

AN EPIDEMIOLOGIC STUDY OF BLOOD SCREENING TESTS AND ILLNESS HISTORIES
AMONG CHEMICAL WORKERS INVOLVED IN THE MANUFACTURE OF
POLYVINYL CHLORIDE

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INTRODUCTION

The recently recognized occurrence of angiosarcoma of the liver among workers in the B. F. Goodrich Chemical Plant in Louisville, Kentucky has provided the opportunity for this study. Following the realization that five deaths attributable to angiosarcoma had occurred among polyvinyl chloride manufacturing workers in the plant, all plant employees were screened for blood chemistry abnormalities using a battery of 12 screening tests. This effort resulted in the identification of two additional cases of angiosarcoma of the liver. In all instances, angiosarcoma occurred among workers in Unit 62, the unit in the plant in which vinyl chloride is used in the production of polyvinyl chloride. The occurrence of the seven cases in a single unit of the plant suggests that workers in this unit have experienced a close contact with a causative agent which has not been experienced by workers in other units.

Because little is known about either the mechanisms of tumor development or the means of early detection of individuals at greatest risk of developing the sarcoma, it was felt that a careful comparison of Unit 62 workers with other plant workers might indicate important areas for further study. The present epidemiologic study was undertaken, then, to discern any detectable blood screening test or illness history differences between currently employed B. F. Goodrich Louisville Plant workers who have work experience in Unit 62 and a similar group of workers who have never worked in Unit 62.

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MATERIALS AND METHOD

Information on date of birth, dates of employment, duration of employment, units or work assignment, and length of time spent within units was obtained from company employment records on each hourly paid worker currently employed by the Louisville B. F. Goodrich plant. In addition, information of sex, race, height and weight measurements at the time of initial employment, and blood chemistry screening tests were obtained from company medical records. Illnesses resulting in days lost from work as well as related illnesses and injuries are recorded in the company medical records of all employees and were abstracted for analysis.

In order to determine whether Unit 62 workers experienced relatively more illness or exhibited differences in blood screening studies when compared to workers in other units of the plant, the study population of 882 hourly paid workers is divided into two subpopulations on the basis of work experience in Unit 62.⁽¹⁾ Four hundred thirteen of these employees have worked in Unit 62 for longer than one month ("Unit 62 workers") and 469 employees have never worked in Unit 62 ("other workers"). The mean for the total number of years employed by the plant is 14 years for Unit 62 workers and 12 years for other workers. In the analyses, the term "work years" denotes the number of years spent in Unit 62 for Unit 62 workers, while for the other workers it denotes the number of years spent in units other than Unit 62. In addition to their Unit 62 work experience, Unit 62 workers have, on the average, 7 years of work experience in units other than Unit 62. All employees in the study are male and non-white employees constitute less than 10% of each subpopulation. Because the number of non-white employees is small and the race distributions

in each subpopulation are similar, race was not included as a control variable. Mean ages are 40 and 41 years for the Unit 62 workers and the other workers, respectively. Employment heights and weights of the two groups are also similar.

The 12 blood chemistry screening tests were done over a several month time period beginning in January 1974. Early morning blood specimens were drawn from each subject after an overnight fast. Colorimetric laboratory analyses were done using a single Technicon SMA-12-60 analyzer and Technicon reagents. All enzymatic reactions were read in the 340 nm wave length range. Three independent standards were used as controls at every 12 sample interval⁽²⁾

Data processing and analyses were done on an IBM 360 computer using prepared computer program systems.⁽³⁾ Overall means and simple statistics for each laboratory test were calculated for each subpopulation. For each screening test, the proportion of subjects with values in the clinically abnormal ranges was determined for each subpopulation. Since the purpose of the analysis was to compare the two subpopulations under study rather than to identify individuals with overt evidence of illness, the clinical laboratory's criteria for normal ranges were felt to be acceptable without further investigation.⁽⁴⁾ In order to describe the effects of both age and work experience on blood chemistry levels, mean values for each laboratory test were plotted by 5-year age groups, and similarly by 5-year work experience categories, within each subpopulation. Least squares regression lines for laboratory tests on both age and duration of work experience were also plotted for each subpopulation. Multiple regression techniques were used to compare laboratory test values of the two subpopulations. These values were adjusted for age in the analysis by the use of an age group co-variable in the statistical model. Finally, categorical illnesses within each subpopulation were enumerated and the proportions

of each subpopulation having a history of illness within each category were compared using Chi square tests.

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RESULTS

FIGURE 1 presents the mean blood screening test values and standard deviations for both subpopulations. There are no differences between the mean values for Unit 62 workers and the other workers. The individual test values were assigned to below normal (low), normal, and above normal (high) categories on the basis of normal ranges as determined by the clinical laboratory.⁽⁵⁾ These results are presented in TABLE I. When a Chi square analysis is used to test for independence of the two variables, subpopulation and category of each blood screening test value (low, normal, high), three tests failed to show independence at the 0.05 probability level; albumin, alkaline phosphatase, and SGOT. It appears that a greater proportion of Unit 62 workers have elevated albumin levels, while elevated SGOT and alkaline phosphatase levels occur more frequently in the other workers.

When multiple regression techniques are used to test for group differences in mean values of each blood screening test, both albumin levels and cholesterol level trends with age are found to be different for the two subpopulations. No other such differences are found in any of the other screening tests.

FIGURE 2 presents mean albumin levels of each subpopulation for 5-year intervals of work years. The superimposed lines represent the least squares regression plot of albumin level on work years for each group of workers. The negative slopes for both groups reflect an effect of age on albumin levels. Using a multiple regression technique to adjust for differences due to age, the albumin levels of the Unit 62 workers are found to be significantly higher than the albumin levels of the other workers ($p < 0.03$).

FIGURE 3 presents mean cholesterol levels for each subpopulation by work years. The least squares regression plot of cholesterol levels on work years is also shown. The increase of cholesterol levels over time reflects an effect

of age on the levels. The cholesterol levels increase less rapidly over time for Unit 62 workers than for the other workers. The observation that initial cholesterol levels are higher for Unit 62 workers reflects the fact that for the 0 - 4 work year category, Unit 62 workers are, on the average, 6 years older than the other workers. However, in the other 5-year work experience intervals, the average age differences are two years or less.

Using multiple regression techniques to assess the interaction between age and cholesterol level in each subpopulation, the effect of age on cholesterol levels is found to be significantly different for the two subpopulations ($p < 0.03$).

The frequency of reported illness by category of illness is presented for the two subpopulations in TABLE II. While most of the illness categories are general, a history of confirmed or suspected peptic ulcer disease and liver-spleen disease (e.g., splenectomy for portal hypertension, cirrhosis, hepatitis, etc.) are felt to be of interest, and consequently, these specific entities are categorized separately from GI illness. When a Chi square analysis is used to test for independence of the two variables, subpopulation and occurrence of each categorical illness in both subpopulations, three of the illness categories failed to show independence at the 0.05 probability level. Although the numbers are small, allergic problems and liver-spleen disease are recorded more frequently in Unit 62 workers than in the other workers, while the other workers have more genitourinary system illness reported.

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DISCUSSION & CONCLUSION

The present study involves a comparison of medical findings in chemical workers of a single plant employed in a unit (Unit 62) where seven cases of liver angiosarcoma have been diagnosed and a control group of similar workers employed in other units of this plant.

Relatively few individuals in either group have had major illnesses resulting in days absent from work. Several instances of group differences in reported illnesses were identified and are presented here without any attempt to assess factors such as length of employment, selective criteria for employment, age, or behavioral differences between groups.

The additional finding that there are many individuals in both groups with abnormal screening tests suggests that clinically abnormal blood chemistry screening results among workers, particularly in the absence of a control group, must be interpreted cautiously. While greater percentages of Unit 62 workers had abnormal albumin levels, greater percentages of the control group had clinically elevated SGOT and alkaline phosphatase levels.

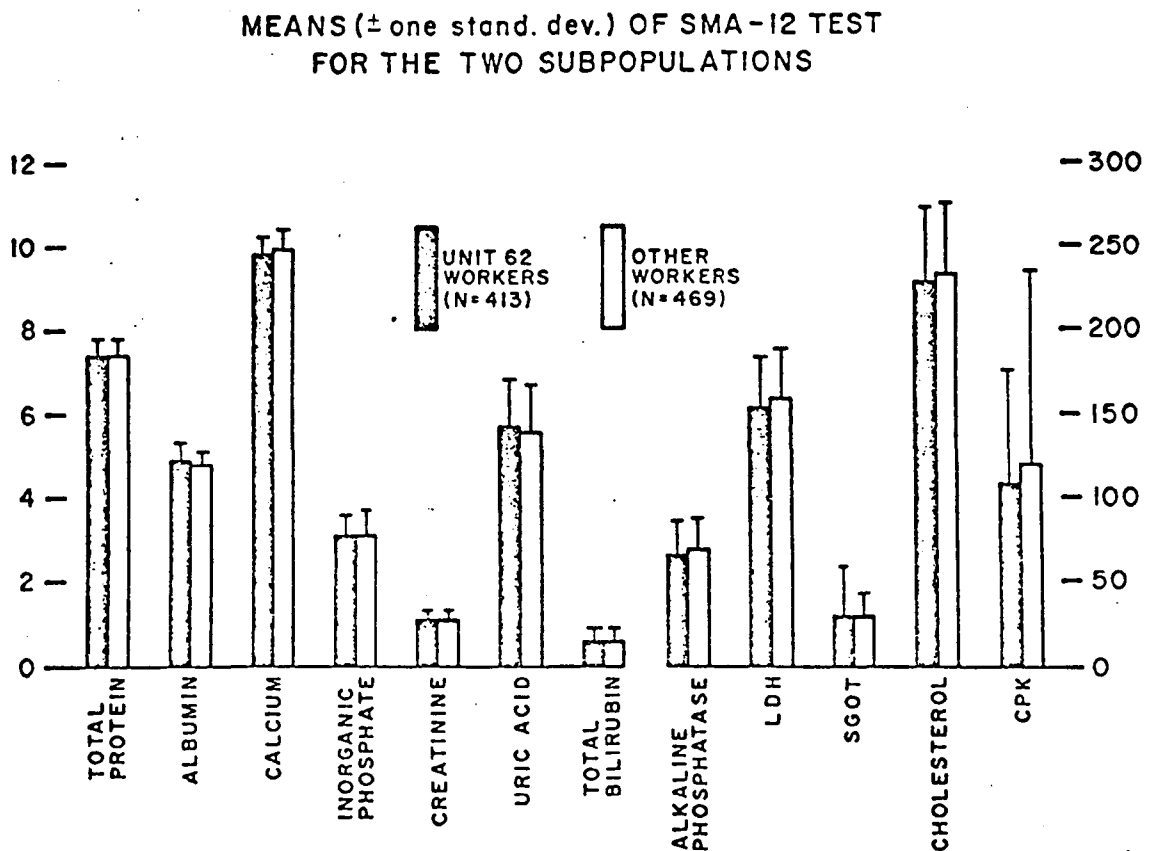
After adjusting for age, the findings of significant group differences in albumin concentrations and in cholesterol trends over time may suggest areas for further study even though they may not clinically differentiate individuals at high risk of developing angiosarcoma.

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FIGURE 1

Means of the individual blood screening tests for both subpopulations;  Unit 62 workers;  other workers. Numerical values of the means are in units of gm% for total protein and albumin; mgm% for calcium, inorganic phosphate, creatinine, uric acid, total bilirubin, and cholesterol, and mu/ml for alkaline phosphatase, LDH (lactic dehydrogenase), SGOT (serum glutamic-oxalic transaminase), and CPK (creatinine phosphokinase). Vertical bars represent one standard deviation of the data for each test.



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FOOTNOTES

- (0) Acknowledgments: This study was made possible through the cooperation and support of the B.F. Goodrich Chemical Company of Louisville, Kentucky. The authors are especially grateful to Mr. P. Lawrence, plant manager, Mr. Ken Pember, industrial relations manager, and Dr. M. N. Johnson, Director of the Department of Environmental Health, Chemical Division, B. F. Goodrich Corporation, Akron, Ohio. The authors also wish to express their sincere appreciation to Dr. J. B. Block, Medical Consultant, Occupational Health and Safety Division, Kentucky State Department of Labor, Frankfort, Kentucky. (see title page)
- (1) Due to incompleteness of either the personnel or medical records of 65 of the 947 total hourly paid workers carried in the plant files at the time of this investigation, these employees were excluded from the study population. (see page 2)
- (2) A description of specific methods used in the analyses is available from the Technicon Instruments Corporation, Tarrytown, N.Y.(see page 3)
- (3) This involved use of the following two standard statistical packages: the Statistical Analysis System (SAS) and the Statistical Package For The Social Sciences (SPSS). (see page 3)
- (4) These normal ranges are being used to clinically single out individuals for further testing. (see page 3)
- (5) These normal ranges are presented in TABLE I.
(see page 5)

TABLE 1

Number and Percent of Workers in Two
Subpopulations Having Blood Screening Test
Values in Low, Normal, and High Categories ^a

Blood Screening Test with Normal Range ^a	Category	Number & Percent of Workers in Each Subpopulation			
		Unit 62 Workers		Other Workers	
		N	%	N	%
Total Protein (5.0-8.0 gm%)	low	0	0.0	0	0.0
	normal	386	94.1	442	94.2
	high	24	5.9	27	5.8
		<u>410</u>	<u>100.0</u>	<u>469</u>	<u>100.0</u>
Albumin ^b (3.5-5.0 gm%)	low	2	0.5	1	0.2
	normal	263	64.1	350	74.6
	high	145	35.4	118	25.2
		<u>410</u>	<u>100.0</u>	<u>469</u>	<u>100.0</u>
Calcium (8.5-10.5 mgm%)	low	0	0.0	1	0.2
	normal	395	95.6	431	91.9
	high	18	4.4	37	7.9
		<u>413</u>	<u>100.0</u>	<u>469</u>	<u>100.0</u>
Inorganic Phosphate (2.5-4.5 mgm%)	low	38	9.2	57	12.2
	normal	372	90.1	410	87.4
	high	3	0.7	2	0.4
		<u>413</u>	<u>100.0</u>	<u>469</u>	<u>100.0</u>
Cholesterol (150-300 mu/ml)	low	5	1.2	8	1.7
	normal	385	93.4	428	91.3
	high	22	5.3	33	7.0
		<u>412</u>	<u>100.0</u>	<u>469</u>	<u>100.0</u>
Uric Acid (2.5-8.0 mgm%)	low	1	0.2	1	0.2
	normal	398	96.4	460	98.1
	high	14	3.4	8	1.7
		<u>413</u>	<u>100.0</u>	<u>469</u>	<u>100.0</u>
Creatinine (0.8-1.4 mgm%)	low	2	0.9	4	0.9
	normal	225	98.7	452	97.0
	high	1	0.4	10	2.1
		<u>228</u>	<u>100.0</u>	<u>466</u>	<u>100.0</u>

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Total Bilirubin (0.3-1.0 mgm%)	low	19	4.6	17	3.6
	normal	366	88.8	405	86.4
	high	27	6.6	47	10.0
		<u>412</u>	<u>100.0</u>	<u>469</u>	<u>100.0</u>
Alkaline Phosphatase ^c (30-85 mu/ml)	low	3	0.7	2	0.4
	normal	366	88.6	392	83.6
	high	44	10.7	75	16.0
		<u>413</u>	<u>100.0</u>	<u>469</u>	<u>100.0</u>
CPK (25-145 mu/ml)	low	3	1.3	10	2.1
	normal	185	80.4	369	79.2
	high	42	18.3	87	18.7
		<u>230</u>	<u>100.0</u>	<u>466</u>	<u>100.0</u>
LDH (100-225 mu/ml)	low	8	1.9	4	0.9
	normal	398	96.4	454	96.8
	high	7	1.7	11	2.3
		<u>413</u>	<u>100.0</u>	<u>469</u>	<u>100.0</u>
SGOT ^d (10-40 mu/ml)	low	2	0.5	3	0.6
	normal	377	91.3	399	85.1
	high	34	8.2	67	14.3
		<u>413</u>	<u>100.0</u>	<u>469</u>	<u>100.0</u>

^a Ranges of normal values for each test are defined by the Technicon Corporation. The categories low, normal, and high refer to values falling below, within, and above these defined normal ranges for each test.

^b Showed significant difference between the two subpopulations using Chi square analysis ($p < 0.005$).

^c Showed significant difference between the two subpopulations using Chi square analysis ($p < 0.05$).

^d Showed significant difference between the two subpopulations using Chi square analysis ($p < 0.05$).

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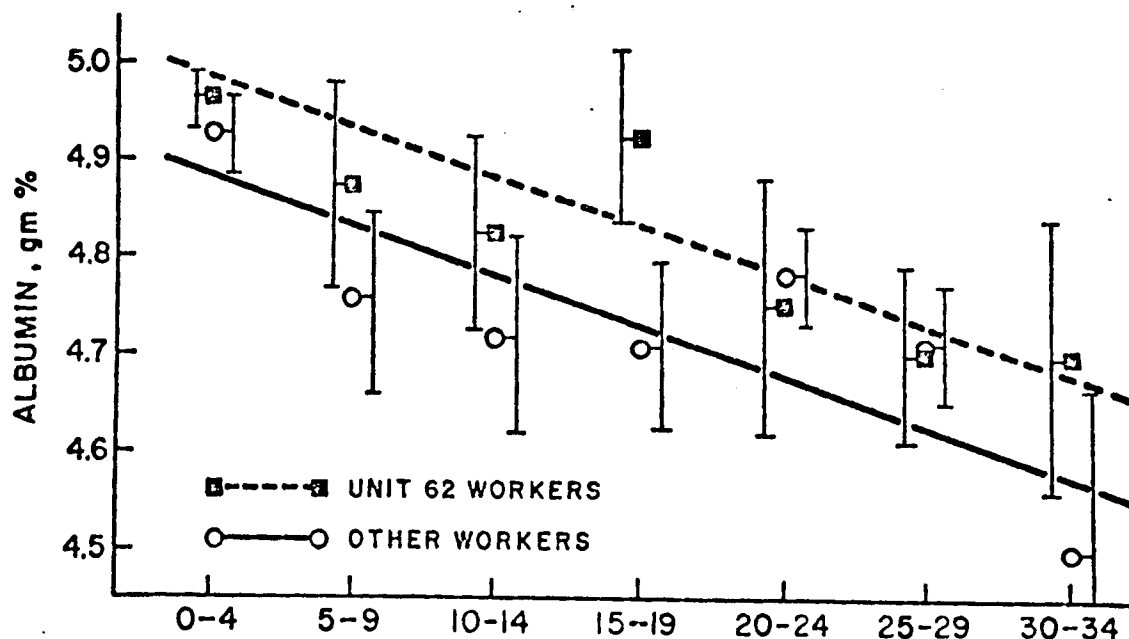
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FIGURE 2

Mean albumin levels (gm%) of the two subpopulations for each 5-year interval of work years: $\square$ Unit 62 workers; $\circ$ other workers. Lines represent linear regression plots for albumin level on work years for each subpopulation: ---- Unit 62 workers; — other workers. Vertical bars are 95% confidence limits of each mean calculated from the Student "t" distribution. N values for each mean are as follows:

<u>Interval of Work Years</u>	<u>Unit 62 workers</u>	<u>Other workers</u>
0 - 4	244	186
5 - 9	59	35
10 -14	27	50
15 -19	34	35
20 -24	28	90
25 -29	16	62
30 -34	5	11
	<u>413</u>	<u>469</u>

MEAN ALBUMIN ($\pm 95\%$ C.L.) VS. WORK YEARS
AND LINEAR REGRESSION

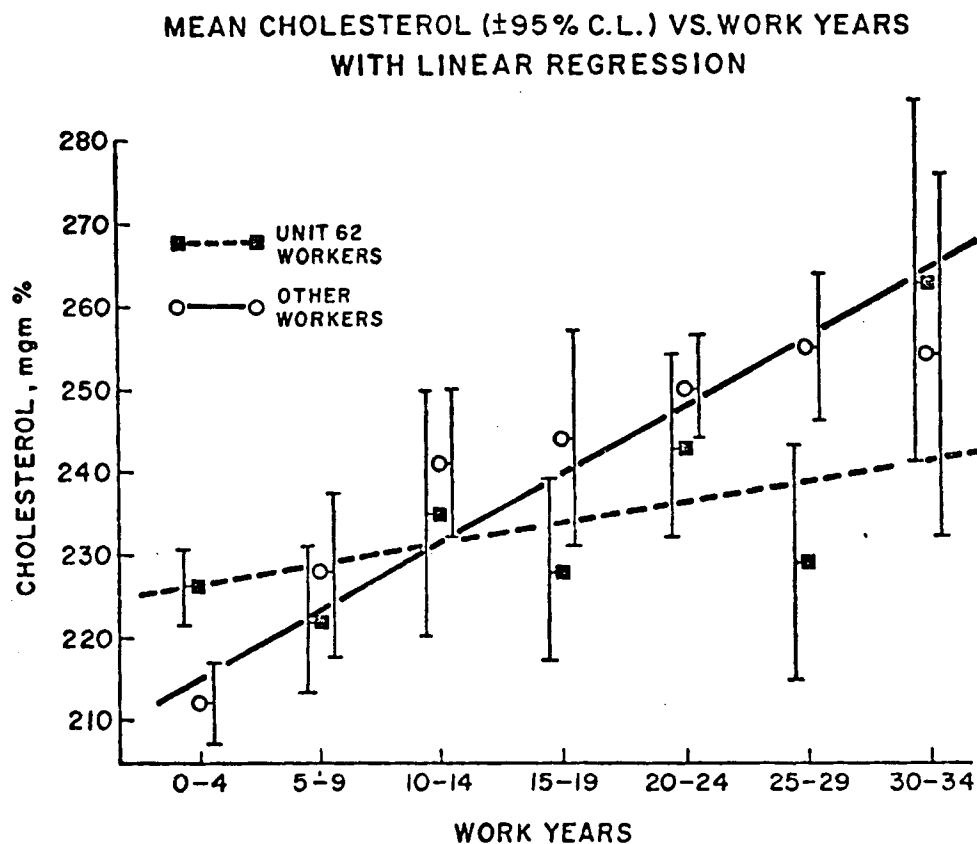


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FIGURE 3

Mean cholesterol levels (mgm%) of the two subpopulations for each 5 year interval of work years; $\square$ Unit 62 workers, $\circ$ other workers. Lines represent linear regression plots for cholesterol level on work years for each subpopulation; ---- Unit 62 workers, — other workers. Vertical bars are 95% confidence limits of each mean calculated from the Student "t" distribution. N values for each mean are found with FIGURE 2.



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TABLE II
Comparison of Two Subpopulations, Unit 62
Workers and Other Workers, by Categorical
Illness History

<u>Category of Illness</u>	<u>Number and Percent of Workers Having Illnesses in Each Category</u>			
	<u>413 Unit 62 Workers</u>		<u>469 Other Workers</u>	
	<u>N</u>	<u>%</u>	<u>N</u>	<u>%</u>
Cardiovascular	13	3.1	21	4.5
Musculoskeletal	10	2.4	11	2.3
Genitourinary ^a	4	1.0	16	3.4
Allergic ^a	12	2.9	5	1.1
Gastrointestinal	10	2.4	7	1.5
Peptic Ulcer Disease	6	1.5	9	1.9
Pulmonary	5	1.2	9	1.9
Neuro-psychiatric	7	1.7	5	1.1
Diabetes	3	0.7	7	1.5
Dermatologic	6	1.5	3	0.6
Liver-Spleen ^a	6	1.5	0	0.0
Endocrine	0	0.0	2	0.4
Toxic	5	1.2	2	0.4

^a Showed significant difference between the two subpopulations using Chi square analysis ($p < 0.05$).

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ANALYSIS OF PREEMPLOYMENT PHYSICALS
MARCH 1974 - MAY 6, 1974

MONITOR USED BUOYS AS SALES WITH ONE SUBJECT ONLY - 100% OF 1971

[illegible]

DATE

No. 80

SUBJECT:

JOB NO.

TITLE

DATE

This is with you - take orders and with notes so anyone can follow.

STATUS: 3rd LIVER FUNCTION TESTING
 MAY 10, 1974

TOTALS								
LOCATION:	ALBC	ALTC	3ALV	HEMRI	W. BEACH	LOUIS	P. TOWN	
NUMBER TESTED	653	415	589	300	146	1183	245	3531
NORMAL	✓ 415	✓ 304	✓ 469	✓ 293	✓ 109	✓ 864	✓ 145	✓ 2599
ABNORMAL	✓ 152	✓ 104	✓ 120	✓ 7	✓ 37	✓ 319	✓ 100	✓ 839
NUMBER REPEATS	164*	92* ①	120	7	25	298	92	798
NORMAL	✓ 76	✓ 44	✓ 58	✓ 7	✓ 9	✓ 110	✓ 66	✓ 370
ABNORMAL	✓ 77	✓ 20	✓ 62	✓ 10	✓ 16	✓ 188	✓ 26	✓ 389
NUMBER PROFILES	14*	0	7	0	14	120 ②	0	155
NORMAL	✓ 5	✓	✓ 6	✓	✓ 12	✓ 118	✓	✓ 141
ABNORMAL	✓ 5		✓ 1		✓ 2	✓ 2		✓ 10
NUMBER JEANS	9	0	1	0	0	120 ②	0	121
NORMAL	✓	✓	✓	✓	✓	✓ 118	✓	✓ 119
ABNORMAL						✓ 2		✓ 2
EMPLOYEES REASSIGNED	9	0	0	0	1	57	0	58
NO. RETURNED	✓ -	-	-	-	-	✓ 4	-	7

* WAITING ON RESULTS

① ALTC STILL DOING REPEATS

② PROFILES & JEANS COMBINED

WILCOX

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