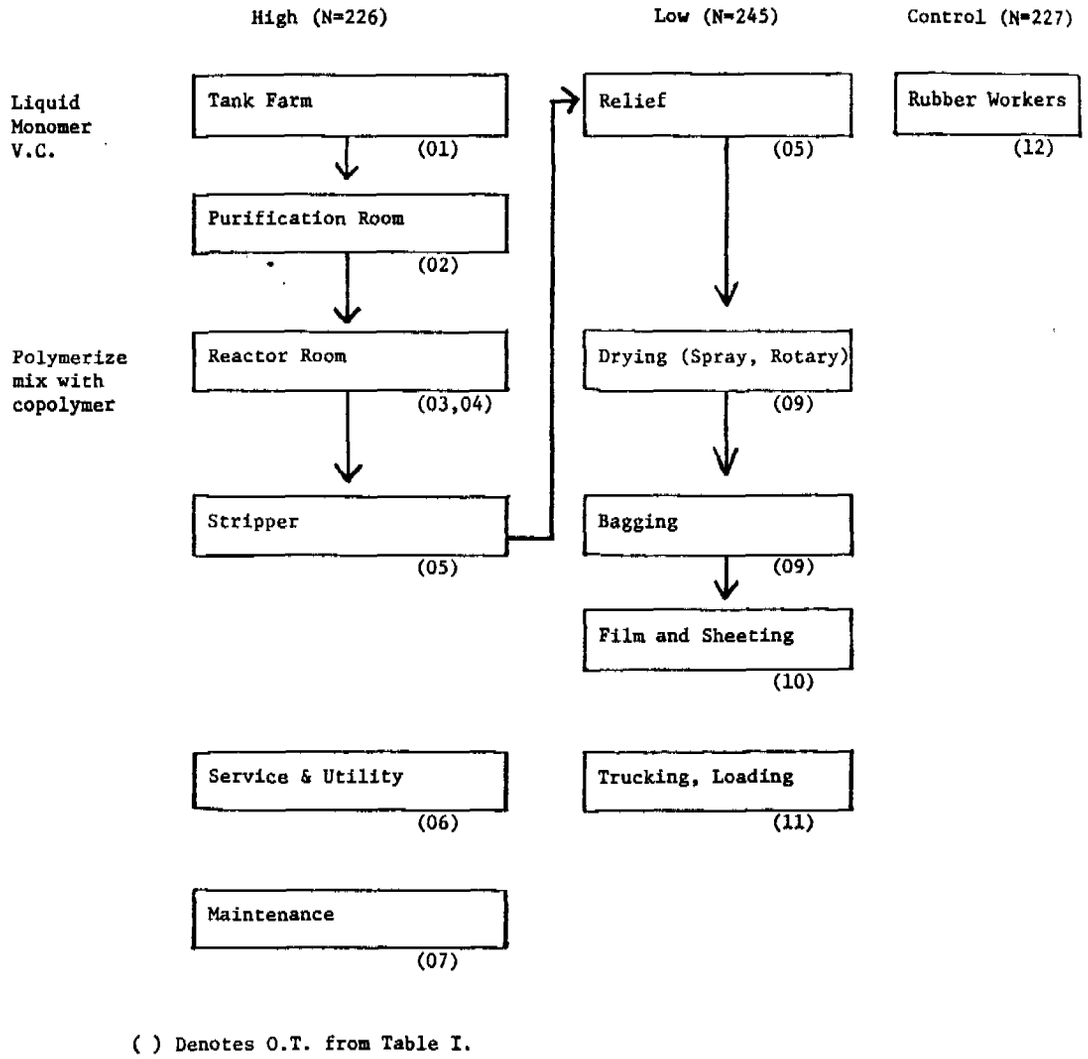

( ) Denotes O.T. from Table I.

Figure 1 – Schematic flow diagram of vinyl chloride polymerization.

procedure for choosing which rubber workers to include in the study entailed taking a systematic one-in-twelve sample with a random starting place from an alphabetical listing, thereby assuring a representative sample of the rubber plant workers. The response rate for current vinyl chloride workers was 200/298 (67%) while the rate for the current rubber plant workers was 89/212 (42%). This difference in response rates may be due to the adverse publicity on vinyl chloride exposure.

In order to evaluate the exposure experiences of each worker, the individual jobs reported on the questionnaire were grouped into 12 categories (see Figure 1). The principles and procedures of regrouping production-oriented categories into health-oriented categories has been recently described.[11]

Industrial hygiene analytic sampling results are present in Tables I, II and III. Table I is based upon data taken by company personnel before major changes were made in controlling levels of vinyl chloride exposure, and should be representative of the relative levels that workers were exposed to during their earlier work history. Table II is based upon company data taken during the installation of environmental controls. Table III contains data taken by University of North Carolina personnel in 1975, after major environmental controls had been installed. By comparing these three tables, it can be seen that the absolute levels of vinyl

TABLE I
VC Exposure Index
Company Data
Grab Sample–Gas Chromatograph
(Prior to 1974)

O.T.	DESCRIPTION	EXPOSURE INDEX
01	Tank Farm Operators	H
03	Reactor Operators	H
04	High Pressure H_2O	H
05	Stripper Operators	H
08	Relief Operators	H
06	Supply Men	H
06	Service & Utility	M
02	Janitors	M
07	Maintenance	M
?	Pilot Plant Janitor	M
09	Centrifuge Operators	L
09	Dryer Operators	L
09	Bagger Operators	L
11	Truck Operators	L

(L) Low	(M) Medium	(H) High
0-50 ppm	50-200 ppm	200 & Above

chloride have decreased, yet the gradient of exposure between job categories appears to have remained the same.

Based on these sampling results, and on general industrial hygiene evaluation of the plant operation, it was possible to create a further grouping of the 12 occupational categories in Figure 1 into three exposure categories representing high, low, and essentially no exposure to VC. Figure 1 illustrates this grouping in the context of a flow diagram of the vinyl chloride manufacturing process.

By defining three exposure categories as noted, several purposes were achieved. If, in fact, VC exposure was causative for some or all of the given symptoms, then it would be natural to expect a dose-response type of pattern between exposure categories and symptom response. Because of the way exposure categories subdivide the population, any potentially confounding effect of other chemicals should be accounted for. Thus, if rubber workers, for example, had more headaches because of solvent exposure, the effect would be to lessen the chances of a dose-response pattern (as defined in the study) emerging. The majority of workers spent time in more than one exposure category. In addition, within the VC plant, the respondents had no knowledge of which exposure category they worked in. Thus, many of the workers served as "controls" on themselves for different jobs, and in addition, some of the VC workers will serve essentially as "controls" on other vinyl chloride workers. It is possible that no real difference in symptoms existed and the workers who answered the questionnaire gave biased answers because of their apprehension of working with vinyl chloride. Because of the internal consistency of the results as well as the external consistency with the findings in previous studies, this possibility is unlikely.

Results

Since the symptoms under consideration are all transitory and reversible, an acute effects model has been employed. Thus, each reported person-job held, rather than each person, is treated as the unit of observation. Each person has been able to contribute to the analysis his experience in more than one job (the average is approximately three jobs per person, and often a person has experienced jobs in more than one O.T. group). By treating the job as the unit of observation, there is a tendency to dampen the effect of individual variability in symptom experience since workers are often acting, in effect, as their own controls. Any

TABLE II
Exposure Data For VC and PVC Workers in a VC and PVC Plant
Company Data
(Second quarter 1974)

O.T.	OTG	# WORKERS	VINYL CHLORIDE MONOMER EXPOSURE	MAXIMUM READING
			HIGH EXPOSURE (most readings—20-30 ppm)	
01	High	3	Tank Farm Attendant	<40
04	High	6	High Pressure Water Cleaner	>50
			MEDIUM EXPOSURE most readings—10-20 ppm	
03	High	10	Reactor Operator—Bldg. 2	>50
08	Low	9	Relief Operator—Bldg. 2	50
06	High	36	Service Utility	>50
			LOW EXPOSURE most readings—0-10 ppm	
03	High	4	Reactor Operator—Bldg. 1	<20
11	Low	12	Shipping Operator	<30
08	Low	3	Relief Operator—Bldg. 1	<20
09	Low	12	Centrifuge Operators	<40
09	Low	4	Dryer Operators	<40
09	Low	8	Baggers	<10
11	Low	9	Truckers	<10
07	High	48	Maintenance	>50

TABLE III
Vinyl Chloride Sampling Results
Chemical Plant (Buildings I & II) and Rubber Plant
(3-24 to 3-26-75)

O.T.	LOCATION	VINYL CHLORIDE LEVELS (PPM) AS DETECTED BY:* MIRAN	V.C. INDICATOR TUBE	GRAB SAMPLE BY G.C.	CHARCOAL TUBE
	BUILDING I				
03,04	Reactor Room				
	Operator's Desk	15±2	20	5-6	11.7
	Desk Cluster (4 tubes)	15±5	—	—	7.0, 11.7, 10.9, 7.4
	Mezzanine	21±2	—	4-5	47.4
	General Room				
	Typical	15±2	—	—	11.7
	Peak	93±2	—		
05	Stripper Area				
	Operator's Desk (PVC & CoPolymer Side)	33±5	24	7	20.0
	General Area	24–32	—	—	——
08	Relief Area				
	Operator's Desk	——	3	—	1.43
	General Area	28–36	—	—	——
09	Second Floor Spray Driers				
	General Room	3	—	—	——
09	Bagging Area				
	Lines 4,6,7	9–16±3	—	—	——
09	Bulk Drying Area (Rotary Driers)				
	Panel Board Area	1.5	3	—	6.1
	Bagger: Line 13	3.5	—	—	——
02	Transfer Pump House				
	No Pumping of V.C.	——	8	—	5.8
	Pumping of V.C.	——	—	—	300(1)
02	Purification Room	——	20	—	26.1
	BUILDING II				
03	Reactor Room				
	Operator	——	—	—	5.2(2)
05	Stripper Level				
	Operator	——	—	—	8.8(2)
08	Relief Area				
	Operator	——	—	—	5.0
07	Maintenance Pipe Fitter	——	—	—	5.9(2)
	RUBBER PLANT				
10	Film and Sheeting				
	Mezzanine Area	1.8–4.0	—	—	——
	Banbury Mill #4 Area	3.2–6.5	10(3)	—	5.0(2)
12	General Room	Not Detectable	—	—	——

(1) Air-supplied respirator required.
(2) Personnel sample
(3) Not breathing zone
*Definitions for V.C. Analytical Techniques
Charcoal Tube Samples: gases and vapors adsorbed to activated charcoal and subsequently analyzed by gas chromatography by OHSG laboratory personnel; reflect time weighed averages.
Grab Samples: gases and vapors drawn into sampling bottles, bottles sealed, and contents analyzed by injecting portion of contents into gas sampling port of AID portable gas chromatograph.
Data obtained in field low due to V.C. loss from sampling bottles
Miran Infra-Red Analyzer: continuous monitoring of V.C. by the direct reading instrument.
Lower detectable limit of instrument: 0.8-1.0 ppm.
Area samples minimum of 10 minutes.
Indicator Tubes: Gastec indicator tubes with range of 0.5-14.0 ppm.
Easy to read and correlate well with other methods (i.e., charcoal tubes and Miran).

differences found with this type of model can then be more easily ascribed to real differences in environmental exposure.

Tables IV-1 through IV-8 present the basic data used in the analysis. Limiting the statistical analysis to white males (who make up 95 percent of the plant population) was necessary in order to provide adequate cell sizes. In Tables IV-1 through IV-8, the categories of response are labelled 0, 1, 2 and 3 to correspond with the questionnaire replies as to frequency of symptoms: never, once, occasionally and often.

By examining Tables IV-1 through IV-8, it can be seen that a certain type of pattern is evident for many of the symptoms. This pattern is most evident for Table IV-1 (corresponding to symptom 1). For the 255 high exposure group jobs recorded on individuals' questionnaires, 94 (37 percent) were reportedly associated with an episode of dizziness or light-headedness at least once. The comparable figures for the low exposure group were 28 out of 236 jobs (12 percent) and the values for the rubber worker jobs were 21 out of 214 jobs (10 percent). The purpose of presenting

TABLE IV-1
Exposure Category by Frequency of Dizziness, Light-headedness

O.T. GROUP	NEVER	ONCE	OCCASIONALLY	OFTEN	ROW TOTAL
High Exposure	161	8	72	14	255
	(63.1)	(3.1)	(28.2)	(5.5)	(100.0)
Low Exposure	208	1	25	2	236
	(88.1)	(0.4)	(10.6)	(0.8)	(100.0)
Rubber Worker	193	5	14	2	214
	(90.2)	(2.3)	(6.5)	(0.9)	(100.0)
Column Total	562	14	111	18	705
	(79.7)	(2.0)	(15.7)	(2.6)	(100.0)

Row percentage applies to Tables IV-1 through IV-8.

TABLE IV-2
Exposure Category by Frequency of Passing Out

O.T. GROUP	NEVER	ONCE	OCCASIONALLY	OFTEN	ROW TOTAL
High Exposure	244	8	2	1	255
	(95.7)	(3.1)	(0.8)	(0.4)	(100.0)
Low Exposure	231	3	2	0	236
	(97.9)	(1.3)	(0.8)	(0.0)	(100.0)
Rubber Worker	212	2	0	0	214
	(99.1)	(0.9)	(0.0)	(0.0)	(100.0)
Column Total	687	13	4	1	705
	(97.4)	(1.8)	(0.6)	(0.1)	(100.0)

TABLE IV-3
Exposure Category by Frequency of Nausea, "Sick" Feeling

O.T. GROUP	NEVER	ONCE	OCCASIONALLY	OFTEN	ROW TOTAL
High Exposure	193	5	42	15	255
	(75.7)	(2.0)	(16.5)	(5.9)	(100.0)
Low Exposure	212	0	20	4	236
	(89.8)	(0.0)	(8.5)	(1.7)	(100.0)
Rubber Worker	190	3	16	5	214
	(88.8)	(1 4)	(7.5)	(2.3)	(100.0)
Column Total	595	8	78	24	705
	(84.4)	(1.1)	(11.1)	(3.4)	(100.0)

TABLE IV-4
Exposure Category by Frequency of Headache

O.T. GROUP	NEVER	ONCE	OCCASIONALLY	OFTEN	ROW TOTAL
High Exposure	187	3	42	23	255
	(73 3)	(1.2)	(16.5)	(9.0)	(100.0)
Low Exposure	194	0	30	12	236
	(82.2)	(0.0)	(12.7)	(5.1)	(100.0)
Rubber Worker	183	0	25	6	214
	(85.5)	(0.0)	(11.7)	(2.8)	(100.0)
Column Total	564	3	97	41	705
	(80.0)	(0.4)	(13.8)	(5.8)	(100.0)

these tables is to describe the patterns of response for each symptom. A measure of the importance of these results is given in the following statistical analysis, which employs a weighting scheme with values 0, 1, 2 and 3 respectively. (For example, if a person answered "occasionally" to the frequency of a given symptom, this response was treated as twice as important as an answer of "once".)

Using the Occupational Title Grouping in Figure 1, a series of statistical analyses were performed to determine the relationship of the questionnaire responses of these groups of workers to their relative exposures to VC.

The differential exposures to VC between the three study groups account for only one of the many possible hazards. Thus, the controls in this study must be viewed as "internal controls" who may be exposed to other chemical exposures. However, the consistency and strength of the results of this study in conjunction with similar results from previous studies, tend to confirm the suspicion that the causative agent in this study is vinyl chloride.

Since questionnaire answers are recorded in categories rather than a continuum, it was therefore appropriate to use statistical analysis techniques designed for categorical data. The

TABLE IV-5
Exposure Category by Frequency of "Pins and Needles" in Arms or Legs

O.T. GROUP	NEVER	ONCE	OCCASIONALLY	OFTEN	ROW TOTAL
High Exposure	219	2	21	13	255
	(85.9)	(0.8)	(8.2)	(5.1)	(100.0)
Low Exposure	216	0	12	8	236
	(91.5)	(0.0)	(5.1)	(3.4)	(100.0)
Rubber Worker	201	1	7	5	214
	(93.9)	(0.5)	(3.3)	(2.3)	(100.0)
Column Total	636	3	40	26	705
	(90.2)	(0.4)	(5.7)	(3.7)	(100.0)

TABLE IV-6
Exposure Category by Frequency of Muscle Weakness

O.T. GROUP	NEVER	ONCE	OCCASIONALLY	OFTEN	ROW TOTAL
High Exposure	211	6	19	9	255
	(86.7)	(2.4)	(7.5)	(3.5)	(100.0)
Low Exposure	224	0	11	1	236
	(94.9)	(0.0)	(4.7)	(0.4)	(100.0)
Rubber Worker	194	2	13	5	214
	(90.7)	(0 9)	(6.1)	(2.3)	(100.0)
Column Total	639	8	43	15	705
	(90.6)	(1.1)	(6.1)	(2 1)	(100.0)

TABLE IV-7
Exposure Category by Frequency of Irritation of Eyes, Nose or Throat

O.T. GROUP	NEVER	ONCE	OCCASIONALLY	OFTEN	ROW TOTAL
High Exposure	166	2	49	38	255
	(65.1)	(0.8)	(19.2)	(14.9)	(100.0)
Low Exposure	158	1	47	30	236
	(66.9)	(0.4)	(19.9)	(12.7)	(100.0)
Rubber Worker	159	0	43	12	214
	(74.3)	(0.0)	(20.1)	(5.6)	(100.0)
Column Total	483	3	139	80	705
	(68.5)	(0.4)	(19.7)	(11.3)	(100.0)

TABLE IV-8
Exposure Category by Frequency of General Fatigue, "Run-Down" Feeling

O.T. GROUP	NEVER	ONCE	OCCASIONALLY	OFTEN	ROW TOTAL
High Exposure	177	1	39	38	255
	(69.4)	(0.4)	(15.3)	(14.9)	(100.0)
Low Exposure	181	0	29	26	236
	(76.7)	(0.0)	(12.3)	(11.0)	(100.0)
Rubber Worker	171	2	28	13	214
	(79.9)	(0 9)	(13.1)	(6.1)	(100.0)
Column Total	529	3	96	77	705
	(75.0)	(0.4)	(13.6)	(10.9)	(100.0)

TABLE V
Results of Statistical Analysis of Eight Symptoms

SYMPTOM	DOSE-RESPONSE PATTERN
1. Dizzyness, lightheadedness	yes
2. Passing out	borderline
3. Nausea, "sick" feeling	yes
4. Headache	yes
5. "Pins and needles" in arms and legs	yes
6. Muscle weakness	no
7. Irritation of eyes, nose or throat	borderline
8. General fatigue, "run down" feeling	yes

procedure used in this analysis was the Categorical Linear Data Model.[12] (This procedure makes use of the cell proportions in a weighted least squares analysis of complex contingency tables.)

The information on frequencies of response in Table IV-1 through IV-8 was input into the categorical data computer program (LINCAT). The statistical model is of the form:

$$F(\pi) = X\beta$$

where π is the vector of empirical probabilities derived from each of the frequency Tables IV-1 through IV-8

X is an arbitrarily chosen design matrix

β is the (unknown) parameter vector.

Although it is beyond the scope of this paper to discuss the statistical procedure, it is sufficient to indicate that this approach to categorical data analysis is analagous to the General Linear Model approach[13] to the statistical analysis of continuous data.

The first set of analyses examined which of the symptoms, if any, exhibited a significant dose-response type of relationship with presumed VC exposure. A dose-response pattern was deemed to exist if the (weighted) symptom response rate for O.T. Group 1 was significantly* greater than for O.T. Group 2 and, in addition, the response rate for O.T. Group 2 was greater than for O.T. Group 3. This takes account of both the direction and magnitude of the respective differences.

It was next decided to determine the importance of age at time of exposure to each job as a possible confounding variable. The study population was subdivided by age at exposure into ≤ 36 and ≥ 37 at time of entry into job. For those symptoms where adjustment by age produced a better fitting model (in the statistical sense), the adjustment for age was made in Table V. Only the statistical models for symptoms 1, 7 and 8 were enchanced by age adjustment. In each of these three cases age was not a significant variable in its own right, but its inclusion resulted in a better fitting model. (The direction of the difference in age groups for all three of these symptoms indicated that younger people tended to exhibit these symptoms more frequently than older people, although this difference was not statistically significant. This may be due to a possible adaptation by older workers or to self-selection by the more sensitive workers.)

The results presented in Table V show a clear dose-response relationship for symptoms 1, 3, 4, 5 and 8. This means that in addition to there being a significant difference in the response rate for all VC workers when compared with rubber workers, there is a further difference between VC workers when they are categorized into high and low exposure groups. For symptoms 2 and 7, the direction of the response gradient was of a nature to indicate a dose-response pattern but the magnitude of the differences was not quite great enough to meet the criteria for statistical significance. These two symptoms have consequently been labelled as "borderline". Symptom 6 (muscle weakness) did not exhbit a dose-response gradient.

Preliminary attempts at utilizing information on smoking, length of service and calendar period of exposure have yielded little to date. Further work is being done in these areas.

In summary, there appears to be a dose-response relationship between certain acute symptoms (predominantly neurological) and level of vinyl chloride exposure. The responses of the workers may have been subject to bias due to prior knowledge of the hazard of vinyl chloride exposure. However, the existance of the dose-response pattern for certain symptoms, as well as the absence of such a pattern for one symptom tend to support the validity of this study.

*Significance here is defined as: probability of a Type 1 error (α) $\leq .05$.

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