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UNIVERSITY OF WASHINGTON

DEPARTMENT OF ENVIRONMENTAL HEALTH

AN OCCUPATIONAL HEALTH STUDY OF THE PREVALENCE OF CHRONIC RESPIRATORY DISEASE IN POTROOM WORKERS IN THE NORTHWEST ALUMINUM REDUCTION INDUSTRY

by

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Errata Sheet for

A STUDY PREPARED FOR THE NATIONAL INSTITUTE

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Errata Sheet

1. p. xiii, paragraph 2, line 1 -- change "co-investigators" to "principal medical and industrial hygiene consultants."

2. p. xiv -- change "Principal Co-Investigators" to "Principal Medical Consultants."

3. p. 22, paragraph 1, line 4 -- add after "exposure" the following phrase: "in their current employment."

4. p. 23, Table 4 title -- delete "LOGIC FOR."

5. p. 39, paragraph 2, last line -- add after "scheme" the following phrase: "and gives definition of terms."

6. p. 41, paragraph 1, line 1 -- delete "atypical, suspicious, positive, and unsatisfactory," and insert "mild atypical, moderate atypical, suspicious (marked atypical), positive, and unsatisfactory."

7. p. 60, paragraph 2, line 2 -- after "Table 15" add: "Analysis of the group with unsatisfactory sputum findings showed that non-smokers predominated, and associated with this was the relative infrequency of respiratory symptoms among persons who were unable to provide satisfactory sputum samples. Thus, the sputum results reflect a significant bias toward the smoking subgroups for both the study group and the control group. This bias would tend to slightly increase the frequency of observed abnormalities for both groups, but no firm conclusions can be made as to the magnitude of the bias."

8. p. 63 -- insert between paragraphs 1 and 2: "An analysis was performed of the prevalence of screening abnormal and phenotype abnormalities for the various dose groups among aluminum workers. Recognizing that not all of the workers in each group had all three tests performed, it was

concluded that no significant difference in the frequency of abnormality for any of these three tests was associated with potroom exposure dose. In fact, the trend of the data suggested that persons in the highest dose group had a higher frequency of abnormality, a trend opposite from that which would be expected if genetic susceptibles had selectively migrated out of the potroom and out of the industry. Frequency of abnormality among the control groups generally paralleled that of the low and intermediate dose group; thus, confirming the interpretation of there being no selection process related to $alpha_1$-antitrypsin deficiency."

9. p. 63, paragraph 2, last line -- delete "all the same" and insert "not remarkably different."

10. p. 64, Table 19 -- change "mg/KG" to "mg/L" and "mg%" to "mg/L". Change "0.422" to "0.0401", "21" to "27", "0.398" to "0.0460", "19" to "25", and "0.409" to "0.0389."

11. p. 68, paragraph 2, line 7 -- insert "See Appendix N for an analysis of occupational exposure history, comparing the study group with the control group for the effect of non-potroom work exposures." (Appendix N is attached.)

12. p. 71, paragraph 3, line 8 -- delete "follow-up studies to date show no evidence of progression."

13. p. 71, paragraph 3, last line -- insert: "Analysis of this comparison will be published elsewhere, but the results indicated that the reviewed agreed in most cases with the original interpretations used in this report; and in those few cases where disagreement existed, the reviewed generally observed a lower order of pathology than that given in our original interpretation."

14. p. 75, paragraph 1, line 3 -- delete "has been alleged to be associated with the occurrence of non-M alleges" and insert: "is principally associated with the Z allele in either the homosygous or heterozygous state, with non-M alleles resulting in $alpha_1$-antitrypsin deficiency if they are present in a homozygous or heterozygous state."

15. Appendix K -- See attached revision; delete K-3.

Appendix K

CLOSING VOLUME CLASSIFICATION SCHEME

Buist in the August 28, 1975 issue of The New England Journal of Medicine indicated the essentials of a classification by reference to a figure (not given herein). Since this classification and set of definitions were used in this study, we make the following quotation from Buist:

> "Four phases are shown: phase I is very small and represents dead-space gas (pure oxygen) from the conducting airways; phase II represents a mixture of dead-space gas and gas from the alveoli; phase III, the alveolar plateau, represents alveolar gas and, in normal subjects, has a slight positive slope. As residual volume is approached, there is an abrupt change in the slope of the alveolar plateau as airways in the lower parts of the lung either physically close or functionally cease to contribute to the expirate, allowing air spaces relatively rich in nitrogen (upper-lung zones) to contribute progressively more to the gas appearing at the mouth. The volume, above residual volume, at which the abrupt increase in nitrogen concentration is seen is called phase IV, or more commonly, the closing volume and is usually expressed as a percentage of vital capacity. When this volume is used as an absolute lung volume (i.e., above zero lung volume, closing volume plus residual volume) it is referred to as closing capacity and usually expressed as a percentage of total lung capacity. The slope of the alveolar plateau is obtained by measurement of the increase in nitrogen concentration per liter along the alveolar plateau. Total lung capacity and residual volume may be derived from the single-breath trace by measurement of the area under the expired nitrogen versus volume curve and application of the alveolar dilution principle."

The following formulas[23], based on the Buist classification scheme, were used to calculate the predicted values for Type 1 and Type 2 parameters:

$$\text{Type 1} \quad (CC/TLC \times 100) = (0.525 \times \text{age}) + 14.348$$

$$\text{Type 2} \quad (CV/VC \times 100) + (0.318 \times \text{age}) + 1.919$$

The deviations from predicted values were calculated by subtracting the observed value from the predicted value and dividing by the standard deviation value for each. The deviation estimated by Buist[23] were as follows: Type 1 = 4.61% and Type 2 = 4.34%.

A typical calculation for Type 2 is given below for a 46-year old potroom worker:

$$PRED(2) = (0.318 \times 46) + 1.919$$

$$= 16.547 \quad \text{(units are per cent)}$$

$$DEV(2) = \frac{20.089^{*} - 16.547}{4.34}$$

$$= +0.816 \quad \text{(deviation units from predicted)}$$

The standard deviation of +0.816 for this 46-year old potroom worker is within the normal range; it is less than 2 standard deviations above the predicted value. If it were greater than 2 standard deviations, the results would have been classified as "abnormal." All minus values were considered normal

Bibliography

A. Sonia Buist, The Single-Breath Nitrogen Test, New England Journal of Medicine, :438 (Aug. 28) 1975.

D. S. McCarthy et al., Measurement of "closing Volume" as a Simple and Sensitive Test for Early Detection of Small Airway Disease, Amer. J. Med. 52:747-753 (June 1972).

R. E. Dolfuss, J. Milic-Emil, and D. V. Bates, Regional Distribution of Ventilation of the Lung Studied with Boluses of ^{133}Xenon, Resp. Physiol. 2:234 (1967).

*The CV was measured as 1.35 liters; VC was 6.46 liters; therefore, the per cent quotient is 20.089.

Appendix N

EVALUATION OF THE POSSIBLE RISK FACTOR OF NON-POTROOM OCCUPATIONAL EXPOSURE HISTORY

Details of past occupational exposures, other than potroom exposures, could not be documented from the questionnaire for either the study group or the control group. Although the data are relatively non-specific, an analysis was performed of the chronic respiratory disease risk associated with questionnaire responses to the following questions:

Have you ever worked in a dusty job:

Question 14. At a coal mine?

15. At any other mine?

16. At a quarry?

17. At a foundry?

18. At a pottery?

19. At a cotton, flax, or hemp mill?

20. At any other dusty job? _____
specify

Have you ever worked in an area where you encountered:

21. Welding and soldering fumes?

Have you ever worked with:

22. Asbestos?

23. Beryllium?

24. Cadmium or its compounds?

25. Chromic acid mist?

26. Epoxy resins?

27. Fiberglass?

28. Other chemicals, gases, fluids or metals that you or your employer considered to be dangerous or hazardous? _____
specify

The interview ground rules used in this study produce a past exposure bias; namely, the control group would be expected to report more past exposure situations than the study group, for reasons indicated below. The significance of any past work exposures in the potroom for the study group and the exposures elsewhere in employment for both the study group and the control group are both important to evaluate, recognizing in this data bank that there is a lack of quantitative exposure data.

This risk factor evaluation is primarily intended to indicate whether persons with potroom exposures and/or work exposures elsewhere had more evidence of chronic respiratory disease then those without these two reported exposures. Potroom exposures were well documented, but the data on exposures outside the potroom were obtained in a crude manner, using the questions given above. All study subjects had potroom exposures, and some also reported inhalant exposures with work elsewhere in the aluminum industry (such as welding in fabrication areas) or outside of that industry (such as coal mining) (Group I). Other study subjects did not report on interview any work exposures elsewhere other than the potroom (Group II). Control subjects included a majority of persons with some past occupational history of inhalant exposure (Group III), and a minority of persons who reported no such inhalant exposures (Group IV).

These four groupings could not be examined in quantitative terms, such as man-years or exposure adjusted for or subgrouped by time-weighted air concentrations of specific noxious chemicals; but the analysis could be indicative of the general effect on disease prevalence of certain patterns of reported past work experiences. Errors in reporting, such as minimizing "minor" exposures in work elsewhere by potroom workers, could

not be evaluated. One source of bias was very apparent: namely, that during the many years a potroom worker was in the potroom, his age-matched control has an additional opportunity for an exposure situation elsewhere, whereas the study worker was not eligible for this type exposure risk. This artifact was assumed in the research design; however, some moonlighting work exposures may have been included by potroom workers without the interviewer realizing it. One might expect that as age and the number of work years increase, reporting of exposures elsewhere among controls would increase; whereas this effect might be less evident for current potroom workers because they were ineligible for exposures elsewhere during their tenure in the potroom.

METHODS USED IN THIS ANALYSIS

The four groups in this study were enumerated as follows:

	"Exposures Elsewhere"	No Work "Exposures Elsewhere"
Potroom Exposure (Study Group)	Group I = 225	Group II = 231
No Potroom Exposure (Control Group)	Group III = 179	Group IV = 49

The above enumeration is based upon a positive answer to any one of 15 questions (Questions 14-28) about "exposures elsewhere."

One could enumerate the groups for each of these 15 or various groupings of these questions. Some questions were specific, and some were somewhat general. Some specific questions were believed to be less likely to represent a significant respiratory disease risk for most workers. Thus the enumeration of the four groups was also performed using

the more specific questions in two successive stages: (1) eliminate 5 questions (Questions 24-28) that indicate exposures that are probably less hazardous for most workers in terms of chronic respiratory disease risk; and (2) eliminate these 5 plus 2 more that represent very general exposure situations (Questions 21 and 20). The following summarizes the enumerations resulting from these three definitions:

	Group			
Positive Responses	I	II	III	IV
Any of 15 (Type 1)	225 } a	231	179 } b	49
Any of 10 (Type 2)	200 } c	256	153 } d	75
Any of 8 (Type 3)	76	380	61	167

The restriction process affected the enumeration of the study group and the control group in a similar manner: a and b in the above table are 11% and 15% reductions, respectively, and c and d are 62% and 60% reductions.

The age and smoking distributions of the four groups would not be expected to be similar. For reasons given above, Groups I and III would likely be older and, therefore, have more pack-years of smoking exposure. The analysis of such data requires adjusting rates to control for such differences prior to any performing comparisons. Another analytic approach to control for age and smoking was to use the data on matched pairs; each control worker was a match for two aluminum workers. For example, if both aluminum workers and the matched control all had exposures elsewhere, this group of triplets had no age or smoking history differences and could be compared without adjustment. This created two concordant

groups (triplets with exposures and triplets without exposures elsewhere) and two discordant groups (triplets where the "exposures elsewhere" were reported by only the study members and those triplets where exposures were in the control member only). The analysis of standardized rates for Groups I-IV and the analysis of the concordant-discordant groups were therefore undertaken to evaluate whether past occupational exposure contributed to the disease risk.

If "exposure elsewhere" was an important risk factor, potroom exposure should then be evaluated principally by comparing Groups II and IV, where there was no such exposure elsewhere. Moreover, the concordant triplets without exposure elsewhere would be the key comparison. If the disease prevalence of Group II equals or is less than that of Group IV, and if the rate is the study group members of concordant negative triplets, then the analysis of those without "exposure elsewhere" directly leads to the conclusion that this past work exposure is not important. If an analysis also shows no additional potroom effect, then one could propose that neither was a significant risk factor for the potroom workers (Group I rate compared with Group II). The control workers formed a similar comparison for exposures in a variety of work situations (Group II rate higher than Group IV).

Using the concordant positive triplets provides an estimate of an additive effect of potroom work in the presence of exposure elsewhere, and the two types of discordant triplets provide a comparison of the two exposure risks.

RESULTS

The following is a comparison of crude rates for chronic respiratory disease by questionnaire and spirometry (as previously defined):

Definition of "Exposure Elsewhere"	Workers with No "Exposure Elsewhere" Group II (Study Group)	Group IV (Control Group)
Type 1	4.0%	4.1%
Type 2	3.5%	4.0%
Type 3	5.0%	6.0%

The differences in the above comparison table were not significant, and thus, allowing for possible changes when the rates are standardized, one would conclude that potroom exposure alone was not significant in increasing disease prevalence. One should note that in using Type 3 data, one has identified 29 of the total of 34 persons with observed chronic respiratory disease in the entire study; whereas, Type 1 data includes only 11 of the 34.

For the concordant triplets without reported "exposure elsewhere," 17 of the 34 cases were identified using Type 3 definitions. The following indicates the prevalence comparison for 114 triplets with this characteristic:

	Number Affected	N	Prevalence
Study Group	9	228	3.9%
Matched Control Group	8	114	7.0%

Again the difference was not significant, and the trend was in the direction of more disease in controls. Similar analyses using Type 1 and 2

definitions also supported the general conclusion that potroom exposure was not a risk factor for those without exposure elsewhere.

Comparisons of Group I with II and Group III with IV were undertaken to evaluate the disease risk of "exposure elsewhere." Since the crude rates had particular difficulties with different age and smoking distributions, the standardized rates were used, and these rates were also used to derive ratios for the study group (I/II) and the control troup (III/IV):

Definition of "Exposure Elsewhere"	Study Group			Control Group		
Type 1	I	5.0%	1.14	III	5.0%	2.00
	II	4.4%		IV	2.5%	
Type 3	I	3.1%	0.63	III	8.7%	1.53
	II	4.9%		IV	5.7%	

No consistent effect of past exposure to occupational agents, presumed to have a risk of producing chronic respiratory disease, was demonstrated by these data. For the control group, the number of cases of chronic respiratory disease was especially small; therefore, the wide range of prevalences (from 2.5% to 8.7%) had little meaning. (The number of disease cases in the numerator for both the 2.5% and the 8.7% was only 2.) All of the other estimates in the above table are based on much more reliable data. In interpreting these ratios, statistical significance of all four ratios was not obtained. It should be noted also that the more specific subset of questions (Type 3) did not yield a consistently higher prevalence for

all four groups, indicating no major advantage for this subset procedure over the more general and complete set of 15 questions.

SUMMARY

A detailed analysis was undertaken of the study group and control group concerning 15 questions dealing with work exposures outside the potroom. It was concluded that such inhalant exposures were not associated with a significant increase in disease prevalence among the control group. Potroom workers disease rates among subgroups with or without such reported exposures were not any greater when compared with controls with or without these inhalant exposures outside the potroom.

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ABSTRACT

An occupational health prevalence study of chronic respiratory disease in 457 male aluminum potroom workers was undertaken in 1974 by the Department of Environmental Health at the University of Washington. Through the cooperation of ALCOA and the Kaiser Aluminum and Chemical Corporation, three plants located in the state of Washington were included in the study. Using mobile laboratory trailers on plant sites, previously identified aluminum potroom workers who had voluntarily given informed consent to participate were tested by a trained technician team. The tests consisted of an interviewer administered questionnaire, forced spirometry, closing volume determination, chest x-ray, sputum cytology, serum $alpha_1$ antitrypsin, serum trypsin inhibitory capacity (and in appropriate cases $alpha_1$-antitrypsin phenotyping), and blood pressure determination. Urine fluoride determinations were also made, and in a 10% subsample a serum unbound fluoride determination was obtained.

A comparison group from the University of Washington Physical Plant and from the General Telephone Company consisting of 388 skilled manual laborers not exposed to significant inhalants on the job was tested. This group consisted of males of a similar socioeconomic status to the aluminum workers.

The results of the 457 aluminum potroom workers were compared with 228 age and smoking category matched comparison subjects. A prevalence of chronic respiratory disease, based upon interview and spirometry, was noted in the aluminum workers to be 4.9% and in the comparison group, 5.3%.

The results were also analyzed comparing the prevalence in the study group with the prevalence in its matched control group, the overall prevalence ratio for chronic respiratory disease being 4.9%/5.3%, or 0.92. The prevalence ratios were examined separately for the sample of workers employed in a plant using the Soderberg process and the workers in the Prebake process; likewise the ratios were compared for three subgroups based on potroom exposure history and three subgroups for current employment status (former potroom worker, new hire in the potroom, or current potroom worker in excess of a minimum tenure). In none of these did the ratios show any significant differences from unity.

Individual test results were examined in a similar manner, using a prevalence ratio for the study group to its matched control group. The questionnaire data on respiratory symptoms and the spirometry data on forced expiratory volume in one second and the total volume were each analyzed in detail, and no remarkable group or subgroup ratios were observed. The closing volume measurements, on the other hand, showed a consistent ratio of higher prevalence of abnormalities in current workers and in those with higher exposure histories, but no difference was found between the two processes in this respect. The chest x-ray interpretation for "obstructive emphysema" showed a similar pattern of prevalence ratios. For both the closing volume and the chest radiographic findings, the significant ratios were considered to be of doubtful clinical significance since the questionnaire and spirometry data are judged to be more valid for clinical assessments. No other important results were found except for sputum cytopathology. Mild atypia, which is a nonspecific clinical finding, showed a significant ratio, but no particular association of the ratio with process or exposure history. The former potroom worker, however, showed a unity ratio of 22.4%/20.4%, comparing aluminum workers to matched controls with respect to atypia, suggesting that atypia was a reversible effect occurring largely among current potroom workers.

CONTENTS

APPENDICES (continued)

ILLUSTRATIONS

TABLES

ACKNOWLEDGMENTS

It is difficult to be comprehensive in noting appreciation and thanks when so many individuals contributed to this undertaking.

We are especially grateful to the co-investigators who provided significant assistance in four principle areas: (1) direct help in planning the study design and data analysis, (2) seeking and obtaining their respective aluminum company's corporate approval and support for undertaking the study, (3) providing excellent acceptance and cooperation at the plant management level, and (4) supplying the important interface between the testing team and the aluminum plant personnel.

The Associate Investigators, Industrial Hygiene Consultants, and Study Consultants gave us expert assistance, advice, and often participated in training, especially in regard to the technical tests used.

We would like to extend special thanks to Frank B. Metting, M.D., of the Kaiser Aluminum and Chemical Corporation, to William J. Bovard, M.D., of ALCOA, and to Charles R. Nuss of the University of Washington Physical Plant who worked so closely with the day-to-day activity of the study during the testing phases.

There were many individuals at the University of Washington who augmented the study and permitted its successful completion. We particularly wish to thank Alan K. Tarr, Assistant Vice President for Business; Robert F. Tomita, Director, Physical Plant; and John T. Wilson, M.D., Chairman, Department of Environmental Health.

Lastly, we would like to express our appreciation for the work by the technical and support study staff.

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SUMMARY

During 1974, an occupational health study to determine the prevalence of chronic respiratory disease in aluminum potroom workers was conducted by a study team in the Department of Environmental Health at the University of Washington. The Aluminum Company of America (ALCOA) and the Kaiser Aluminum and Chemical Corporation (Kaiser) cooperated and provided assistance in undertaking the study at three aluminum reduction plants in the state of Washington.

A specially trained technician team tested 457 potroom workers at Kaiser-Tacoma, ALCOA-Vancouver, and ALCOA-Wenatchee, using on-site mobile laboratory trailers. All of the aluminum potroom workers at these plants were identified, and a sampling technique to assure representativeness was used to identify a study group. Those workers selected were contacted in advance of testing, and informed consent to participate was obtained.

A comparison study group of 388 skilled manual laborers were similarly tested. This group was made up of Physical Plant employees from the University of Washington and a small group of equipment operators and linemen from the General Telephone Company in Kirkland, Washington. These subjects were tested on site by the same testing team and equipment used to test the aluminum potroom workers.

The testing, administered by appointment, required approximately 45 minutes for each subject to complete. The tests included an interviewer administered questionnaire that obtained basic identification data, past occupational exposures, current work history, past medical history, current respiratory symptomatology, and a tobacco smoking

history. A blood pressure determination was made. A minimum of five trials of forced spirometry, principally to determine FEV_1, and FVC, was obtained. Three acceptable closing volume determinations using the Nitrogen method were obtained. Two test measurements were used, both expressed as percentages. One was the closing volume divided by the vital capacity and the other was the closing capacity divided by the total lung capacity. A PA chest x-ray was made, which was interpreted by two radiologists reading independently and then resolving discordances. Using a three-minute ultrasonic nebulizer induction with a 5% propylene glycol solution, a sputum specimen was obtained for cytologic examination. Serum was prepared for laboratory testing for $Alpha_1$ Antitrypsin by (1) Radial Immunodiffusion and (2) Serum Trypsin Inhibitory Capacity (STIC); Pi phenotyping was carried out on serum with intermediate and low values. Preshift urine fluoride determinations were obtained, and a 10% subsample of potroom workers was tested for a serum unbound fluoride determination.

The testing response rate was 86% for the ALCOA plants and 71% for the Kaiser plant. Additional information from plant medical records showed that the nonrespondent workers at the Kaiser plant were similar to the tested workers. An 82% response rate was obtained in the entire comparison study group.

Using random selection techniques, 228 of the comparison study group were matched (by age within two years, and by being in the same smoking category) to the aluminum study group, using the guideline of identifying one comparison study group subject with two aluminum study group subjects.

Evaluation of the aluminum worker group and the matched comparison group as to race, marital status, height, weight, and education showed good comparability. There were about twice as many comparison workers

(3.9%) found to have elevated systolic or diastolic blood pressure (equal to or greater than 150 systolic or 95 diastolic) as there were aluminum potroom workers (2.1%). This difference was not significant. The aluminum workers were approximately four pounds heavier and one centimeter taller, the principal difference being at the Prebake plants when compared with controls.

Based on questionnaire response to respiratory disease symptomatology, one or more respiratory symptoms of cough, phlegm, wheezing, and dyspnea were found to be present in 46% of the aluminum workers and 42% of the matched comparison group. For two or more major respiratory symptoms the percentages were 22% and 26%, respectively. Symptoms of chronic bronchitis (major morning cough and major morning phlegm and/or major late phlegm) were observed to be 14.2% for the aluminum group and 14.0% for the matched comparison group. None of these differences was found to be statistically significant; moreover, comparisons made between the specific aluminum reduction processes used (Soderberg and Prebake) showed that these methods were not associated with any additional differences.

Studies of forced spirometry revealed 9.6% of the aluminum workers and 7.5% of the matched comparison workers had abnormal (equal to or less than 1.645 duration units of predicted for age and height) FEV_1 and/or FVC.

Comparison of those with an abnormal FEV_1 and/or FVC <u>and</u> one or more major respiratory symptoms showed 4.9% for the aluminum study group and 5.3% for the matched comparison group. This combination of questionnaire and spirometry results was used by investigators as the principal definition of chronic respiratory disease.

Closing volume results that were abnormal (equal to or greater than two standard deviations from predicted) revealed the aluminum study group to have 6% and the matched comparison group to have 3% for closing capacity/total lung capacity results. For closing volume/vital

capacity the results were 7% and 3% respectively, and when both of these tests were abnormal the results were 4% and 2%, respectively. Only the closing volume/vital capacity differences were found to be statistically significantly different. This represents a statistical difference, but not a clinical difference.

Evaluation of PA chest x-rays for current and old primary pulmonary disease showed the aluminum study group with 22% and the matched comparison group with 16%, which was not statistically different.

Sputum cytology results were found to be as follows. The aluminum study group/matched comparison gave these percentages: negative 68%/82%, atypical 30%/18%, suspicious 1.3%/0%, postive 0.3%/0%. These results were obtained from 85% of the two groups that had satisfactory sputa for analysis. The results are statistically significant only for atypical; therefore, the interpretation does not support a specific cancer risk.

Although there were minor differences in some test results, there were no important or statistically significant differences between the aluminum study group and the matched comparison group in respect to the prevalence of chronic respiratory disease.

The results of the sputum cytology test, which is directed more to metaplasia and neoplasia than chronic respiratory disease, seem to suggest a greater metaplasia risk in the aluminum study group than in the matched comparison group, but this difference was statistically significant only in nonspecific categories of mild to moderate metaplasia and was not significant for advanced metaplasia or frank neoplasia.

I INTRODUCTION

The purpose of this research was to determine the prevalence of chronic respiratory disease (CRD)* among workers exposed to dusts, fumes, gases, and vapors in aluminum reduction plant operations and to compare the findings with an appropriate control group. Specifically, the study group and control group samples were selected so as to detect at a high level of probability a two-fold risk or greater of chronic respiratory disease, if such a risk existed among the aluminum potroom workers in three plants as compared to a sample of control workers with no known injurious agents associated with their occupation. Although this study was not intended to provide meaningful data on lung cancer risks among potroom workers, preliminary information was to be obtained on the distribution of sputum cytology findings compared with controls.

The study was undertaken through the auspices of the Department of Environmental Health, School of Public Health and Community Medicine; it started in July 1973 and was completed in April 1975. As indicated in Tables 1 and 2, there were 474 aluminum workers tested at three aluminum reduction plants which included Kaiser Aluminum at Tacoma, Washington (Soderberg process), ALCOA at Vancouver, Washington (Prebake process), and ALCOA at Wenatchee, Washington (Prebake process). Of these 474,

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*Chronic respiratory disease, also known as chronic obstructive lung disease (COLD), for purposes of this study will be defined as any major respiratory symptom (cough, phlegm, wheeze, and dyspea at defined severity and frequency levels) and an observed FEV_1 and/or FVC less than predicted for age and height (at a designated level below the mean for males using a regression formula with age and height constants).

Table 1

TOTAL SAMPLE AND RESPONSE OF THE SAMPLE
TO THE TESTING PROGRAM

	Total Sample	Total Tested	Non-Respondents
Soderberg Process Group (100% sample of all potroom workers)	267	188	79 (29%)*
Prebake Process Group (25% random sample of all current and former potroom workers and 100% sample of all new hires)	333	286	47 (14%)*
	600	474	126 (21%)*
University of Washington Physical Plant employees and General Telephone telephone equipment operators (100% sample of selected units)	476	388	88 (18%)*
Total	1076	862	214 (20%)*

*Percentage of total sample.

Table 2

CONSTITUTION OF THE STUDY GROUP AND CONTROL GROUP FROM THE TOTAL TESTED

	Total Tested	Not Included	Constituted Group
Study Group			
Soderberg	188	5*	183
Prebake	286	12*	274
Subtotal	474	17*	457
Control Group	388	160†	228
Total	862	177	685

*Found to be erroneously identified as a potroom worker.

†Excluded because not matched with Study Group (see text).

17 turned out to be ineligible because they were not potroom workers, leaving 457 study group workers. A control sample of 388 workers was obtained from two sources: (1) shop personnel and other manual workers in the Physical Plant Department at the University of Washington, Seattle, Washington, and (2) linemen and equipment operators from General Telephone in Kirkland, Washington. Of the 388, 228 serve as a matched control group to the 457 study group workers on the basis of one control worker for every two aluminum workers. Although the study group and the matched control groups were composed of 457 and 228 workers, respectively, a total of 862 were tested out of a sample population 1,076 (a response rate of 80%).

II REVIEW OF LITERATURE

Employees of the aluminum reduction industry are exposed to a variety of airborne fumes, gases, and vapors; however, the two specific agents that are of greatest concern are fluorides, in the form of hydrogen fluoride and particulate fluoride, and coal tar pitch volatiles. Most pertinent reports in the medical literature appear to be related to the possible chronic systemic and respiratory effects of fluoride inhalants on the incidence of CRD among aluminum workers, but recent reports have also suggested the existence of carcinogenic risks from pitch volatiles. Investigators in the USSR[1]* reported a significantly higher incidence of cancer of certain sites among workers in aluminum "electrolyzer shops" than in the general population in the same cities. Another USSR study has vaguely suggested that community cancer mortality risks and bronchitis-pneumonitis morbidity risks were both associated with aluminum industry effluents.[2] Neither of these Russian studies were sufficiently documented to allow one to draw any firm conclusions, however. An excellent epidemiologic study[3] of the steel industry has implicated coal tar pitch volatiles in the etiology of excess lung cancer risk among men working on coke ovens. Animal data[4-8] suggested a carcinogenic risk with benzopyrene, a known component of such volatiles. A preliminary study by NIOSH[9] of coal tar pitch volatiles in the aluminum industry has been undertaken, and a mortality study to elucidate the lung cancer rises of workers exposed to volatiles is in progress.[10] In addition to these serious questions of cancer risk, any effect of potroom exposures on the

*References are listed at the end of this report.

incidence and severity of chronic obstructive lung disease is not clearly understood.

Although fluorides have been alleged to produce chronic lung disease--such as asthma, emphysema, chronic bronchitis, or interstitial fibrosis--the evidence is not impressive. By their wide distribution in nature, their inevitable presence in man's food and drink, and their consequent presence in the tissues of the human body, fluorides form a natural part of man's environment; yet, when present in excess, they are known to be harmful.[11]

In 1932, Møller and Gudjonsson[12] reported on clinical findings of 78 Danish workers engaged in crushing and refining cryolite ($Na_3Al\ F_6$), which is used as a flux in aluminum reduction. They reported a high turnover of workers "because of the working conditions:" only 18 out of 100 workers had been there longer than ten years. They also noted the following "fluoride effects" in the 78 workers they studied: silicosis (39/78); osteosclerosis and ligamentous calcification (30/78); anorexia, nausea, vomiting, belching, excessive salivation or obstipation (42/78); immobility of the spine (2/78) and anemia (14/30).

As a result of this study Kaj Roholm[13] was assigned by the Danish Inspectorate of Factories and Workshops to investigate chronic fluoride intoxication. He concluded in 1937 that the symptoms and findings were dependent on the dose, the time factor, the age of the individual, the composition of the diet, and other factors, some of them unknown. He stated that with these chronic exposures fluoride effects were especially localized to bones and teeth. On acute inhalation of gaseous fluorine compounds he noted irritation symptoms of the mucus membranes of the eye and the respiratory airway. Post mortem findings in those cases showed hemorrhagic inflammation of the lungs.

Roholm[13] noted the frequency of complaints of 68 Danish cryolite workers: anorexia 56%, nausea 53%, shortness of breath 43%, constipation 28%, localized joint pains 28%, susceptibility to colds 19%, vomiting 16%, cough 15%, tiredness 13%, stuffiness 12%, skin rash 12%, and others in lesser percentages. X-ray evidence of "pulmonary fibrosis" was found in 34 out of 68 workers and "emphysema" in 11/68. He reported on 14 deaths among cryolite workers, who had recorded an average work time of 13 years and average age at death of 55.6 years. Causes of death were as follows: pulmonary tuberculosis (five cases), cancer in the alimentary tract (four cases), bronchial asthma (one case), pneumonia (one case), diabetes (one case), syphilitic heart disease (one case), and post-surgical death-appendicitis (one case). Roholm concluded that there was nothing to show that working with cryolite reduced the period of life or that cryolite workers acquired recognizable organic lesions apart from the bone changes.

In 1938, Evang[14] investigated a Norwegian aluminum plant and reported that 18 out of 190 workmen had "asthma" compared to 32 out of 3,800 in the local inhabitants. Three-fourths of the workmen who developed asthma had no family history of asthma. He concluded that there was a causal connection between potroom work and asthma. Evang also noted another unpublished study of 48 men who had worked in potrooms from 5 to 40 years, performed by the Industrial Pulmonary Disease Committee of the Medical Research Council in 1936. None of the men was noted to have had silicosis, but three had "slight fibrosis" and four had signs of "a little emphysema." Clinically, one had asthma and one had chronic bronchitis. Evang also referred to an unpublished study of 101 potroom workers by A. Bradford Hill, which was undertaken in 1931-35. The potroom workers were compared with 124 "non-pot workers," with the conclusions that illness was slightly more frequent in potroom workers, but the types of illness were not different.

In 1938, Hjort[15] reported on 48 Norwegian aluminum potroom workers who sought medical attention during a 2-1/2 year period (1932-34). The 48 were out of a total of 98 men working in the potroom; three were seen for asthma and two for "industrial dyspnea." The three workers with asthma were noted to have cleared their asthmatic symptom following vacation.

Tourangeau[16] in 1944 reported from France on working conditions of potroom workers in aluminum plants. Medical records showed the average number of respiratory illnesses over a four-year period did not vary among potroom workers as compared with unexposed employees, 5.9% and 5.3% respectively. Physical examination of 104 potroom workers, aged 20-55 years, with exposure periods ranging from 1 to 20 years, were reported to show no significant pathology. Chest x-rays of 105 potroom workers exhibited increased hilar markings or accentuation of the reticulum of stroma in 16 (15.2%) workers, and deformation of the cardiac shadow in 17 (16.2%) workers. These abnormalities seemed to be more frequent in men who had worked three years or more in the potroom. Four workers (3.8%) showed scarring of tuberculous lesions, and 3 (2.8%) exhibited pleural sequalae.

Agate et al.,[17] in 1949 reported clinical, radiological, hematological, and biochemical findings of 323 workers from two aluminum electrolyte reduction factories and 75 persons residing in the area. The 323 aluminum factory workers were identified as furnace-room workers (254--232 men, 22 women) and nonfurnace-room workers (69--44 men, 25 women). The incidence of cough persisting over a number of weeks and accompanied by the production of sputum was higher in the furnace workers (12.8%) than in the nonfurnace workers (6.9%), or in the community group. Standardization for age and sex was used in comparing these percentages. No complaints of dyspnea on exertion were elicited from any of the groups.

Midttun[18] reported in 1960 on "bronchial asthma" among aluminum workers and noted two forms. One form was acute asthma which occurred on first contact with the potroom and caused workers to leave work immediately (four cases were noted). The chronic form of asthma was stated to be more common (32 cases); it was characterized by an acute cough, especially if exposed to increased pot effluent fumes. At this time, auscutation of the chest indicated protracted respiration, rough inspiration, and stridor. He noted the occurrence of increased cough, especially night and next morning, a complaint of pressure over the precordium, soreness in the chest, and dyspnea on exertion. The cough was aggravated by the recumbency; the night cough would increase and progress to orthopnea, and dyspnea and "bubbling in chest" were noted with attacks lasting up to one hour. Subsequent attacks became longer and some individuals developed "status asthmaticus." He also noted that if an affected individual left work, the symptoms would usually clear after a few days or weeks. In a three-year period (1944-57), 33 cases of asthma in pot workers were noted among a total of 400 pot workers. Those so affected had an average length of exposure of four years. One of the 33 had a family history of asthma, and 13 had a previous medical history of asthma or bronchitis.

In 1958 Derrberry et al.[19] examined the health status of workers in a fertilizer manufacturing plant in relation to fluoride exposure and made the following observations. No statistical differences were noted between the exposed and the control groups in respect to blood pressure, RBC count, WBC count, hemoglobin, thymol turbidity, or urinary sugar. Statistically significant differences were noted in respect to being overweight--control group (18/67), exposed group (11/74)--and albuminuria (degree not given)--exposed group (9/74), control group (3/67). X-ray study of the chest revealed pulmonary changes (emphysema, nonspecific fibrosis, costrophrenic angle adhesions, and/or healed tuberculous lesions) in 11/74 of the exposed group versus 4/67 of the controls ($p < 0.01$).

Rybicki[20] reported in 1970 on the effects of fluoride on the upper respiratory tract in Polish aluminum workers. The staff of the "electrolysis hall" consisted of 170 men in the 20-45 year age group. Twenty-nine percent had been employed less than one year, 48% one to two years, 20% two to three years, and only 3% over ten years. One to three percent of these workers had complaints of intermittent headaches and respiratory distress, but they were otherwise noted to be free of symptoms. Examinations revealed catarrhal and hypertrophic changes in the upper respiratory tract. Workmen with less than two years' exposure exhibited evidence of atrophy of the nasal mucus membranes, histories of nose bleeds, and acute episodes of inflammation of the upper respiratory tract; on the other hand, most older workers were affected with chronic respiratory and ear infections. The investigator noted that the "HF concentration exceeded the maximum allowable concentration," but no further exposure data were given.

Recently, Kaltreider et al.,[21] reported on two prevalence surveys of aluminum works with special reference to fluoride exposure. The first study reported findings relative to respiratory disease and was performed in 1945-46 at Niagara (New York) aluminum works, which used an unhooded prebake reduction process. Average values for fluoride in urine were recorded as follows: pot tender 8.7 ppm, tapper-carbon charger 9.8 ppm, craneman 9.6 ppm, and control 0.7 ppm. Clinical findings in the Niagara workers were as follows: (1) hypertension, 25/107 in the exposed group versus 13/108 in the control group (15/107 in the exposed group had diastolic pressures of 90-100 mm of Hg as compared to 6/108 in the control group, and 10/107 in the exposed group had diastolic pressures greater than 100 mm of Hg as compared to 7/108 in the control group); and (2) lung disease, mean vital capacity determinations (reported as observed V.C./predicted V.C.x 100) were 96.9% in the exposed group and 97.3% in the controls.

In summary, nine case reports or small epidemiologic studies (Roholm, Evang, Hjort, Tourangeau, Agate et al., Midttun, Derryberry, Rybicki, and Kaltreider) have been undertaken and no clear conclusions regarding the risks of chronic respiratory disease among potroom aluminum reduction workers can be deduced from them.

III METHODS AND MATERIALS

A. Planning, Scheduling, and Notification of Results

1. Initial Contacts

The initial contacts with the corporate medical directors of the ALCOA, Kaiser, and Reynolds Aluminum companies during early 1973 were made to enlist their cooperation for the performance of the chronic respiratory disease study in the state of Washington. ALCOA and Kaiser Aluminum agreed to participate.

2. Application for Approval

An application for approval of investigation entailing the use of human subjects was made to the University of Washington Human Subjects Review Committee and was approved for the period of July 13, 1973, through July 12, 1974. Reapplication was made and approved for the period July 13, 1974, through July 12, 1975.

3. Study Questionnaire

Approval was sought and given for the study questionnaire from the Federal Office of Management and Budget. The number assigned was OMB-68-R-1343 PC, which expires July 1, 1975.

4. Notification

Notification of the study was given to the Washington State Medical Association, the Washington State Department of Social and Health Services, and the Washington State Department of Labor and Industries.

5. Study Team and Dose Committee

At a meeting on August 31, 1973, in Seattle, Washington, representatives of ALCOA, the Kaiser Aluminum Company, and the University of Washington met to form an advisory study team to aid in implementing the study project. For the purpose of establishing worker occupational exposure estimates for specific aluminum reduction plants in the study, a subcommittee (Dose Committee) was formed of designated physicians and industrial hygienists from the advisory study team. Team meetings were also held on February 8, 1975 and April 16, 1975.

6. Plant Visits

Plant visits for the purposes of identifying the aluminum workers at potential risk were completed on the following schedule: Kaiser Aluminum Company at Tacoma on September 11, 1973; Spokane (Mead Works) on September 18, 1973; ALCOA at Wenatchee on September 24, 1973; Vancouver on October 1, 1973. Visits at each plant included general informational meetings with members of the plant management and labor union officials, a short plant tour, and meetings with personnel department managers to begin identifying a roster of aluminum workers.

7. Categorizations

On October 17, 1973, the Dose Committee met in Richland, Washington to consider categorizations of exposure for specific jobs related to potroom effluent exposure. As a result of this meeting, subsequent correspondence and a meeting in Seattle, Washington on December 7, 1973, specific categorizations were proposed by ALCOA and Kaiser Company industrial hygienists working in concert. Existing urinary fluoride excretion data were used as the principal determinant for this classification. The Dose Committee and the Investigators concurred with the recommendations. From this, three worker groups were defined for each of the

two types of processes, and a method was agreed on for obtaining estimated total dosage exposure for each study group member.

8. Personnel Records

Arrangements were made at each aluminum plant to obtain photocopied personnel records of each worker on our roster who agreed to take part in the study. From this information the worker could be exactly classified as to worker group and be given an estimated total dosage exposure number (see Section III.B for definitions). These records were verified by interview with each worker in the study at the time he was tested.

9. Written Consent of Worker

In order to enlist the interest, cooperation, and consent of the individual workers selected to take part in the study, plant newspaper releases were made describing the study (see Appendix A). Next, letters were sent in sealed envelopes through each plant mailing system to selected workers describing the details of the study and requesting participation (see specimen in Appendix B). Meetings were then held with small groups of five to twenty workers at the plants, at which time one of the investigators (Breitenstein) gave a further explanation of the study and obtained written consent from each worker to participate (see Appendix C). It was emphasized at these meetings that the testing was entirely voluntary in nature and that the results would be kept confidential between the study team and the individual worker--and in addition, his physician, if the subject permitted it.

10. Test Hours for Aluminum Workers

Arrangements for testing at the plants were made through the plant medical directors who were instrumental in interfacing the testing

team with the plant supervisory personnel. Testing times were arranged so as to provide the least work disruption at each plant, and specific appointment times were arranged before moving the mobile equipment on site. Since there were four shifts of aluminum workers with three consecutive eight-hour shifts and one shift off each day, the testing schedule included hours other than regular 8-5 daytime working hours. It was found that testing three workers an hour, usually over eight hours, allowed for the most efficiency. Since each aluminum plant was visited at least twice, most of the workers who had any unsatisfactory test (e.g., x-ray, sputum, pulmonary function) were retested. Occasionally, a special trip without the full testing unit was made to conduct a repeat test.

11. Test Dates for Aluminum Workers

The testing schedule of the study group was as follows (all dates 1974).

- Kaiser Aluminum Company in Tacoma, Washington: 2/22-3/7, 5/17-5/30, and 6/28-7/3.
- ALCOA in Vancouver, Washington: 3/8-3/18 and 7/8-7/10.
- ALCOA in Wenatchee, Washington: 3/19-3/27 and 7/11-7/17.

12. Physical Plant and Telephone Company Employees

Initially it had been planned to test a group of air frame riveters and mechanics of the Puget Sound area Boeing Company, and initial permission to do so had been obtained. This group was believed to be well suited in most characteristics as a comparison group for the aluminum workers, especially in regard to type of work and socioeconomic characteristics. However, during the summer of 1974 Boeing officials declined participation.

Consideration was then given to other appropriate groups, and permission was obtained to test the Physical Plant Department employees of the University of Washington in Seattle and a small group of General Telephone Company employees from Kirkland, Washington. Several planning meetings with the administrative staff of the University of Washington Physical Plant were held during August 1974. Initial contact with the General Telephone Company administration occurred in October 1975, when it was evident that a small group of additional subjects in the 20 to 30 year age group would be necessary to complete the defined control group.

The same procedure was undertaken in obtaining consent and giving information to the control subjects as had occurred with the aluminum workers. The University Police and the Kirkland General Telephone employees were given the information and completed the consent form immediately before testing, rather than weeks or days before their appointment.

On site testing took place on the following schedule (all dates 1974).

- University of Washington Physical Plant: 9/23-9/27, 9/30-10/4, 10/7, and 10/17-10/18.
- Kirkland General Telephone: 11/7-11/8.

13. Referral to Private Physician

As the test results from each plant became available they were reviewed by one of the investigators (Breitenstein), and early referral of a worker with any significant study finding was made to his designated private physician. This was done by first contacting the worker directly by telephone and then contacting his physician. John Butler, M.D., Professor of Medicine and Head of Respiratory Diseases at the University of Washington Medical School in Seattle agreed to examine any subject with

abnormal tests who had no physician, and to provide consultation on a formal or informal basis to any study subject's physician who so requested it.

14. Test Subject Advised of Results

After all results of each of the tests were completed, a letter was sent to each participant indicating the test results and their significance. Since one of the tests (alpha$_1$ antitrypsin) required two procedures to complete, one in Seattle and one in California, and the chest x-rays required two readings, the final letters (Appendix A) were not sent until December 1974. However, any subject with significant findings had already been notified, usually one to three weeks after the completion of testing, by the early referral method.

B. Definitions of Subgroups and Sampling Procedures

1. Aluminum Worker Classification

The definitions of the potroom workers used in the selection of the aluminum potroom worker study group were as follows.

- Current potroom worker (C): Any currently employed aluminum reduction plant worker who, between November 1, 1972 and November 1, 1973, worked at least five hundred hours (0.25 year) in the potroom.
- New hire potroom worker (N): Any currently employed aluminum reduction worker hired between November 1, 1972 and November 1, 1973, with less than five hundred hours in the potroom.
- Former potroom worker (F): Any aluminum reduction plant worker with a cumulative potroom work history of at least 2,000 hours but less than 500 hours in the potroom between November 1, 1972 and November 1, 1973.

These definitions allowed for stratification and an allocation of sampling such that approximately 80% of the study effort was allocated to current potroom workers and 20% to former potroom workers. In addition

to this allocation, all newly employed potroom workers were included in a major attempt to identify any early effects among them.

Using the worker classifications (C, N, and F) and working with the personnel section of each of the aluminum plants, rosters of each group of workers were identified.* A 25% random sample was selected from each of three age groups (≤ 35, 36-50, and ≥ 51 years) of the identified current and former potroom workers at the Prebake plants (ALCOA Vancouver and ALCOA Wenatchee) and 100% of the new hires were selected.† From the Soderberg process plant (Kaiser Tacoma) it was planned to test 100% of the potroom worker categories.

In addition, a 10% random subsample was selected from the entire aluminum potroom worker sample for the purpose of a pilot evaluation of serum unbound fluoride values.

2. Exposure Levels

In order to identify any dose response relating potroom occupational exposure to adverse health effects that might be detected by the study, exposure levels of High, Medium, and Low were assigned to each aluminum worker, based on his job title as shown in Table 3. Arbitrary numerical values were assigned: 3 for each year of work at a high exposure job, 2 for each year at a medium exposure job, 1 for each year at a low

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*It had initially been planned to test a similar sample fraction at the Kaiser-Mead (Spokane) Prebake plant and a sample was drawn. Testing equipment delays and difficulties in finding testing time suitable to obtain completion of the study within the allotted contract period, plus the determination that we had tested a large enough group of prebake process workers at other plants brought about the decision to delete this group from the study.

†Excluded from the rosters were employees on military, educational, or extended leave. Specifically included were those on sick leave.

Table 3

EXPOSURE LEVEL ASSIGNMENTS

	Job Title or Occupation	
Exposure Level	Prebake Process (ALCOA, Vancouver and ALCOA, Wenatchee)	Soderberg Process (Kaiser, Tacoma)
High	Anode changer, carbon changer, tapper-carbon changer, sweeper operator, craneman with controls, spare man, laborer, and siphon cleaner.	Pot operator, utility man, spare man, anode tender, sweeper operator, and paste tender.
Medium	Pot operator, potman, mechanized cell operator, craneman without controls, pot tender, potroom helper, potroom trainee, pot liner, pot repairer, burner, pot lifter, digging machine operator, pot rebuilder, tapper, and siphoner.	Siphoner, crane operator, mobile equipment operator (MEO), pot rebuilder, pot rebuilder MEO, and supervisor.
Low	Foreman leadman, service man, toolroom personnel, air control personnel, technicians, control, process control checker, maintenance man, welder, electrician, and craftsman.	Service man.

exposure job, and 0 for each year at a job having no potroom exposure. Then, by multiplying the number of years worked at an exposure level times the exposure level number and summing, a single cumulative dose value was assigned to each worker. In making these calculations, less than one-fourth of a year in a dose category was counted as zero. Figure 1 gives the cumulative percentage distribution of dose for the study group.

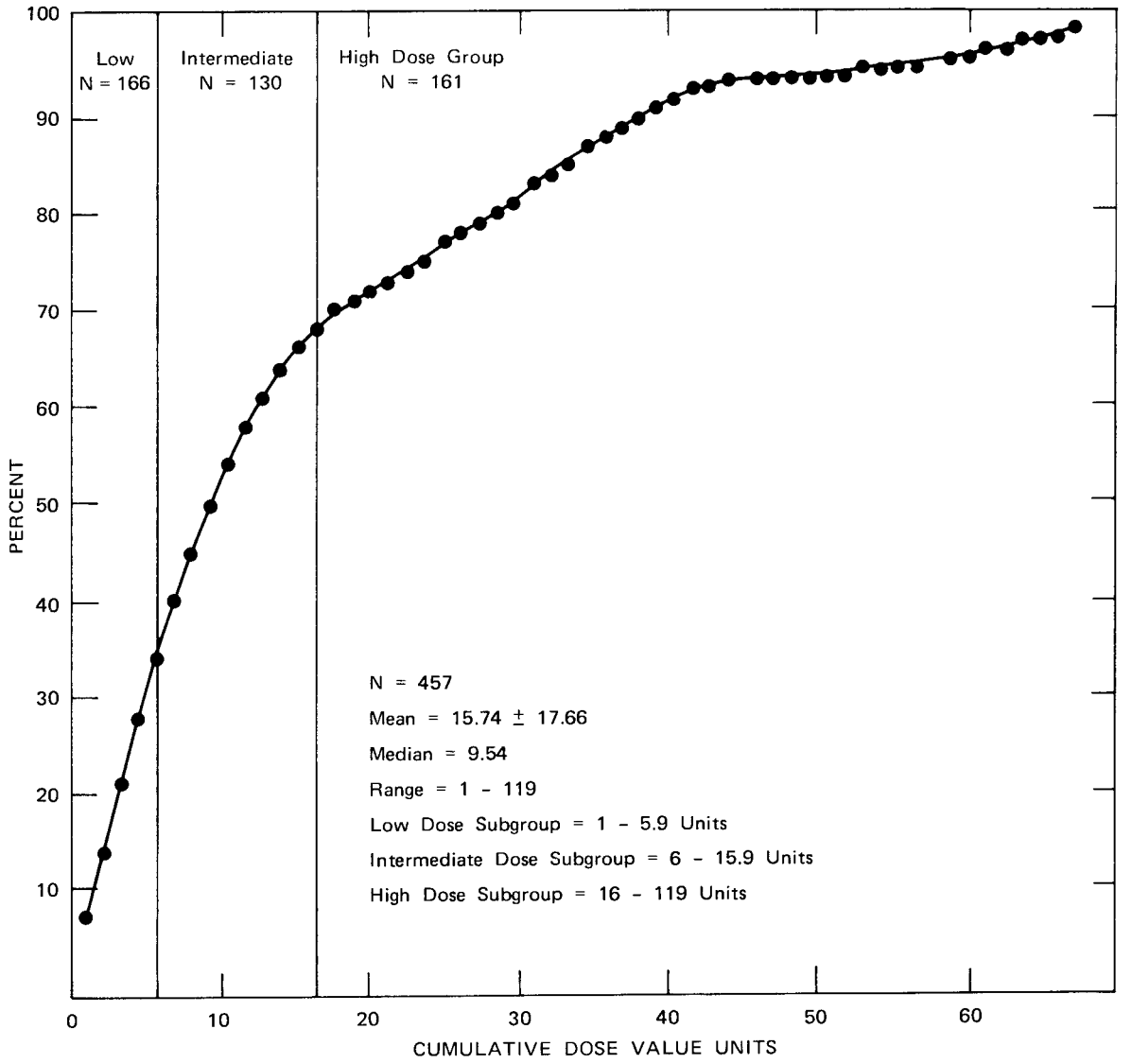


FIGURE 1 CUMULATIVE PERCENTAGE DISTRIBUTION OF STUDY GROUP DOSE VALUES

3. Comparison Group

The comparison group was defined as a sample selected from a universe of male skilled manual laborers of a socioeconomic background similar to the aluminum potroom workers, but who had no significant occupational inhalant exposure. This sample was further refined by matching for age (within two years) and for smoking (same category) on a ratio of 2:1; i.e., two aluminum worker subjects for one control worker subject.

The primary control group selection was made from University of Washington (Seattle) Physical Plan Shop workers. This group met the criteria as defined. There were approximately 400 such workers identified by the University Plant Administrators which in total number was more than adequate for the study design. A 100% sample was selected to be tested from the group. Evaluation of a preliminary age-smoking categorizing questionnaire administered to this entire group indicated an age distribution older than the Aluminum Study Group. To improve matching, the age smoking questionnaire (Appendix E) was administered to the custodian division of the University of Washington and all respondents in this younger age group (35 years and younger) were selected for testing. In addition, the under 36-year-olds from the parking division motor pool and University Police were invited to participate. After completion of the University of Washington phase of testing, a small group of equipment operation and linemen from the General Telephone Company at Kirkland, Washington, under age 31, were tested to allow matching to be completed.

4. Age and Smoking Category Definitions

For the purposes of analysis all tested subjects were placed in three age categories: 35 years and younger, 36 through 50 years, and 51 years and older. The smoking categories were those given in Table 4.

Table 4

LOGIC FOR SMOKING CATEGORIES

Category	Definition
1	Never smoked, or total lifetime consumption has been less than 12 cigars, 12 pipefuls, or 400 cigarettes.
2	All exclusively current and former cigar and/or pipe smokers, regardless of quantity, and current or former cigarette smokers with a total consumption of less than ten pack years.*
3	Former cigarette smokers who have smoked equal to or more than ten pack years, but less than 39 pack years.
4	Former cigarette smokers who have smoked equal to or more than 39 pack years.
5	Current cigarette smokers who have smoked equal to or more than ten pack years, but less than 39 pack years.
6	Current cigarette smokers who have smoked equal to or more than 39 pack years.

Note: For individuals who smoked combinations of cigarettes, cigars, and/or pipes, the category designation was based on cigarette consumption.

*One pack year is one package (20 cigarettes) per day for one year, or a variant thereof with the same total (e.g., two packages per day for six months).

5. Matching

A roster of the aluminum study group and the control group subjects was arranged by age and smoking category. Two aluminum study subjects were matched with one control subject--excpet for one aluminum

subject who was matched with one control subject since there was an uneven number (457) in the aluminum group. The matching was done as close to the exact age as possible and extended no further than two years on either side of the age except in the few cases enumerated below. The same smoking category was matched in almost all cases except as noted below. In all, 228 control subjects were matched with 457 aluminum workers.

When more than one possible choice was available from the controls, controls from the physical plant shops were given preference since they were the primary group selected as a comparison group. The selection was made in a random fashion from a list of identification numbers with no knowledge of individuals by name or testing results. The matches that did not exactly meet the matching specifications were:

- Twenty control subjects, who were matched within in the specified age range, were category 1 smokers matched with aluminum workers in category 2. (This occurred in the 21 through 36 age range only.)
- One control subject, who was matched within the specified age range, was a category 3 smoker matched with a category 4 aluminum worker.
- One 29-year old smoking category 1 control subject was matched with a 23-year old smoking category 2 aluminum worker.
- One 50-year old smoking category 1 control subject was matched with a 46-year old smoking category 2 aluminum worker.

Table 5 shows the percentage distribution of the study group and the control group by smoking history and age. The youngest age strata (under age 36) contained 59% and 57% of the study group and control group, respectively. Workers over the age of 50 years accounted for about 19% of both groups. Smoking below the lowest cutoffs (defined in Table 4) was reported in 14% of the study group and 19% of the controls.

Current smoking and former smoking histories documented to be at least ten pack-years was reported among 35% and 17% for the study group, and among 32% and 19% for the control group, respectively.

Table 5

STUDY GROUP AND CONTROL GROUP BY AGE STRATA AND SMOKING HISTORY CATEGORY

Smoking Category	Age Strata (years) ≤ 35	36-50	≥ 51	Total (all ages)
1	10.3%/15.0%*	2.4%/2.6%	1.5%/1.3%	14.3%/18.9%
2	27.2%/24.2%	3.7%/3.5%	3.1%/2.6%	34.0%/30.4%
3 or 4	3.1%/3.1%	4.8%/6.2%	9.0%/9.7%	16.9%/18.9%
5 or 6	18.6%/14.5%	11.2%/12.3%	5.0%/4.9%	34.9%/31.7%
Total	59.2%/56.8%	22.2%/24.7%	18.6%/18.5%	100%/100%

*The entry 10.3%/15.0% means that 47 of 457 (10.3%) Study Group workers and 34 of 228 (15.0%) Control Group workers were less than 36 years of age and were in smoking category 1.

Tables 6 and 7 show other comparisons between the matched groups. The Soderberg study group and their matched controls had an average of about 33 years; whereas, the Prebake group averaged five years older. The average exposure rating (see pages 19-21) was seven dose units (exposure level x years) greater for the Prebake workers than for the Soderberg workers. The Prebake workers were slightly taller than all other groups; and the Prebake controls were somewhat smaller in weight compared with all other groups. The combined study group heights

Table 6

STUDY GROUP SUBDIVISIONS AND CONTROL GROUP
SUBDIVISIONS BY SELECTED CHARACTERISTICS

	Soderberg		Prebake	
	Study Group	Control Group	Study Group	Control Group
Number of workers tested	183	91	274	137
Mean age (years)	33.3 ± 0.7	33.5 ± 0.7	37.6 ± 0.8	37.8 ± 0.8
Potroom status (number of workers)				
Current	130	65	178	69
Former	37	18	27	13
New hires	16	8	69	35
Exposure rating	11.8 ± 0.7	0	18.4 ± 1.3	0
Mean height (inches)	70.4 ± 0.2	70.2 ± 0.2	70.8 ± 0.2	70.4 ± 0.2
Mean weight (pounds)	180.7 ± 2.0	180.7 ± 2.0	181.5 ± 1.4	174.8 ± 1.5

Table 7

COMPARISON OF STUDY GROUP AND CONTROL GROUP BY SELECTED CHARACTERISTICS

	Study Group	Control Group
Mean age (years)	35.9 ± 0.6	36.1 ± 0.8
Mean weight (pounds)	181.2 ± 1.14	177.2 ± 1.67
Hypertension (proportion)	0.02	0.04
Mean height (inches)	70.7 ± 0.12	70.3 ± 0.21
Mean education (years)	11.7 ± 0.09	13.0 ± 0.14
Race (proportion)		
Black	0.07	0.06
Chicano	0.01	0.02
Oriental	0.00	0.01
White	0.91	0.87
Other	0.00	0.02
Unknown	0.01	0.02
Marital status (proportion)		
Single	0.10	0.21
Married	0.85	0.68
Widowed	0.00	0.02
Separated	0.00	0.03
Divorced	0.04	0.05
Unknown	0.00	0.02
Past work history by industry (proportion)		
Coal mining	0.02	0.01
Other mining	0.04	0.02
Quarrying	0.02	0.04
Foundry	0.07	0.08
Pottery	0.004	0.04
Cotton, flax, hemp	0.02	0.01
Other dusty trade	0.27	0.50
Past work history by exposure (proportion)		
Welding	0.15	0.38
Asbestos	0.02	0.13
Beryllium	0.004	0.00
Cadmium	0.01	0.03
Chromic acid mist	0.004	0.01
Epoxy resin	0.04	0.12
Fiberglass	0.06	0.17
Other selected chemical	0.13	0.47

and weights reflected these subdivision differences: the study group was slightly heavier (about four pounds) and taller (about one centimeter).

The mean education level was higher for the controls, more were single or were in other unmarried categories, and there was a trend toward more nonwhites among the controls. A past work history of foundry work accounted for the most common industry group, with significant inhalant exposure accounting for 7% of the study group and 8% of the controls. Mining appeared to be slightly more common among study group workers, but pottery and quarrying work were even more of a trend in the opposite direction. Likewise welding, asbestos, epoxy, and fiberglass work, and a variety of chemical exposure jobs, were all more common among the controls. It should be noted that accumulated inhalant exposure was not quantified, and the study group had a mean dose of almost 16 units in potrooms.

In summary, the matching process was successful for most characteristics but some minor differences were noted in educational level, racial status, marital status, and past work exposures.

C. Testing Procedures, Equipment, and Materials

1. General

The field testing was undertaken in two mobile laboratory trailers. The smaller trailer, 20 feet in length, was used principally as an office to meet the study subjects, obtain height, weight, blood pressure, and administer the questionnaire. In addition, it provided a resting place for the testing technicians when subjects were not being tested, and for cleaning equipment. The second trailer was 30 feet long and contained x-ray equipment (inspected and approved by the University of Washington Radiation Safety Officer), pulmonary function equipment, and areas for collection of sputum and blood. Both trailers were equipped with propane furnaces and air conditioning so that comfortable testing

conditions could be maintained in any weather. The trailers were parked adjacent to each other in a convenient location at each testing site, where the test subjects had easy walking access from their places of work and where electric power, water, and drainage facilities were available.

Under optimal testing conditions, three subjects to be tested would arrive together at trailers each hour of scheduled testing. After identifying the individuals and obtaining their questionnaire folders that had been prepared in advance, height in inches and weight in pounds was measured, and blood pressure obtained. These measurements, along with age, were recorded on a previously prepared card that identified the subject by name and by assigned study number and to which were attached labels with the study number to be used to identify the specimens and data obtained during the testing procedure (see Appendix D). After the initial procedures were completed, one subject was directed to one of the three testing areas, which were:

- Questionnaire by interview
- Pulmonary function tests
- X-ray, blood, and sputum collection.

Since each area required approximately 12 to 15 minutes to complete, the test subjects were rotated, usually with very little waiting. The entire procedure required 35 to 45 minutes.

2. Questionnaire

The format of the questionnaire (see Appendix E) was a precoded form except for Section 1, which was the assurance of confidentiality, consent to participate, and authorization to release medical information. Section 2 contained identification data including date of interview, interviewer number, name, address and telephone number of subject, assigned worker classification, age, sex, race, marital status, education,

height, weight, and blood pressure. Section 3 contained relevant past work history relating to specific occupational exposures that have a known potential for respiratory disease. Section 4 (for the aluminum study group only) contained a dosage exposure estimate. Also included in this section was an estimate of respirator usage at the aluminum plant by the subject. Section 5 listed the last four hospitalizations that the subject might have had, particularly with reference to respiratory disease admissions; the year of the hospitalization; a subject-supplied "diagnosis," which was coded (see Appendix F); and estimated length of stay. Section 6 was the current respiratory history, which ascertained the frequency and severity of cough, phlegm, wheeze, and dyspnea based on the breathmobile questionnaire format.[22] Section 7 obtained information on specific previously diagnosed respiratory diseases in the subject and in his closest relatives with specific questions about asthma, emphysema, acute and chronic bronchitis, pneumonia, pulmonary tuberculosis, sinusitis, and lung tumor. In addition, questions about cancer, heart attack, and high blood pressure were asked. Section 8 obtained a tabacco smoking history from which the subject could be categorized as to smoking habits into the previously described six-way classification. After the interview was over, the questionnaire was checked for completeness and given to data personnel for further processing.

3. Spirometry

Equipment used for measuring the forced expiratory spirometry included the following component parts of the electronic spirometry system:

- Ohio 840 spirometer.
- Tektronics 601 storage display scope.
- Bell and Howell datagraph 5-134.
- Beckman DRS 1000 digicorder with A-D converter and nine-track tape recorder.
- Electro/Med 780 calibrating spirometer.

This test entailed a flow/volume measurement of the subject's forced exhalation on separate trials. A technician entered the subject's height, weight, age, sex (male), and the ambient temperature; the test site location and its altitude above sea level; and a technician identification number by digital code into the Beckman DRS 1000 digicorder. The technician instructed each subject in the performance of the forced expiratory maneuver, and encouraged him to obtain a maximal effort in rapid exhalation into the spirometer. A nose clip was not used with this test, and the subject was tested in a standing position. Cigarette smoking was discouraged for a minimum of five minutes before the test. Five trials were attempted by each subject, and the technician made every effort to obtain two maximum trials within 10% of each other as displayed as a flow volume loop on the storage display scope. Additional trials were obtained, as necessary, to obtain maximum performance by each subject.

The flow and volume signals from the transducers of the electronic spirometer were simultaneously recorded on light sensitive paper of the datagraph, and the volume signal was digitized and recorded on the digital nine-track tape. The datagraph recording was primarily used as a backup to obtain forced expiratory volume at one second (FEV_1) and forced vital capacity (FVC) when the digital tape system was not functioning. All tape recordings were on 1/2-inch wide magnetic tape with a nine-track data format at 800 bits per inch (BPI) using the IBM NRZI system.

Calibration of this equipment was performed using four signals:

(1) Electronic-millivolt--A one-millivolt signal was generated within the Beckman digicorder and recorded directly on the nine-track tape.

(2) Electronic-volt--Electronic signals of 1, 3, and 6 volts, respectively, generated within the Ohio 840 spirometer, were recorded on the nine-track tape.

(3) Mechanical-pump--Five liters of air were mechanically pumped over three seconds in and out of the 840 spirometer by the motor drive of the electro/med 790 calibrating spirometer. This volume change was recorded on the datagraph and on the nine-track tape.

(4) Mechanical-secondary source--Displacement of air using a calibrated one-liter syringe or a Collins spirometer was pushed into the 840 spirometer. The volume was recorded on the datagraph and the nine-track tape.

Calibrations were made by the following protocol:

- Both electronic signals (1 and 2) before each test subject.
- Both electronic signals and the mechanical-pump (1, 2, and 3) at the beginning of each test day.
- Both electronic signals and the mechanical-pump at each new location.
- Mechanical-secondary source (4) approximately every four months.

4. Closing Volume

The equipment and materials for making the closing volume determination included:

- Ohio 840 spirometer reservoir for 100% oxygen
- Ohio 700 nitrogen analyzer and sampler head
- Ohio x-y recorder with pen stylus and chart paper
- Triplett 626 flowmeter
- Sargent-Welch 8805 vacuum pump
- Victor two-stage gas regulator
- One-hundred percent oxygen.

The subject was seated on an adjustable stool and during the test had an air occlusive noise-clip in place and a rubber mouthpiece that fit inside the mouth for a tight lip seal. Each subject's test result was recorded

on calibrated paper on the x-y recorder, which indicated nitrogen percentage on the y axis and volume of air on the x axis. At the beginning of each trial the 0% and 80% (or recorded ambient air) nitrogen concentration were marked on the record. The Ohio 840 spirometer, which acted as a reservoir for 100% oxygen, was filled after several oxygen flushing maneuvers through a three-way valve. The subject then breathed room air in and out in a normal manner through the nitrogen concentration sampler attached to the three-way valve. When end-tidal nitrogen concentration approached 80% on the x-y recorder, the subject was asked to breathe out to residual volume (RV). The valve was then turned to connect him with the oxygen containing spirometer, the recording marker on the x-y recorder was activated on the plotting paper, and the subject was instructed to breathe the oxygen in to total lung capacity (TLC). This point (TLC) was determined by observing no further movement of the recording marker on the x-y plot. No attempt to control inspiratory flow was made, and the oxygen was usually taken in over one or two seconds. When the subject was at TLC, he was asked to begin exhaling at a rate of approximately 0.4 liters per second, which was controlled by the subject observing his exhalation flow visually on the Triplett 626 flow meter dial. Any trial in which this flow rate exceeded 0.5 liters per second was voided by the technician. The exhalation continued until the subject again reached RV, after which the subject had the mouthpiece removed and was given a short rest while the equipment was readied for the next trial. Each subject had a minimum of three acceptable trials, with additional trials as needed when trials were voided for technical or testing reasons.

Calibrations of the equipment included:

- Periodic calibration of the spirometer with a one-liter syringe to assure accuracy on the x axis of the x-y recorder.

- Periodic calibration of the nitrogen analyzer using precision gases containing 0%, 5%, 40%, and 80% nitrogen concentration.
- Daily checking of 0% nitrogen concentration and room air (80%) nitrogen concentration.

5. Chest X-ray

The following equipment was used for the x-rays:

- General Electric CMS 110 with tube 11DB4/HRT 1.0, 2.0, and a Videx 10945-11 collimator.
- Kodak 90-second X-omat developer.

A single posterior-anterior chest x-ray was obtained on each subject using appropriate coning and filtration along with a gonad shield for subject protection. The x-rays were developed by the radiology technician at the University of Washington Medical School Hospital Radiology Department. The films were delivered for initial reading to Melvin Figley, M.D., professor and Chairman of the Radiology Department. Repeat x-rays were obtained, whenever possible, when technically unsatisfactory films were reported. In addition, 31 films were obtained from the medical departments of one of the aluminum plants or the Health Service of the University of Washington on those subjects who had an unsatisfactory x-ray and where repeat test in the trailer could not be scheduled.

6. Sputum Cytology

The equipment and materials used for the sputum cytology tests were:

- Mistogen En 145 electronic ultrasonic nebulizer.
- Five percent propylene glycol in sterile water as nebulizing solution.

- Preservative solution of 2% propylene glycol and 48% ethanol.
- Eight-ounce plastic sputum jars with lids.

The subject breathed through the mouthpiece attached by a flexible plastic tube to the nebulizer. The mist was generated at a rate of six ml per minute. Inhalation was performed in a small room in the larger testing trailer with an exhaust fan to the outside. The subject was instructed to expectorate any material coughed up during the course of the mist inhalation or immediately afterward into the sputum jar. The duration of the mist inhalation was approximately three minutes as determined by a mechanical timing device. In the event of a scanty production, the mist inhalation was continued a few minutes longer and/or the subject was encouraged in voluntary hard coughing. Most subjects could obtain some specimen by this technique. Approximately 15 to 30 cc of preservative solution was added to the sputum jar at the conclusion of the test. The sputum sample was processed at the University of Washington Harborview Hospital Cytology Laboratory. See Appendix G for details of processing.

7. Serum $Alpha_1$ Antitrypsin

The equipment and materials for the $alpha_1$ antitrypsin test included those used for venipuncture and an IEC centrifuge. Using standard sterile technique with the subject supine, approximately 14 ml of venous blood was removed from an antecubital vein. After completion of the venipuncture, the subject applied direct hand pressure over the puncture site through a cotton pledget for a few minutes to reduce the possibility of hematoma formation. After this time a bandaid was applied to the venipuncture site.

The blood was allowed to clot and was centrifuged. The serum was transferred in equal proportions to two plastic vials, which were sealed with plastic caps. The serum was frozen on the same day, usually within a few hours. Dry ice in a styrofoam ice chest was used when necessary to maintain the specimens in a frozen condition. The two vials were delivered to a freezer at the University of Washington Medical School Hospital laboratory for initial processing. See Appendix H for processing details.

8. Urine and Serum Unbound Fluoride

The equipment for this test was the same as described in paragraph 7 above plus a fluoride ion specific electrode and a PH meter.

All urine fluoride samples were collected with the aluminum worker off work for at least 24 hours. Since it was not possible to accomplish this complicated schedule during the testing stays at each aluminum plant, arrangements were made to have this urine test done through the medical departments at each plant. A clean voided specimen was then analyzed for fluoride content. The specific gravity of each specimen was obtained and the fluoride result adjusted to a specific gravity of 1.024. See Appendix I for processing details.

A 10% subsample of the aluminum workers had a serum unbound fluoride test performed. Since it seemed important to correlate the urine fluoride value with the serum unbound fluoride value, the blood specimen for this subsample was obtained in the medical department of the aluminum company at the same time as the urine specimen for fluoride analysis. The serum was frozen and transported to the University of Washington for further processing in the Chemistry Laboratory of the Department of Environmental Health. Appendix I gives detailed methods.

D. Data Processing and Interpretation

1. Questionnaire

After keypunching, the data on the cards were listed on sheets for a review and a quality check. Any necessary corrections or additions were made on cards. The data cards were then delivered to the School of Public Health and Community Medicine computer center to be entered into the study file program.

The respiratory symptomatology categories we used are shown in Table 8. They are patterned after the Breathmobile Project Questionnaire,[22] and use the same categories of major and minor symptoms. The Breathmobile Project question quantified the number of years of phlegm production was inadvertently omitted from our questionnaire, so that persons with only one year of 50 days of phlegm production were categorized in our study as having a major symptom, and therefore the major results tend to be over estimated in comparison with the Breathmobile data.

A subject was classified as having chronic respiratory disease if he had one or more major respiratory symptoms and an FEV_1 and/or FVC less than 1.645 deviation units below predicted values[22] for his age and height.

2. Forced Expiratory Spirometry

The spirometry tapes were evaluated by a computer program that not only assembled the spirometric data, but selected the best trial effort and gave an interpretation category for FEV_1, FVC (normal, borderline, and abnormal), and a reliability code.[22] Although data for peak flow and flows at 50% and 75% of FVC were determined, no analysis is reported at this time. Some tapes had minor input errors and required special transcribing before they could be used. Other spirometry tapes were technically unsatisfactory, and in such instances, the datagraph

Table 8

CRITERIA USED IN ESTABLISHING MAJOR AND MINOR RESPIRATORY DISEASE SYMPTOMATOLOGY CATEGORIES

Major Symptomatology Category

- Morning cough 50 or more days during the past year and a duration of more than one year.
- Sputum production (in the morning or later in the day) on 50 or more days during the past year.
- More than one period of increased cough and sputum lasting for three weeks or more during the past three years.
- Wheezing or nonexertional attacks of dyspnea occurring 50 or more times during the past year.
- Dyspnea while walking on level ground with person of own age or while walking on level ground at own pace.

Minor Symptomatology Category

- Morning cough either less than 50 days during the past year or of a duration of one year or less.
- Sputum production (in the morning or later in the day) less than 50 days during the past year.
- One period of increased cough and sputum lasting for three weeks or more during the past year.
- Wheezing or nonexertional attacks of dyspnea occurring less than 50 times during the past year.
- Dyspnea while hurrying on level ground or walking up slight hill, but not while walking on level ground with person of own age or at own pace.

printout was measured for all trials. These measurements were keypunched and analyzed on a "back-up" program that gave the same output format as was obtained from the tape data for FEV_1 and FVC. The spirometry results from both tape and datagraph were then keypunched, quality checked, and put into the computer file. Appendix J is the classification scheme.

3. Closing Volume

The closing volume determinations were made following the "Suggested Standardizations Procedures for Closing Volumes (nitrogen method)" distributed by The Division of Lung Diseases of the National Heart and Lung Institute. Two percentage values, closing volume divided by vital capacity (CV/VC%) and closing capacity divided by total lung capacity (CC/TLC%) were calculated for each of the three trials, and interpretation was made for the best trial effort for the two values, using prediction equations[23] and cut-offs for normal, borderline, and abnormal. When a subject was abnormal on CV/VC he was considered as having a Type 2 abnormality, and when he was abnormal on CC/TLC he was considered as having a Type 1 abnormality. These results were then keypunched and prepared for analysis. Appendix K is the classification scheme.

4. Chest X-ray

The chest x-rays were read independently by two radiologists who were not aware of which x-rays were from the study group and which were from the control group. Any film in which there was a significant difference in interpretation was reviewed by the radiologists a second time for the purpose of reaching a consensus.

In categorizing the chest x-rays two separate classifications were made, as outlined in Table 9. Multiple findings were recorded in the data set. The first classification (0 to 8) was related principally

to current respiratory disease, and the second classification related to noncurrent pulmonary conditions and nonpulmonary conditions. This information was then keypunched for inclusion in the analysis.

Table 9

CHEST X-RAY CLASSIFICATION

Current respiratory disease condition

0. No significant current respiratory disease abnormality
1. Nontuberculosis infiltrate
2. Lymphadenopathy
3. Emphysema, bullous
4. Emphysema, obstructive
5. Suspect TBC
6. Suspect lung carcinoma
7. Suspect chronic bronchitis
8. Other--e.g., prominent right hilum

Other x-ray finding

10. No other abnormality
12. Calcified hilar or paratracheal nodes
13. Calcified lung foci, nodule(s), gramloma
14. Pleural scarring, thickening or calcification (other than apical)
15. Apical scarring or thickening
16. Diaphragm variant or elevation
17. Scoliosis
18. Cardiomegaly
19. Vascular abnormality--e.g., widening of aorta, anomaly of aortic arch
20. Aortic arteriosclerosis
21. Rib anomaly or fracture evidence
22. Azygos lobe or variant
23. Other--e.g., gynecomastia, previous surgery, thyroid mass, prominent cardiac fat pad, obesity
30. No film
31. Unsatisfactory film

5. Sputum

The sputum results were classified as negative, atypical, suspicious, positive, and unsatisfactory. It was necessary to identify two pulmonary macrophages in each specimen in order to be acceptable for interpretation and classification. Appendix G gives the classification.

6. Serum Alpha$_1$ Antitrypsin, Serum Trysin Inhibitory Capacity, and Phenotyping

Serum, which had been separated from blood by centrifuging in the field and freezing in two separate serum vials, was delivered to the University of Washington Medical School Clinical Laboratories. The determination of serum alpha$_1$ antitrypsin by radial-immunodiffusion technique was made. Initially only specimens with values lower than 200 mg% were sent to the City of Hope, Duarte, California for phenotyping; however, some discrepancy was noted between the serum alpha$_1$ antitrypsin results by radial immunodiffusion performed at the University of Washington and serum trypsin inhibitory capacity (STIC), which measured the same phenomenon, performed at the City of Hope, Duarte, California. A normal STIC value of greater than 1 unit was considered normal. It was elected to examine all of the specimens by both techniques and to do phenotypes on only those with STIC values equal to or less than 1 unit.

7. Urine Fluoride Values

Urine fluoride values in mg/liter (ppm) were keypunched after correcting all the values to a specific gravity of 1.024. The results of the serum fluoride performed only on a subsample (approximately 10%) were recorded in mg%.

IV RESULTS

The prevalence of respiratory symptoms did not differ between the study group and the control group. Figure 2 shows the comparisons of prevalence rates for the study group versus the control group by plant process. The prevalence rates were examined using four cutoffs: (1) workers with major cough and major phlegm ("chronic bronchitis"), (2) with two or more major symptoms, (3) with one or more major symptoms, and (4) with one or more major or minor symptoms. The principal cutoff used in our definition of CRD prevalence was (3); this prevalence rate was examined in detail for significant differences among workers in three exposure dose subgroups and the three worker classification subgroups (see Figure 1 and page 18, respectively).

The ratio of prevalence rates for the intermediate dose group was 46.2%/41.5%, or 1.11, very similar to the values for the entire study group compared to the entire control group. The specific rates for a given study subgroup cannot be compared with another study subgroup because the age and smoking characteristics are different. The ratio comparisons between study and control groups shown in Table 10 are not statistically significant, and no consistent trend is apparent, such as significantly larger ratios for high exposure groups or former potroom workers. The high exposure group was also compared with the remainder of the study group, controlling for age and smoking history and using successive cutoffs of 1, 2, 3, and 4 or more major symptoms. No differences were observed, as shown in Figure 3.

The prevalence of abnormal spirometry was examined using two ventilatory parameters (FEV_1 and FVC) and two cutoffs ($<1\%$ and $<5\%$), as

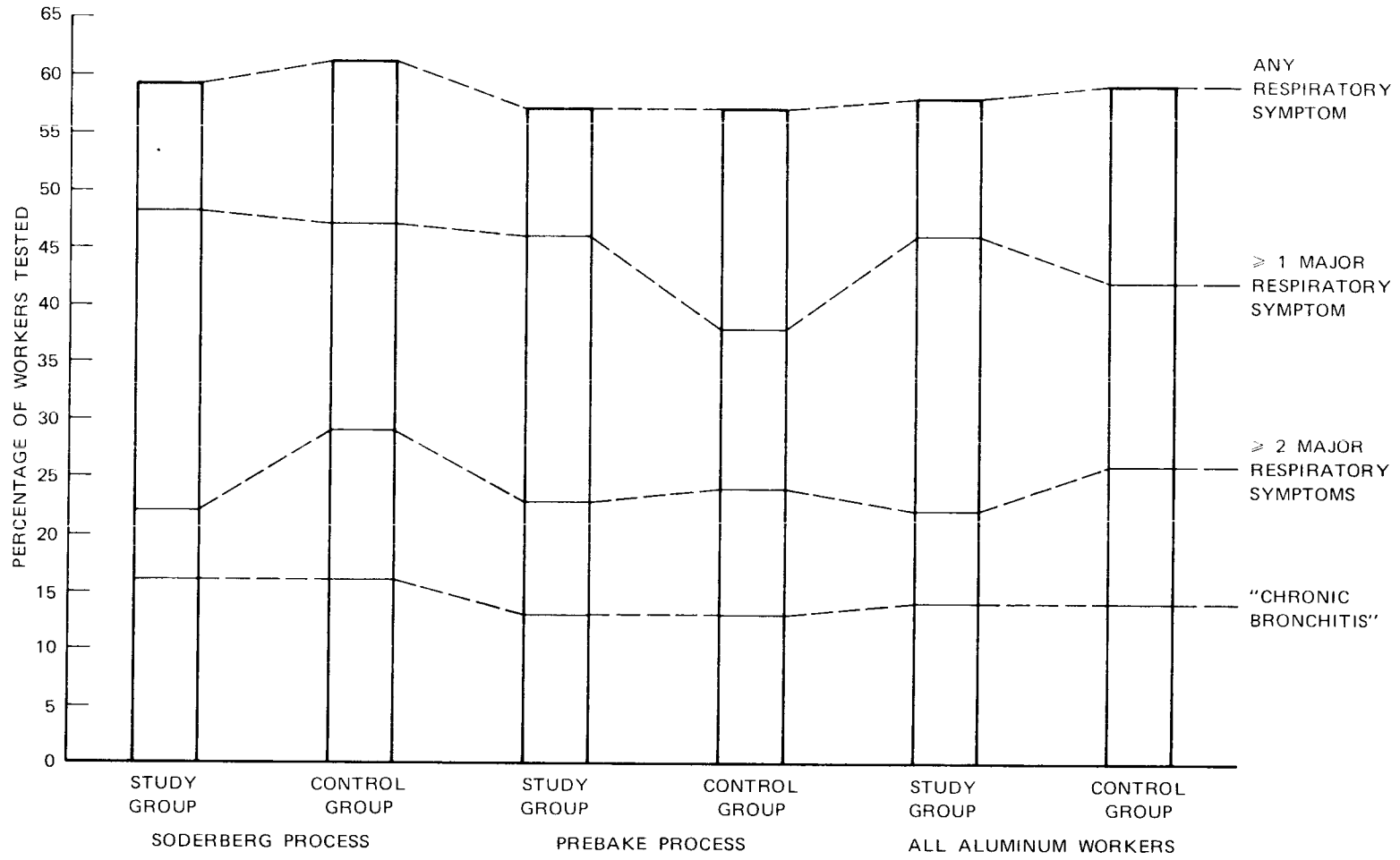


FIGURE 2 RESPIRATORY SYMPTOM CATEGORIES BY GROUP: SODERBERG, PREBAKE, AND ALL ALUMINUM

Table 10

FREQUENCY OF ONE OR MORE MAJOR RESPIRATORY SYMPTOMS FOR DOSE AND WORKER CLASSIFICATION SUBGROUPS

		Exposure Level			Worker Classification		
	Total Groups	Low Dose Group	Intermediate Dose Group	High Dose Group	Current	Former	New Hire
Study Group (SG)	212/457 (46.4%)	81/166 (48.8%)	60/130 (46.2%)	71/161 (44.1%)	169/308 (54.9%)	25/64 (39.1%)	18/85 (21.2%)
Control Group (CG)	95/228 (41.7%)	31/83 (37.3%)	27/65 (41.5%)	37/81 (45.7%)	79/154 (51.3%)	10/32 (31.3%)	6/43 (14.0%)
Ratio (SG/CG)	1.11	1.31	1.11	0.96	1.07	1.25	1.51

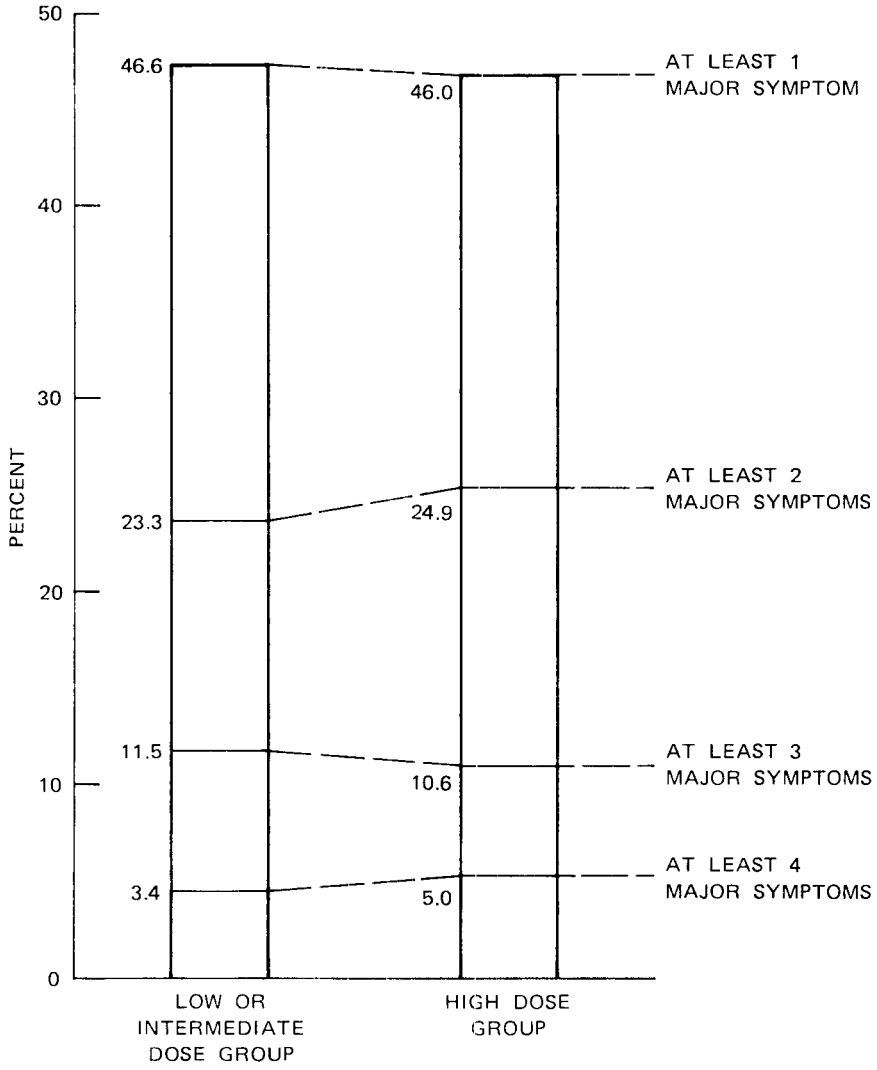
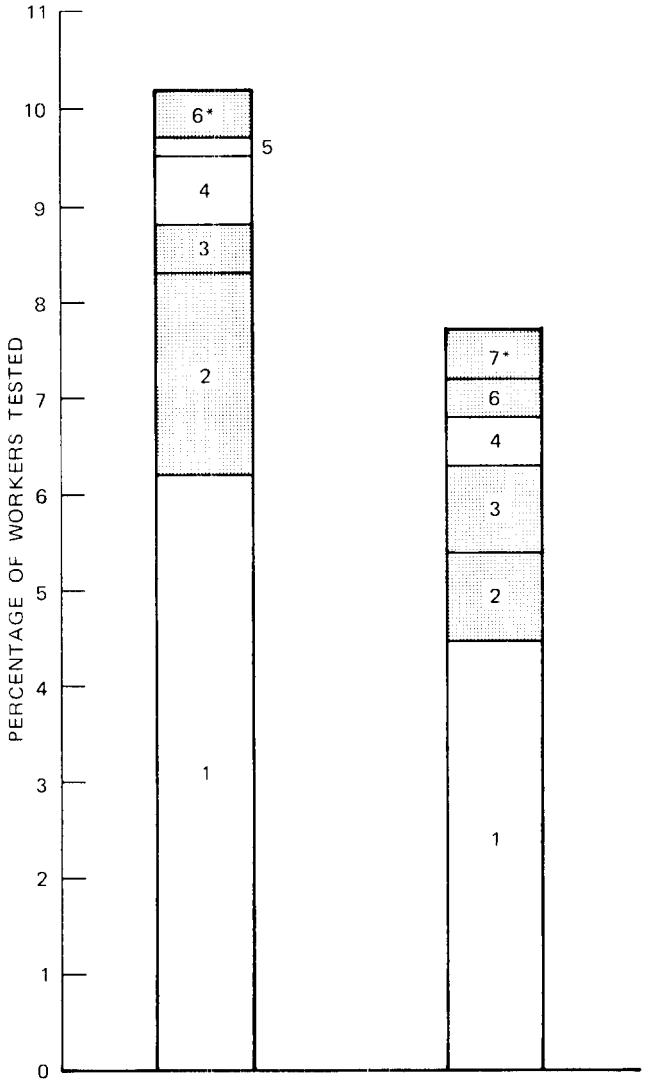


FIGURE 3 PERCENTAGE FREQUENCY OF MAJOR SYMPTOMS FOR HIGH DOSE GROUP COMPARED WITH THE REMAINDER OF THE STUDY GROUP

indicated in Appendix J. The prevalence for the eight possible combinations of these spirometry abnormalities is shown in Figure 4. No significant differences were observed between the study group and the control group. (The frequency of either the FEV_1 or the FVC being below the 1% cutoff is demarcated in Figure 4.) The prevalence ratio, using as the basis that either parameter or both were below the 5% cutoff, was 1.28 for the entire study group compared with the matched control; moreover, the ratios were 1.26 and 1.34 for the Soderberg process and Prebake process groups, respectively. The ratios for FEV_1 below the 5% cutoff were also studied for the three dose groups by process group, and the ratios were near unity for all groups except for the high dose group where it was 1.47 for the Soderberg group and 1.54 for the Prebake group. None of these ratios were significant. The effect of exposure level and worker classification were also examined by making t-test comparisons of means of absolute liter values and deviation units for various subgroups.

In Table 11 both liter differences and deviation unit differences between study group and matched control groups, and their subgroups for exposure level and worker category, are compared. The deviation unit values for FEV_1 and FVC are plotted in Figure 5. For the entire study and control groups, the FVC and deviation FVC differences were statistically significant; the study group values were significantly larger for the study group. No statistical significance was found for $FEV_{1.0}$ differences except for the former potroom workers who had lower mean deviation values compared with their matched controls. This same subgroup comparison showed no significant mean difference in FVC deviation units (i.e., the mean value for study group former potroom workers was 0.337 units above predicted values, whereas the mean value for their age-smoking matched controls was 0.348 units above predicated values, controlling for age and height). For both current and new hire groups, the deviation FVC values were statistically significant in favor of the potroom workers.



*Coded as follows:

		FVC		
		NORMAL	1% TO 5%	<1%
FEV_1	NORMAL	–	5	8
	1% TO 5%	1	4	7
	<1%	2	3	6

FIGURE 4 ABNORMAL SPIROMETRY CATEGORIES BY GROUP: ALL ALUMINUM WORKERS

Table 11

SPIROMETRY MEASUREMENTS BY DOSE AND WORKER CLASSIFICATION SUBGROUPS
(Milliters, Mean Value ± Standard Error)

Group	$FEV_{1.0}$		FVC	
	Measured	Deviation from Predicted*	Measured	Deviation from Predicted*
Study group	4053 ± 42.5	-0.099 ± 0.061	5215 ± 45.0	+0.415 ± 0.052
Control group	4053 ± 53.6	+0.003 ± 0.075	5044 ± 59.6	+0.242 ± 0.063
Low dose				
Study group	4453 ± 56.6	+0.184 ± 0.080	5601 + 69.0	+0.577 ± 0.088
Control group	4390 ± 55.7	+0.222 ± 0.084	5407 ± 65.4	+0.452 ± 0.073
Intermediate dose				
Study group	4080 ± 79.2	-0.155 + 0.119	5210 ± 76.4	+0.386 ± 0.095
Control group	4123 ± 67.2	+0.050 ± 0.098	5080 ± 77.6	+0.220 ± 0.083
High Dose				
Study group	3617 ± 69.7	-0.346 ± 0.106	4824 ± 75.0	+0.272 ± 0.087
Control group	3645 ± 59.4	-0.264 ± 0.091	4635 ± 62.8	+0.040 ± 0.071
Current				
Study group	4002 ± 47.5	-0.109 ± 0.070	5161 ± 50.6	+0.386 ± 0.059
Control group	4011 ± 43.8	-0.044 ± 0.063	5000 ± 48.5	+0.200 ± 0.051
Former				
Study group	3987 ± 129.5	-0.289 ± 0.170	5119 ± 115.9	+0.337 ± 0.130
Control group	3986 ± 93.3	+0.060 ± 0.126	5007 ± 104.4	+0.348 ± 0.108
New Hire				
Study group	4606 ± 99.1	+0.290 ± 0.162	5846 ± 145.3	+0.787 ± 0.185
Control group	4530 ± 98.0	+0.327 ± 0.151	5488 ± 123.1	+0.443 ± 0.141

*Minus sign designates below predicted, and plus sign designates above predicted values.

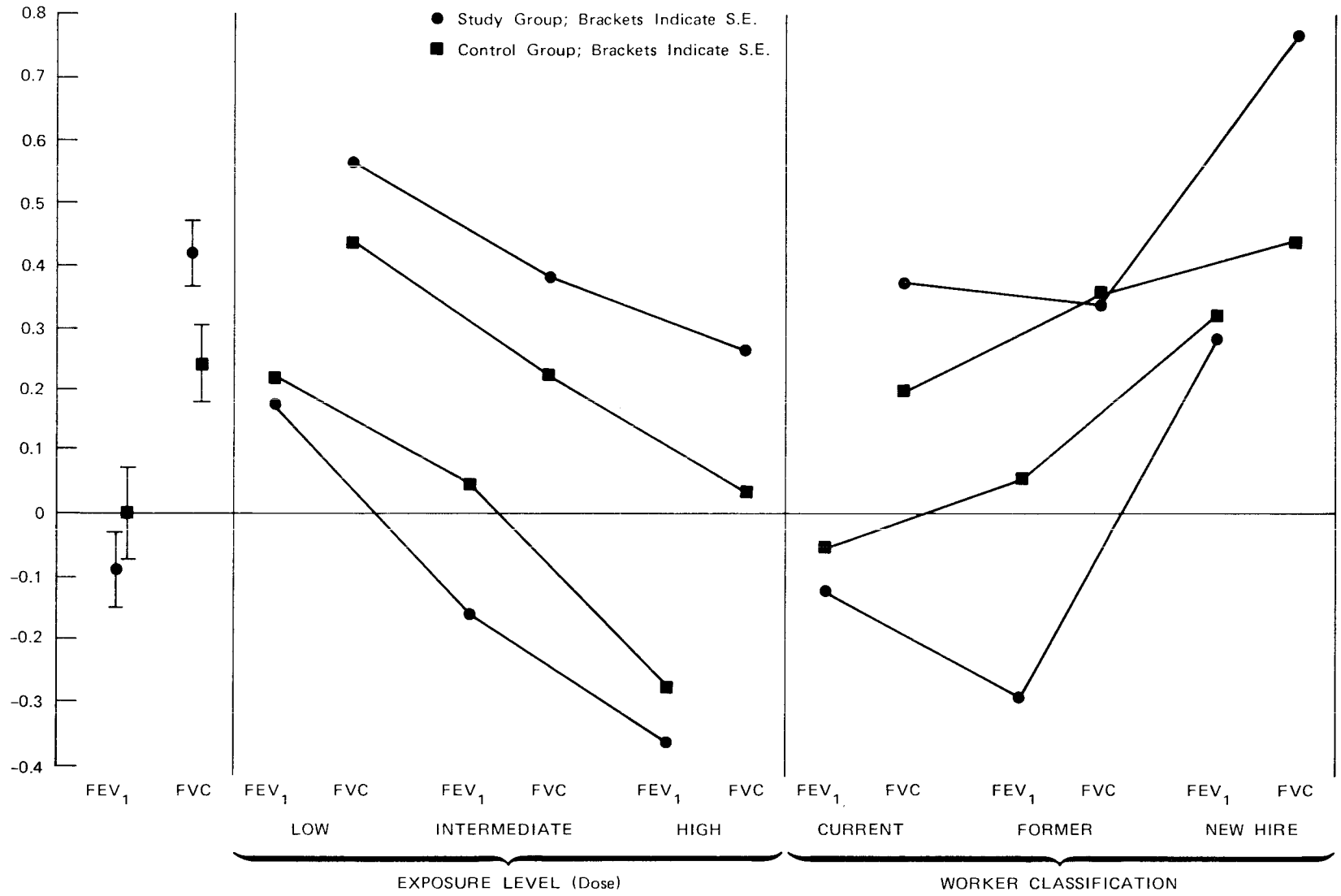


FIGURE 5 MEAN DEVIATIONS FROM PREDICTED SPIROMETRY VALUES FOR DOSE AND WORKER CLASSIFICATION SUBGROUPS

The trend is for higher exposure level subgroups to have a relatively higher FVC compared with lower dose groups when controlling for smoking, as shown in Figure 5; however, this trend was not statistically significant. In summary, the only observations suggesting a significant effect of potroom exposures is in mean $FEV_{1.0}$ among former potroom workers; however, the inconsistency of this $FEV_{1.0}$ finding when compared by exposure dose places this effect in doubt. Moreover, the lack of a significant difference in the prevalence of abnormal FEV_1 values using either the 5% or the 1% cutoffs also supports this contention of a no exposure effect.

The combination of one or more major symptoms and abnormal spirometry (below the 5% cutoff) was used as the definition of chronic respiratory disease (CRD). Figure 6 shows no significant difference in comparing the prevalence of CRD in potroom workers (4.9%) versus the controls (5.3%), or in the Soderberg (3.8% versus 5.5%) and Prebake (5.5% versus 5.1%) processes. The prevalence comparisons of abnormal spirometry and normal questionnaire, and the converse, also showed no significant differences between the study group and the control group. These prevalences are shown in Figure 6; also given are the percent prevalences by plant process.

The difference in prevalence of an abnormality in closing volume measurement was not significant for Type 1 (CC/TLC) ratios when the study group was compared with the control group or for the corresponding groups composed of persons representing the two plant processes. Appendix K gives the measurement criteria for abnormalities. The Type 2 (CV/VC) comparison for all workers was significant at the 5% level, however. The aluminum worker group prevalence of this abnormality was 7.2%, and the matched control group prevalence was 3.1%. The significance of the prevalence difference between subgroups of aluminum workers and matched controls for the two processes was borderline ($p < 0.10$) for Type 2

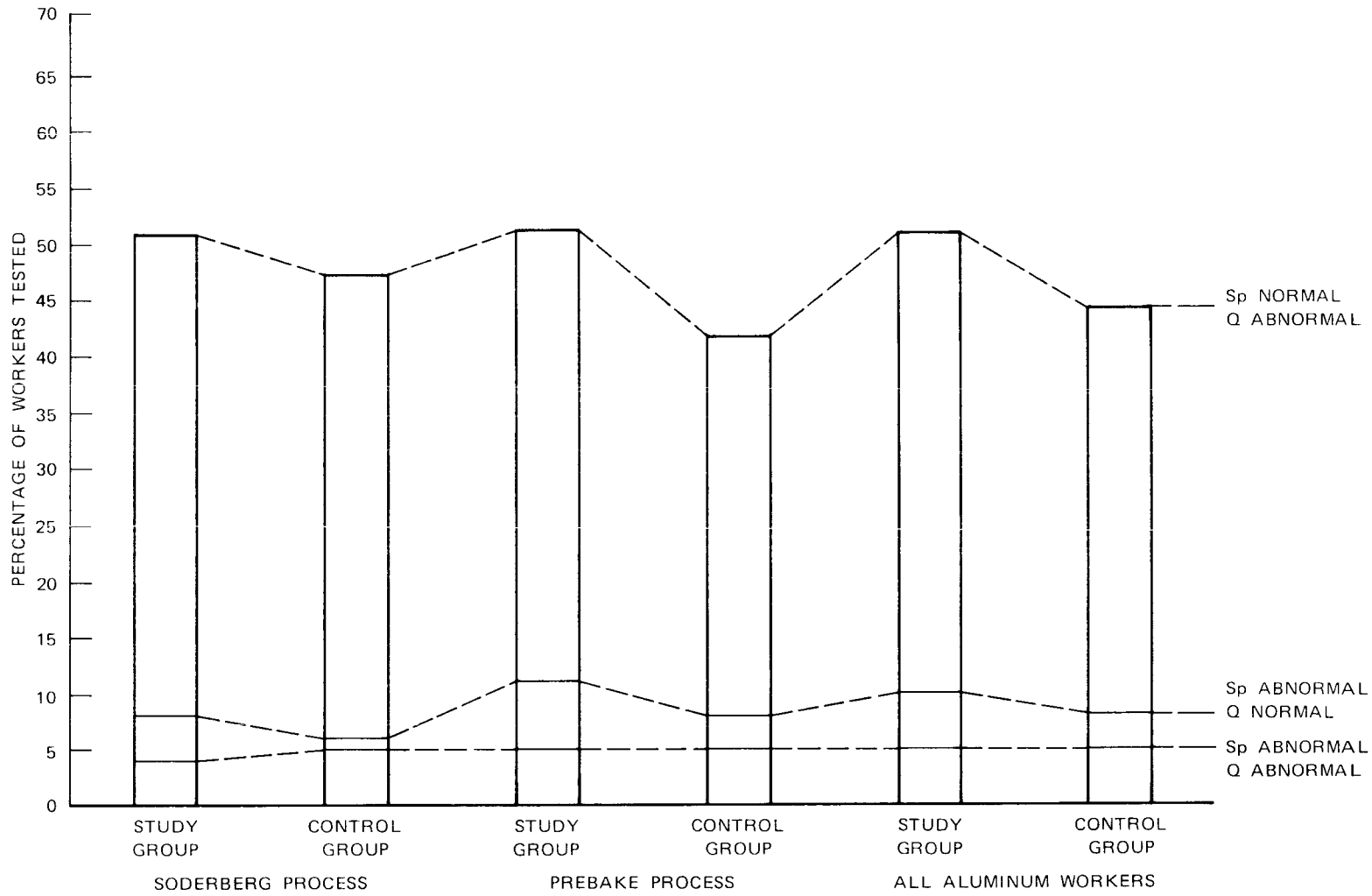
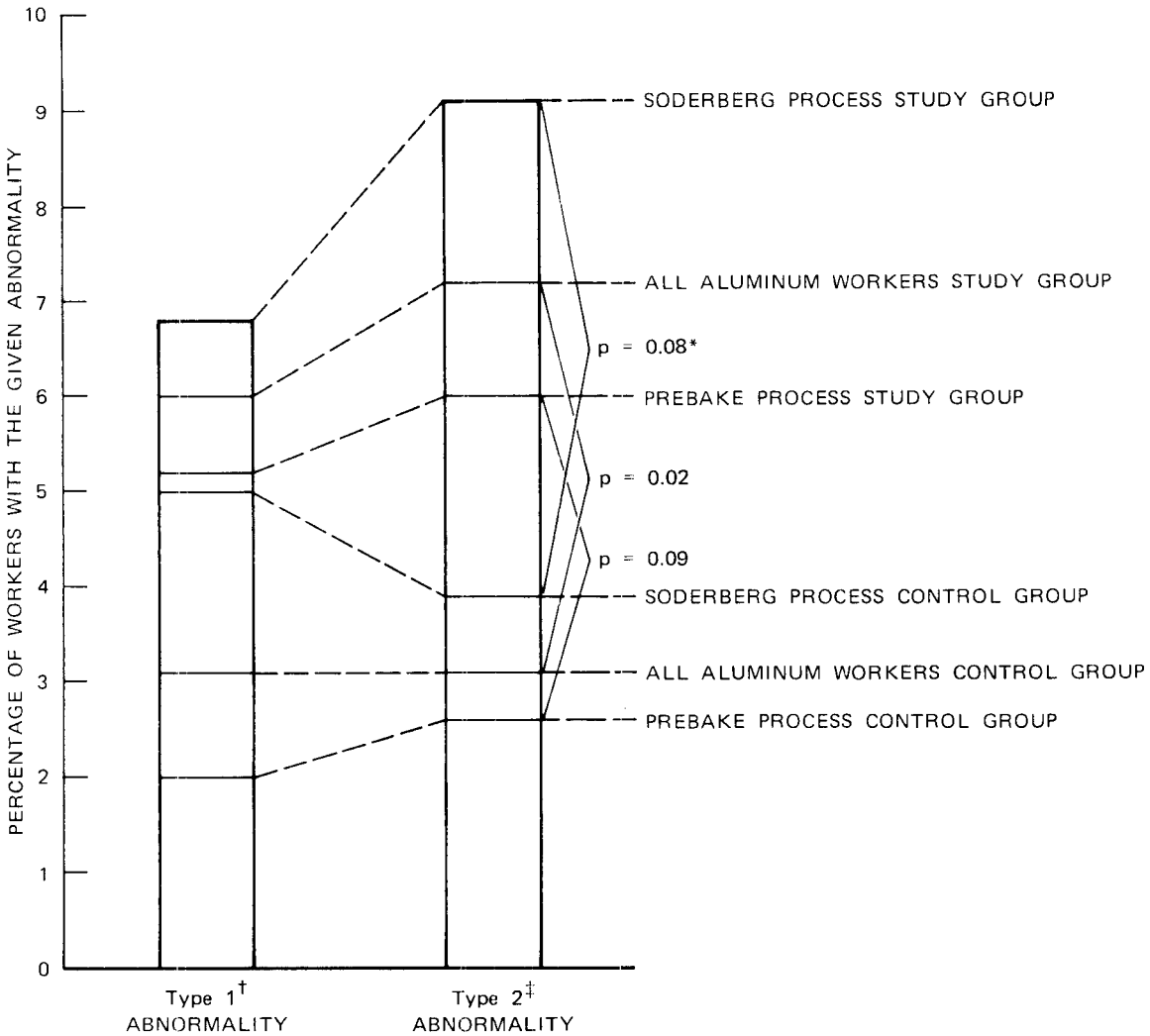


FIGURE 6 QUESTIONNAIRE SYMPTOMS, Q, AND/OR SPIROMETRY, Sp, BY GROUP: SODERBERG, PREBAKE, AND ALL ALUMINUM

abnormalities. Figure 7 shows the comparison values for the two types. Table 12 gives prevalence comparisons for the three exposure levels and three worker classifications. Significant differences ($p < 0.05$) for the high exposure group were found for Type 1 abnormality prevalence, Type 2 abnormality prevalence, and for the prevalence differences for a person having a combined (both Type 1 and Type 2) abnormality. No differences were found in the worker classification, but the number of new hires was perhaps too small (38 aluminum workers and 20 controls) to expect to make such inferences. Table 13 shows that the subgroup data do not produce any different conclusions when examined separately for the two processes, and the high dose subgroup effect is evident in both the Soderberg and Prebake groups. The clinical significance of abnormal closing volume measurement remains in doubt, although it has been proposed to detect a condition known as "small airway disease," a possible precursor to some cases of chronic obstructive lung disease.

The chest x-ray findings for the study group compared with the control group were not remarkable except for interpretations of "obstructive emphysema," as shown in Table 14. The radiographic definition of obstructive emphysema in this study is given in Appendix L. Figure 8 shows a trend for an increasing prevalence ratio as a function of dose level. The prevalence difference was significant ($p < 0.05$) only for the entire study group and the high dose subgroup. The worker classification results showed no significant difference. Figure 9 summarizes other survey data obtained on the 30 aluminum workers with "obstructive emphysema" reported on the chest x-ray and compares the frequency of selected abnormalities on questionnaire, spirometry, closing volume, and sputum cytology obtained on the 30 versus their 15 matched control workers. The numbers of workers are extremely small, and statistical testing cannot be expected to be useful; however, a trend was observed suggesting more abnormal obstructive flow rates ($FEV_{1.0}$ and closing volume) among those



*Statistical significance of the difference using a two-way Z-test of the difference of two proportions.

†Definition of abnormality: CC/TLC ratio greater than two standard deviations above the mean value for a male of that age (see text).

‡Definition of abnormality: CV/VC ratio greater than two standard deviations above the mean value for a male of that age (see text).

FIGURE 7 CLOSING VOLUME ABNORMALITIES (TYPE 1 AND TYPE 2) BY GROUP AND SUBGROUP

Table 12

CLOSING VOLUME CLASSIFICATION BY DOSE
AND WORKER CLASSIFICATION SUBGROUPS

	Percentage with Type 1 Abnormality	Percentage with Type 2 Abnormality	Percentage with Both
Low dose			
Study group	3.8%	5.0%	3.8%
Control group	3.7	4.9	3.7
Difference	+0.1	+0.1	+0.1
Intermediate dose			
Study group	3.1	7.0	1.6
Control group	3.9	2.3	2.3
Difference	-0.8	+4.7	-0.7
High dose			
Study group	10.2	9.6	7.0
Control group	1.9	1.9	0.6
Difference	+8.3	+7.7	+6.4
Current			
Study group	5.8	7.3	4.1
Control group	3.2	3.2	2.0
Difference	+2.6	+4.1	+2.1
Former			
Study group	3.2	4.8	1.6
Control group	1.6	1.6	1.6
Difference	+1.6	+3.2	0.0
New hire			
Study group	10.5	10.5	10.5
Control group	2.5	2.5	2.5
Difference	+7.5	+7.5	+7.5

Table 13

CLOSING VOLUME CLASSIFICATION BY GROUPS AND SUBGROUPS

Abnormality and Dose Subgroup	Process Group			
	Soderberg		Prebake	
	Study Group	Control Group	Study Group	Control Group
Type 1 abnormality				
Low dose	5.66%	5.45%	2.83%	2.78%
Intermediate dose	4.23	4.17	1.75	3.57
High dose	11.54	5.66	9.52	0
Type 2 abnormality				
Low dose	7.55	5.45	3.77	4.63
Intermediate dose	8.45	2.78	5.26	1.79
High dose	11.54	3.77	8.57	0.96
Both Type 1 and Type 2 abnormalities				
Low dose	5.66	5.45	2.83	2.78
Intermediate dose	2.82	2.78	0	1.78
High dose	7.69	1.89	6.67	0

Table 14

PRIMARY AND SECONDARY CHEST X-RAY CONSENSUS INTERPRETATIONS BY GROUP

	Study Group	Control Group
Primary interpretations		
Obstructive emphysema	7%	4%
Suspect TB	0.4	0
Nontuberculous infiltrate	0.4	0
Suspect lung cancer	0	0.4
Bullous emphysema	0.2	0
Other suspect bronchiectasis	0.4	0
Subtotal	8%	4%
Secondary interpretations		
Calcified hilar or paratracheal nodes	2	0.8
Calcified granuloma	4	2
Pleural scarring or calcification(nonapical)	4	5
Apical scarring	4	4
Subtotal	14%	12%
Totals	22%	16%

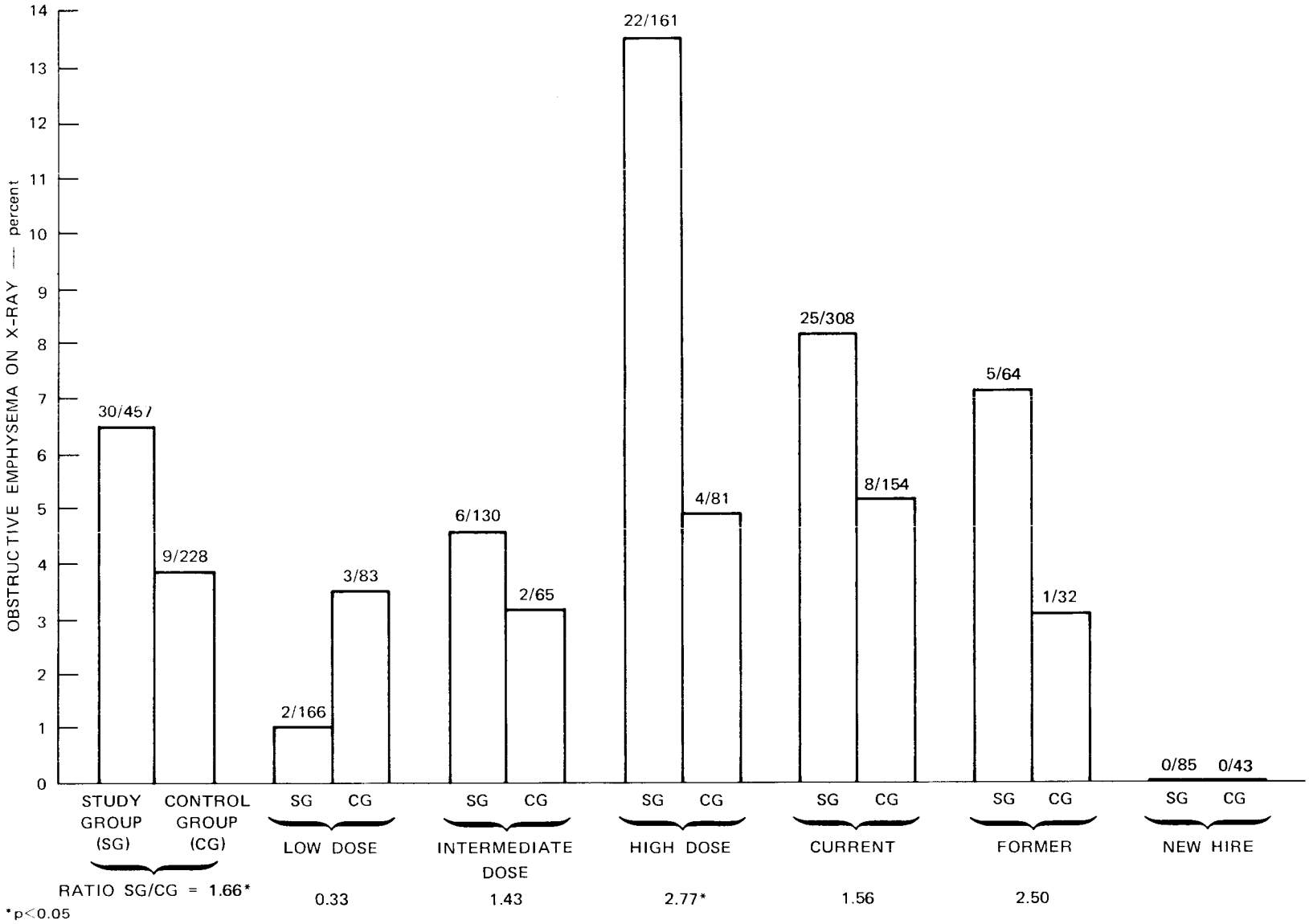


FIGURE 8 OBSTRUCTIVE EMPHYSEMA ON CONSENSUS X-RAY READING BY DOSE AND WORKER CLASSIFICATION

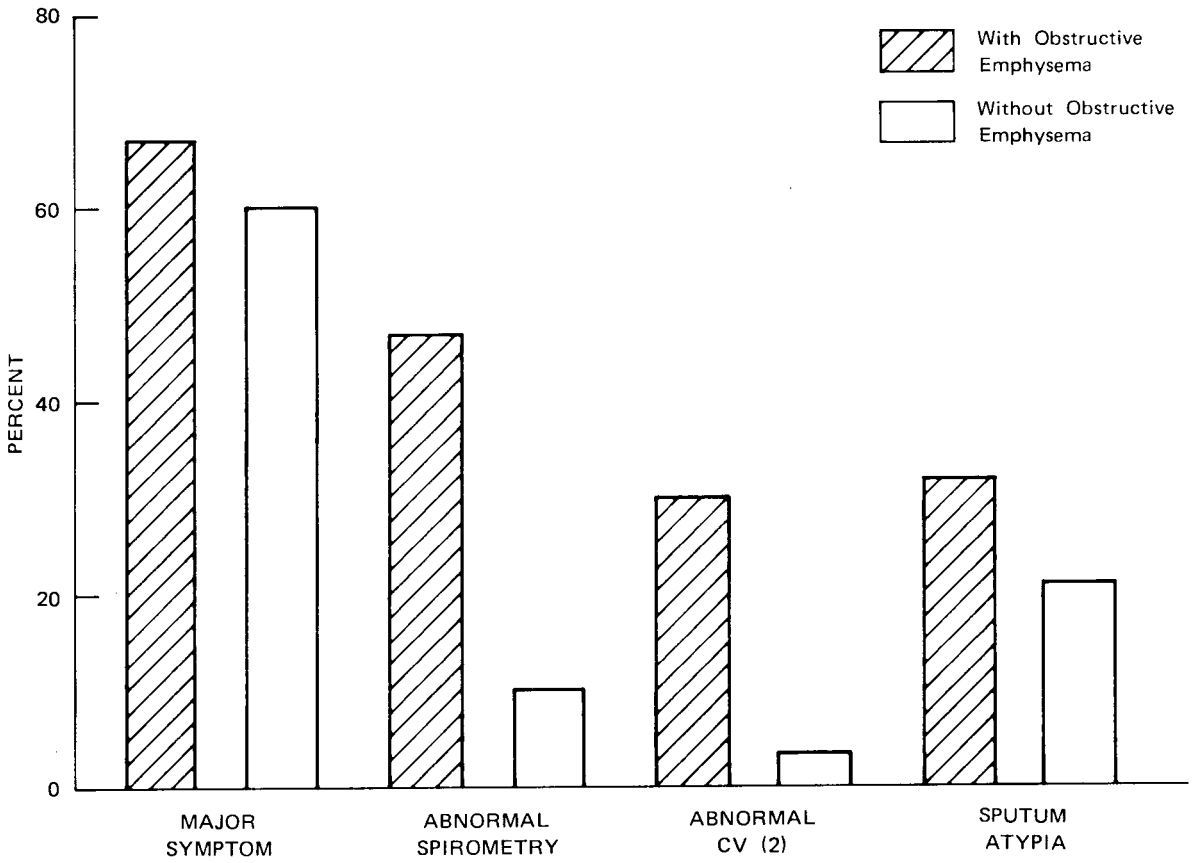


FIGURE 9 FINDINGS ON PERSONS WITH OBSTRUCTIVE EMPHYSEMA ON X-RAY COMPARED WITH PERSONS WITHOUT OBSTRUCTIVE EMPHYSEMA

with radiographic evidence of "obstructive emphysema." It should also be noted that many workers with this x-ray evidence had normal questionnaire and spirometry. The absence of any significant increased prevalence of respiratory symptoms or spirometry abnormalities, comparing the study group to the control group, as noted above, would strongly reject the contention that these x-ray findings are indicative of a true excess of chronic obstructive lung disease in the study group. It has long been recognized that radiographic evidence of obstructive emphysema has a low specificity for clinical emphysema, and the standardized respiratory symptoms questionnaire and spirometry are also more sensitive tools in this regard. Because of the much lower validity of the radiographic procedure as an epidemiologic tool for chronic obstructive lung disease prevalence studies, the interpretation of higher prevalence of x-ray evidence is a guarded one and does not refute the much stronger conclusions made from the prevalence of symptoms and spirometry findings.

Cytopathologic findings on sputum were obtained in approximately 85% of the study group and controls, as indicated in Table 15. The prevalence of mild atypia was significantly higher ($p < 0.01$) in the study group compared to the control group, as shown in Table 16. Figure 10 shows no specific trend in cytopathology with exposure level; however, the differences were significant ($p < 0.05$) for all three dose groups. The former workers had a prevalence of cytopathology very similar to that of their matched controls, and the difference for the limited number of new hires was not statistically significant. Current potroom workers had a significantly higher prevalence ($p < 0.05$) of cytopathology compared with controls. It should be noted that mild atypia was the predominant difference in all of these prevalence differences, and mild atypia is regarded as a nonspecific finding, not necessarily indicative of a lung cancer risk.

Table 15

SPUTUM CYTOPATHOLOGIC FINDINGS BY GROUP:
SATISFACTORY SPECIMEN YIELD RATES

	Study Group	Control Group
Satisfactory	390 (85.4)	193 (84.4)
Unsatisfactory	62 (13.6)	31 (13.6)
Unknown	5 (1.0)	4 (2.0)
Total Groups	457 (100%)	228 (100%)

Table 16

SPUTUM CYTOPATHOLOGIC CLASSIFICATION BY GROUP

Classification	Study Group	Control Group
Negative	266 (68.2)	159 (82.4)
Atypical		
Mild	94 (24.1)	29 (15.0)
Moderate	24 (6.2)	5 (2.6)
Subtotal	118 (30.3)	34 (17.6)
Suspicious	5 (1.3)	0 (0)
Positive	1 (0.2)	0 (0)
Total Satisfactory	390 (100%)	193 (100%)

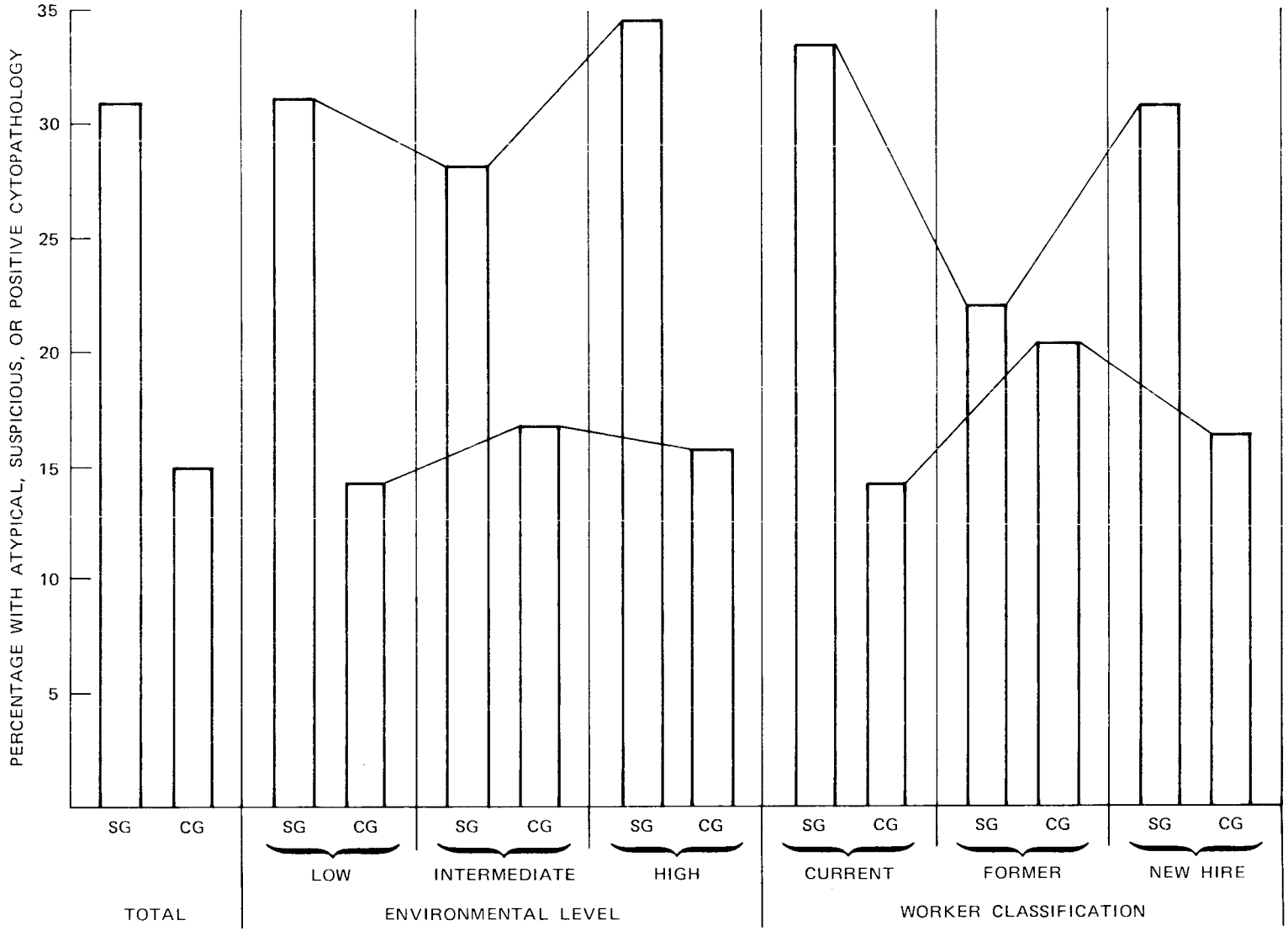


FIGURE 10 SPUTUM CYTOPATHOLOGY BY DOSE AND WORKER CLASSIFICATION SUBGROUPS

Comparison of the two screening tests for detecting abnormal phenotypes for alpha$_1$ antitrypsin deficiency disease is given in Tables 17 and 18. About one-fifth of the workers tested were below normal values for the STIC screening test and about one-fourth below normal values by the radial immunodiffusion screening test. (In this analysis, no distinction was made between aluminum workers and controls.) Table 18 shows that the abnormal STIC tests account for about one-half of the abnormal phenotypes, and normal STIC values negatives account for about nine-tenths of the normal phenotypes. The prevalence of abnormal phenotypes accounted for one-sixth of all those subjected to phenotyping. It should be noted that there were no homozygotes other than the normal MM phenotype; MS occurred among 64% of the heterozygotes, MZ among 32%, and MP and MI accounted for the remainder.

Table 19 shows that the preshift urine F values were higher in the Soderberg workers ($p < 0.05$); whereas, the mean serum Fs for the subsample of these two groups of workers and a group of unmatched controls were all the same.

Table 17

COMPARISON OF YIELD OF TWO SCREENING TESTS FOR ABNORMAL ALPHA$_1$ ANTITRYPSIN PHENOTYPES

	Alpha$_1$ Antitrypsin ($\leq$ 200 mg%)		
	Positive	Negative	Total
STIC ($\leq$1.000)			
Positive	69	45	114 (20.6%)
Negative	70	387	457 (79.4%)
Total	139	432	571 (100%)

Table 18

COMPARISON OF STIC SCREENING TEST
WITH PHENOTYPE CLASSIFICATION

	Phenotype		
	Abnormal	Normal	Total
STIC			
Positive	37	47	84
Negative	36	333	369
Total	73	380	453
Sensitivity	$\frac{37}{73}$ (51%)	--	
Specificity	--	$\frac{333}{380}$ (88%)	

Table 19

URINE FLUORIDE IN STUDY GROUP BY WORKER CLASSIFICATION AND PROCESS
AND SERUM FLUORIDE IN A SUBSAMPLE OF THE STUDY GROUP

	Pre-Shift Urine F (mg/lg)		Serum F (mg%)	
	N	Mean ± S. E.	N	Mean ± S. E.
Soderberg			17	0.422 ± 0.010
Current/New Hire	51	2.17 ± 0.17		
Former	15	2.24 ± 0.43		
Prebake			21	0.398 ± 0.009
Current/New Hire	201	1.43 ± 0.07		
Former	22	0.99 ± 0.10		
Control			19	0.409 ± 0.009

V DISCUSSION

The principal question to be addressed by this industrial prevalence study can be stated as follows: Does work in the potroom lead to a doubling of the prevalence of chronic obstructive lung disease? Several key reservations were inherent in our analysis of this question, and each can be discussed in detail:

(1) Does our population of current and former aluminum potroom workers in three plants in the Northwest remain in the plant workforce such that the aluminum plant roster is representative of all occupational risk groups? A corollary is: Do workers with early disease leave the workforce?

(2) Does our cross-sectional randomized and stratified sample of a risk population, consisting of 457 potroom (183 Soderberg and 274 Prebake process) workers (308 current, 64 former, and 85 new hires), represent that population so as to estimate expected prevalence rates to detect a true two-fold greater prevalence in the population at risk? A corollary is: Does the sample represent a reasonable allocation of doses such that the response can be applied across dose subgroups?

(3) Does a control population for aluminum workers exist such that all important extraneous sources of disease risk are comparable to the aluminum study population? A corollary is: Does our matched group of 228 University Physical Plant employees and telephone workers reasonably well correspond to the risk group so that potroom exposure is the principal difference?

(4) Does our methodology for identifying persons with chronic obstructive lung disease have such reliability and validity that one can be confident of numerator events? A corollary is: Are our measurements clinically meaningful?

Each of these basic epidemiologic questions for this industrial prevalance study expands into a series of subsidiary questions and could generate a set of contrasting questions for alternative studies, such as longitudinal morbidity and mortality studies. Basic to all of these

research studies is the question of whether a specific agent of disease, such as fluorides, may be interacting as an occupational potpourri, including perhaps polycyclic hydrocarbons, with nonoccupational exposures, such as cigarette smoking, or constitutional factors, such as alpha$_1$ antitrypsin deficiency heterozygosity.

Therefore, in addition to the central question of a two-fold risk chronic obstructive lung disease, the study team labored over the design of the study with respect to pulmonary fibrosis, lung cancer, alpha$_1$ antitrypsin serum levels and phenotypes, and urine and serum fluorides. Each of these ancillary questions was addressed, albeit in a somewhat cursory manner, as the more specific designs for such studies could mitigate the efficient accomplishment of our principal project objective. Therefore, in this discussion of each of these ancillary objectives, our considerable limitations will be explained.

Returning to the four key reservations, the results should be viewed with the following cautions:

(1) No retired, terminated, or otherwise separated employees who were former potroom workers were included in this study. The former potroom workers were in actuality a subgroup of those still employed by the aluminum industry! Moreover, our roster was a current one, so that active employment (and perhaps its corresponding health selection bias) was an implicit requirement for participation. Fortunately, the numerator condition we were studying is not disabling until many years have elapsed. However, if acute irritation is particularly objectionable to a new worker, this particular job may not be acceptable, and the new hire may seek transfer or quit. Moreover, if this irritancy tendency is correlated with chronic disease susceptibility, a survivor group may be resistent; for example, no workers with alpha$_1$ antitrypsin deficiency would remain if this were a risk factor that is associated with both serious and obvious acute effects, such as susceptibility to "potroom asthma." A small study of potroom employee turnover was performed. Of the 308 current potroom workers on November 1, 1972 (see definitions on page 18), 8.4% were no longer in the potrooms one year later;

and for 85 new hires on the same date, 36.0% were no longer in the potrooms one year later. Over 75% of this turnover was in the group under 36 years of age. It was judged to be questionable that we could very effectively identify from our cross-sectional data whether self-selection factors related to future chronic respiratory disease were operating in this turnover among young potroom workers.

(2) The sample size was calculated to optimize estimates of prevalence of chronic respiratory disease among current, former, and new hire potroom workers in the two processes. A sample of 457 study group aluminum employees matched to 228 control group workers was shown to be sufficient to detect a study group prevalence of 10% of chronic respiratory disease (46/457) and recognize a significant difference at the 5% level (alpha error), assuming a prevalence of 5% in the age-smoking history matched control group (12/228). The power of this sampling design was 80% (beta error = 20%). Stratified random sampling was performed from a composite three-plant roster using a sampling fraction of 100% for one low risk group, namely new hires. (If a 25% sample had been used for this group, perhaps only about 25 such persons, rather than 85, would have been studied, and far fewer inferences could have been made concerning the group.) This new hire subgroup serves to provide a low dose internal control. The second decision to allocate the sample was related to the two processes, wherein current potroom workers in the Soderberg process were assigned a 100% sampling fraction rather than 25%; this increased the yield of this group to 130 persons rather than 50 current potroom workers in the Soderberg process, and markedly improved our ability to compare processes. The sample of the two groups, study group and control group, was of borderline quality from the standpoint of response rate. This was especially the case for the Soderberg process subgroup, wherein the nonresponse rate was 29%. A special study of the Soderberg plant medical records of the nonrespondents was performed, and the frequency of abnormalities documented in those records was found to be comparable to the respondent group. The frequency of abnormal spirometry at the 5% cutoff was 4% for the nonrespondent group, about the same for respondents of a similar age distribution. The frequency of hospitalizations during the past ten years for respiratory disease was 2% for the nonrespondent group. About 10% of them had a diagnosis of chronic respiratory disease, 36% were moderate or heavy smokers, 20% turnover occurred, the ratio of Current to Former to New Hires was 7:2:1, and the ratio of the three

age groups (≤ 35, 36-50, ≥ 51 years) was 7:2:1--all of this being data consistent with the contention that the respondents and nonrespondents at this plant do not differ in relevant characteristics.

(3) A control group of similar age, smoking history, family history for chronic obstructive lung disease, childhood respiratory infection rates, and so on, would be ideal to compare the prevalence in the study group to a control group. In our study, matching was only performed for age and smoking, and some other factors were examined for comparability after the matching was completed. It should be noted that only minor differences were observed in education, size, blood pressure, and the like; moreover, it was our judgment that inferences drawn from comparisons of matched groups do not suffer from an imbalance of any known extraneous sources of chronic respiratory disease risk. The study group prevalance ratio was examined in dose subgroups. There were three approximately equal groups: high, intermediate, and low. Another key internal comparison was the prevalence among the former potroom subgroup compared to its matched control; former potroom workers may be a key subgroup since they may no longer be in the potroom because of effects of long exposure. In this manner the study design included the elements of external controls (matched controls) and internal controls (dose and worker subgroups), as well as the comparison of the two process groups.

(4) The reliability and validity of the questionnaire and spirometry for detecting chronic respiratory disease has been well established by numerous epidemiologic studies, although the clinical application of these data to individual patients is controversial because the impact of this as a form of disease detection is dubious from the standpoint of reversing the disease process by any known therapeutic means. In general, the clinical problem is that <u>early</u> chronic obstructive lung disease cannot be detected by questionnaire and spirometry; and clearly established disease patterns for epidemiologic purposes usually require combined test results, as defined in this study. The validity of the test cannot be asserted for closing volume or radiographic interpretation. No clear cutoffs for the closing volume test can be stated that are indicative of "small airway disease" or any other chronic obstructive lung disease. In this study we used regression formulas for predicted mean values and classified workers as "abnormal" if their CC/TLC or CV/VC quotients were in excess of two standard deviation units above those values. It should be noted that this specific epidemiologic

> classification has not been validated, and our inferences concerning a higher prevalence associated with high doses in the potroom, therefore, cannot be considered as indicating a disease risk, only a specific physiologic difference. Likewise, radiographic criteria for "obstructive emphysema" have been considered unacceptable except as crude epidemiologic indicators. For example, a normal functional state is frequently observed in many young people with good quality chest radiographs interpreted by consensus as abnormal. The sensitivity of chest radiography has been observed to be low, especially for mixed chronic bronchitis and emphysema. In persons with radiographic abnormalities, such as hyperlucency, and abnormal closing volumes but normal spirometry and no respiratory symptoms, a wise clinical course might be to be vigilant for "small airway disease" as a prelude to emphysema; however, the hypothesis has not been tested and remains speculative. The fact that both findings occurred more frequently in the potroom workers in the high dose subgroup raises some concerns that might not have otherwise arisen; however, the clinical significance of this statistical inference must be held in reserve.

There were nine suspect lung cancer cases in this study; of these six were among the study group, one was among the control group, and two were among the unmatched controls. All of these were detected by sputum cytology except for one case of suspect lung cancer found on chest x-ray in a control group worker. This man was a 28-year-old light smoker with no respiratory symptoms and mild atypia; followup thus far has showed no significant pathology.

Followup thus far on the eight with positive or suspicious sputum results has also been unrewarding except for the one with a positive sputum. He was a 58-year-old current potroom worker in a Prebake process plant who had reported major cough, phlegm, and both exertional and non-exertional dyspnea. He was a heavy smoker with an abnormal FEV_1 and a borderline result on his closing volume test. His chest x-ray was read as "obstructive emphysema" by consensus reading. Followup began with fiberoptic bronchoscopy and esophagram, both of which were negative.

Bronchial washings were positive from the left lung, and tomograms revealed a left upper lobe lesion 2 cm. in diameter. A left upper lobectomy was performed.

Followup on the other seven with suspicious sputum has been negative so far; moreover, six of the seven have had repeat sputum, and four of these were rated as moderate atypia and the remaining two as mild atypia on the repeat specimen. Only one of the seven worked in the Soderberg process plant where the lung cancer risk might be presumed to exist; of the remaining six, two were unmatched controls and four were in Prebake process plants. Table 20 gives the pertinent data on these seven men.

Table 20

PERTINENT DATA ON CASES WITH SPUTUM CATEGORIZED AS SUSPICIOUS

Case Number	Age	Potroom-Dose	Smoking History	Findings
8133	45	Control--0	Light	Medical workup negative
8800	55	Control--0	Nonsmoker	Pleural thickening on x-ray
2028	19	Current--3	Light	None
4025	60	Current--66	Ex-smoker	Abnormal FEV_1; "obstructive emphysema" on x-ray
4048	47	Current--15	Moderate	Chronic respiratory disease
4119	53	Current--16	Ex-smoker	None except heterozygote (MZ)
6017	24	New hire--4	Light	Chronic bronchitis symptoms

The dose level for the five potroom workers (cases 2028, 4025, 4048, 4119, and 6017) was not significantly higher than the mean for their subgroup and process, and case 2028, the one Soderberg process worker with a suspicious sputum, had been employed in the potroom for only a

little over one year. None of the 37 Soderberg process or 27 Prebake process workers who were former potroom workers had suspicious sputa.

In comparing the workers with mild or moderate atypia with the workers with negative results on sputum examination, the following conclusions were reached:

(1) The age of workers with this level of atypia was not significantly different from those with negative results.

(2) The distribution of smoking history was equivalent in the two groups.

(3) The prevalence of "obstructive emphysema" on chest x-ray or a history of morning cough was greater among the group with mild or moderate atypia.

It was concluded that perhaps the atypical epithelium results from inflammatory agents, rather than from carcinogens. The significance of mild and moderate atypical squamous metaplasia must be weighed against the assumption that only a small proportion, if any, of these will necessarily progress to outspoken cancer. Some may regress, some may persist. It is impossible to say that the proportionately larger number of study group subjects with mild or moderate atypia will progress compared with the control group. Followup studies to date show no evidence of progression. It was also noted that the prevalence of atypia in our study group was strikingly lower than reported in a nonmining control group by another team of investigators;[26] however, the comparability of the two groups is subject to question. We have arranged to have a sample of slides taken from our group reviewed by Saccomanno as our first step to follow up on this point.

It should be recalled that our induction technique was aimed to obtain a satisfactory specimen in less than ten minutes, and as many as three inductions were attempted at separate times at least four weeks apart. From this we found 79% of workers provided satisfactory sputum on the

first induction and an additional 6% were able to give a satisfactory sputum specimen by the second or third induction. Considering the fact that our overall nonresponse rate was 20%, the added unsatisfactory rate of 15% of those tested (80% of the study and control groups recruited for the sample) adds to the uncertainty of our estimates.

Several other problems in interpretation of the sputum cytopathology can be cited that relate to the natural history of mild atypia in relation to lung cancer, particularly since the prevalence of more advanced and more specific neoplastic findings were not statistically significant in the difference between study group and controls. One possible set of hypotheses would be that mild atypia does occur in a susceptible fraction of all potroom workers fairly soon after being assigned in the area, and that this irritant response of the mucosa remains, or even progresses to moderate or marked atypia, during the many years that a worker is assigned in the potroom. Former potroom workers, assuming this hypothesis, would have a sputum cytologic pattern similar to that of controls, because the inflammatory process would be reversible. This extended hypothesis would also propose that high cumulative doses would have no greater effect on incidence or severity rates than low doses, since the irritant threshold effect for those that are susceptible would be easily exceeded in the potroom. Whether this speculation has any validity would depend on sputum data from longitudinal studies and is beyond the scope of this report.

One alternative hypothesis would be that an inflammatory process at some stage progresses to neoplasm, and the potroom worker with mild or moderate atypia or suspicious cells is at special risk of lung cancer. For a variety of reasons, this alternative is difficult to contend with within the context of this prevalence study; most significant is the fact that insufficient persons were placed under observation so as to expect enough lung cancer in the study group so that statistical significance could be achieved unless the risk rates were approximately two orders of

magnitude greater in study group compared with the control group. The fact that one case of lung cancer was found in the aluminum workers and none was found in the 228 controls does not provide evidence for or against the alternative hypothesis. As indicated in the introduction, unlike chronic obstructive lung disease, the prevalence of frank lung cancer found by sputum cytology or on x-ray even in a high risk group would be expected to be so low that retrospective cohort mortality studies would be more efficient for estimating a potroom exposure risk (in excess of that caused by cigarette smoking) for lung cancer. The justification of such sputum studies arises out of the ready opportunity to perform a nonspecific test for atypia that might suggest the importance for undertaking more definitive studies as indicated above. Fortunately, mortality studies can be fairly conclusive since, unlike chronic obstructive lung disease, most of the attributive incidence is accounted for in death certification and correctly coded as a primary cause.

The question of lung tissue responsiveness to potroom inhalants also includes questions of the impact of hereditary factors such as $alpha_1$ antitrypsin heterozygosity and other unidentified constitutional factors. Thus far, epidemiologists and geneticists have little to offer for identifying familial and other elements dealing with workers' susceptibility save the arduous process of phenotyping for $alpha_1$ antitrypsin alleles. The homozygote ZZ worker would be clearly at risk; however, the various heterozygotes, being common among new hires and subject to selective forces thereafter, would constitute a vital subgroup if we could economically detect such persons and if they were proven to be susceptible. In this study we concentrated on screening methods, since the susceptibility question would require longitudinal study. The results showed the futility of STIC and RID screening in terms of heterozygote yield. We have no effective and efficient screening tool for detecting phenotypes. Moreover, phenotyping has yet to be justified as a predictor of future occupational

lung disease. This prediction, controlling for smoking, needs to be derived from cohort studies of potroom workers using a logitudinal design.

Urinary fluoride measurements on a single grab sample--whether preshift or postshift--were evaluated by the study team to be superficial tests, since the dose estimates could be constructed from the plant's periodic bioassay program with greater validity than we could from a single urine determination. Thus, the study team decided to provide the data to NIOSH, but we did not use individual results for dose calculations. The doses were applied to occupations by examining relative urine F levels for hundreds of workers in particular job categories over many years, rather than limited data that might have been produced from a single grab sample for a worker and/or the mean of such samples for his job category. We provided in Table 19 the results of a single grab sample as preshift values, with more than 24-hours off work, since such values are more indicative of long term exposure, a parameter perhaps more pertinent to chronic obstructive lung disease risk. Serum F was studied because recent literature suggested a better discrimination of this test for peak estimates, but since the blood was obtained coincident with the urine, the question of acute peak correlations could not be addressed. In the process of examining preshift values for serum, however, we did establish that such baseline levels are fairly similar for study subjects and controls.

In summary, no chronic obstructive lung disease risk could be deduced; however, some less valid measures than questionnaire and spirometry for detecting that disease, such as closing volume and chest x-ray, were positive for abnormalities whose relationships to chronic obstructive lung disease remains an enigma. This, together with an excess of mild atypia on sputum cytology results, suggests that some type of inflammatory reaction may be resulting from potroom exposures, but little evidence is present to judge the long term significance, if any, to such findings. Other study protocols have been recommended to deal with these issues,

including the remote possibility of a lung cancer risk among such workers. The inherent susceptibility in the general population to pulmonary irritants has been alleged to be associated with the occurrence of non-M alleles. Phenotype classifications of allele pairs can be determined on workers, using very expensive techniques. Screening tests for the phenotypes were obtained and evaluated in comparison to results of phenotyping. These data are especially important for new hires who leave the industry or complain of respiratory symptoms from potroom work. The validation test results were very discouraging in that sensitivity for determining heterozygotes was about 50% and specificity was about 90%. Since the yield from screening tests was very poor, phenotyping will be required to examine the question in future longitudinal studies, unless a new screening test is developed.

Appendix A

NEWSPAPER RELEASES

PROPOSED INSERT FOR PHYSICAL PLANT BULLETIN BOARD

UNIVERSITY OF WASHINGTON PHYSICAL PLANT AND ALUMINUM WORKERS OCCUPATIONAL HEALTH STUDY

The Department of Environmental Health at the University of Washington, in cooperation with the University's Physical Plant Department, ALCOA, and the Kaiser Aluminum Company is undertaking an Occupational Health Study. The Study Team is made up of physicians, industrial hygienists, and other investigators from the University of Washington, Boeing, and the two aluminum companies. This research is being funded by the National Institute for Occupational Safety and Health (NIOSH).

The study is to determine the frequency of chronic lung disease among workers in the employ of the University's Physical Plant and these aluminum companies in the state of Washington, and to test methods that may be useful for early detection of lung disease. It will not be possible to examine each worker at the plants; however, a total selected sample of about 1,000 workers will be studied, about 400 being University of Washington physical plant employees.

Preliminary arrangements suggest that the first individual employee contacts at the physical plant will be made in July and August of this year. Early contacts will be in the nature of a screening questionnaire to obtain information about age and smoking habits. Approximately 300 to 500 physical plant employees will then be selected to be studied. This group will then be given further explanation of the study to obtain full cooperation of all those selected. The examination, using two mobile laboratory vans to be located at each plant, will be completed during September and October of 1974. The examinations will be scheduled during the regular work shifts.

ALUMINUM WORKERS OCCUPATIONAL HEALTH STUDY

PROPOSED INSERT FOR PLANT NEWSLETTER

The Department of Environmental Health at the University of Washington, in cooperation with ALCOA and the Kaiser Aluminum Company is undertaking an Occupational Health Study. The Study Team is made up of physicians, industrial hygienists, and other investigators from the University of Washington and the two aluminum companies. This research is being funded by the National Institute for Occupational Safety and Health (NIOSH).

The study is to determine the frequency of chronic lung disease among current and former pot room workers in the employ of these companies in the State of Washington.

The aluminum reduction plants selected for the study are the ALCOA Plants at Vancouver and Wenatchee, and the Kaiser Aluminum Plants at Spokane (Mead), and Tacoma. It will not be possible to examine each worker at these plants; however, a total selected sample of about 750 workers will be studied.

Preliminary arrangements suggest that the first individual employee contacts of those selected to be tested will be made in November or December of this year. The first contacts will be in the nature of further explanation of the study to obtain full cooperation of all those selected. The examination, using a mobile laboratory van to be located at each plant, will be completed during the first four months of 1974. The examinations will be scheduled during the regular work shifts.

Union officials representing the workers at each of the plants have been meeting with members of the Study Team, and are providing important help in the setting up of this study.

Appendix B

NOTIFICATION LETTERS

UNIVERSITY OF WASHINGTON
SEATTLE, WASHINGTON 98195

December 1974

School of Public Health and Community Medicine
Department of Environmental Health, SC-34

Dear Mr.

During the past year you were tested by a University of Washington medical technician team as part of an occupational health study.

The tests that were made on you included: chest X-ray, pulmonary function (breathing tests), sputum cell examination, blood sample for an enzyme called alpha$_1$ antitrypsin, and blood pressure. All these tests were within normal limits except as noted below:

No exception ____

Thank you for taking part in this testing.

Sincerely,

Bryce D. Breitenstein, Jr., M.D.
Project Director

UNIVERSITY OF WASHINGTON
SEATTLE, WASHINGTON 98195

School of Public Health and Community Medicine
Department of Environmental Health

Dear Mr.

We are asking you to participate in an Occupational Health Study being undertaken by the University of Washington and in cooperation with your employer and your union. Enclosed with this letter is information which explains the nature of the study.

I will be meeting with you at your plant within the next month or two to explain the study further, answer any questions you may have, and to obtain your consent to participate.

It is anticipated that we will begin testing at your plant sometime within the next three months. We are presently scheduling on-site testing at four plants (ALCOA-Vancouver, ALCOA-Wenatchee, Kaiser-Spokane, Kaiser-Tacoma) where the study will take place.

Sincerely,

Bryce D. Breitenstein, Jr., M.D.
Project Manager

BDB:rk

At a meeting to be held at your plant, the purpose of the study will be explained in more detail. We will ask you to sign a consent form to participate in the study, and to give us permission to contact your private physician if any of your study findings require this to be done.

The consent form contains a statement to you that your identity in the study and your relation to any of the information obtained in the study will not be revealed by the investigators, except to your personal physician. The second part of the consent form is a statement of your agreement to voluntarily enter the study and an explanation of the procedures that will be used. Briefly, these will include answering a questionnaire, having a sample of blood drawn, the collecting of a specimen of urine and sputum, obtaining X-rays of the chest, and the measuring of your breathing ability. These procedures will be explained in greater detail below. The third portion of the consent form is your request that any significant findings discovered in the course of this study be given to the personal physician that you indicate.

For ease in collecting the information and undertaking the laboratory tests and X-rays, several station areas in our mobile laboratory van will be set up. These will be described below.

At one station the questionnaire will be completed in private with the help of a trained interviewer. It contains several sections. Sections 2, 3, 4, and 5 may have been partially or totally filled out from existing records, but may need additional information from you at the time of your private interview. The following is a description of these sections:

1. The first section is the consent form explained above.

2. The second section is an identification section that gives general information about you, including your name, address, phone number, age, sex, race, marital status, and education. The name, address, and phone number are primarily taken down so that you could be contacted if necessary, but these will not appear in any reports or conclusions drawn from the study.

3. The third section asks about your past work history. It will include the years you worked at a particular job, what the industry was and what type of product was made. We are especially interested in previous work exposure to dust, gases, fumes, or chemicals and to their types, if known. If you worked where you did not have exposure to these substances, the details are not as important in this section.

4. Section four deals with your present work history as to the company you are working with now, how long you have been with that company, and what your present job is. Then there is a detailed section of the different types of work that you may have done at your current place of employment. We would like this filled out, starting with your first job as to the number of years, second job as to the number of years, etc. If the job you have done is not listed, there is space to fill it in by writing in the name.

5. Section five lists the hospitalization you have had and asks for the year of hospitalization and how long you stayed. This is for your last four hospitalizations, if you have had that many.

6. Section six is a set of questions about your lungs as to cough, wheezing, phlegm, and shortness of breath.

7. Section seven asks about some of the major illnesses that you and your immediate family have or may have had, and asks in your case for details as to age of onset, and length of illness, and whether medication is being taken for any of the illnesses you may list.

8. Section eight is a history of your smoking habits, if you are or have been a smoker.

9. Section nine asks about the use of a respirator at your job.

In the same general area where the questionnaire is being completed, your height, weight, and blood pressure will be recorded.

Depending on the order of scheduling, the following additional procedures will be done in specified areas:

1. A breathing test which will measure how well you breathe and which will show how much air you can hold in your lungs and how fast you move it in and out of your lungs. You will simply be asked to take in a deep breath and blast the air out into the machine as fast as you can and empty all the breath you can into the machine. This will be repeated five times to get your best effort.

2. A breathing test which will measure how much gas you remove from your lungs, especially through the passages in the deepest part of your lung. First, you will simply hold some oxygen gas in your lungs, and then slowly breathe out into a machine for a short period while we measure the gases in your breath.

3. X-rays of your chest will be made. Proper shielding will be given you to protect you from the radiation.

4. A sample of blood will be drawn from your arm under sterile conditions.

5. A sample of your sputum (spit from your lungs) will be collected. To assist you we will have a fine mist for you to inhale; this mist is harmless but helps you bring up sputum.

6. A sample of urine will be obtained under clean conditions.

In the event that you cannot have these things all accomplished at one time, you may be rescheduled for a later time.

In all these procedures there appears to be minimal or no risk in accomplishing them.

You will be given the opportunity to have any questions you may have about this study answered by the investigators. It is important for you to realize that you are entering this study entirely voluntarily and are free to withdraw without any penalty at any time.

It is also important to note that the data collected in this research study will be kept as confidential data shared only among the various investigators and your personal physician if you have designated him to receive the information. The investigators are as follows:

Principal Investigator:	David P. Discher, M.D.
Principal Co-investigators:	Miles O. Colwell, M.D., William J. Bovard, M.D., Bertram D. Dinman, M.D., Sherman Williamson, M.D., James P. Hughes, M.D., Frank B. Metting, M.D., and Bryce D. Breitenstein, M.D.
Associate Investigators:	Donald R. Peterson, M.D., Donovan Thompson, Ph.D., Peter Breysse, M.P.H., Danny L. Dunham, M.S., and Albert L. Keller, Jr., M.A.

UNIVERSITY OF WASHINGTON
SEATTLE, WASHINGTON 98195

School of Public Health and Community Medicine
Department of Environmental Health, ~~RH-94~~ SC-34

Dear Mr.

We are asking you to participate in an Occupational Health Study being undertaken by the University of Washington's Department of Environmental Health and in cooperation with its Physical Plant Department. Enclosed with this letter is information which explains the nature of the study.

I will be meeting with you at or near your place of work within the next month to explain the study further, answer any questions you may have, and to obtain your consent to participate. It is anticipated that we will begin testing physical plant employees in September 1974.

Sincerely,

Bryce D. Breitenstein, Jr., M.D.
Project Manager

At a meeting to be held near your place of work, the purpose of the study will be explained in more detail. In general terms, the Department of Environmental Health at the University of Washington in cooperation with the University's Physical Plant Department, ALCOA, and the Kaiser Aluminum Company is undertaking an Occupational Health Study.

The study is to determine the frequency of chronic lung disease among workers in the employ of these companies in the State of Washington, and to test methods that may be useful for early detection of lung disease. The examination of University of Washington physical plant workers, using two mobile laboratory vans to be located on campus, will be completed during September and October of 1974. The examinations will be scheduled during the regular work shifts.

We will ask you to sign a consent form to participate in the study, and to give us permission to contact your private physician if any of your study findings require this to be done.

The consent form contains a statement to you that your identity in the study and your relation to any of the information obtained in the study will not be revealed by the investigators, except to your personal physician. The second part of the consent form is a statement of your agreement to voluntarily enter the study and an explanation of the procedures that will be used. Briefly, these will include answering a questionnaire, having a sample of blood drawn, the collection of a sputum specimen, obtaining an x-ray of the chest, and the measuring of your breathing ability. These procedures will be explained in greater detail below. The third portion of the consent form is your request that any significant findings discovered in the course of this study be given to the personal physician that you indicate.

For ease in collecting the information and undertaking the laboratory tests and x-rays, several station areas in our mobile laboratory van will be set up. These will be described below.

At one station the questionnaire will be completed in private with the help of a trained interviewer. It contains several sections. Sections 2, 3, 4, and 5 may have been partially or totally filled out from existing records, but may need additional information from you at the time of your private interview. The following is a description of these sections:

1. The first section is the consent form explained above.
2. The second section is an identification section that gives general information about you, including your name, address,

telephone number, age, sex, race, marital status, and education. The name, address, and telephone number are primarily taken down so that you could be contacted if necessary, but these will not appear in any reports or conclusions drawn from the study.

3. The third section asks about your past work history. It will include the years you worked at a particular job, what the industry was and what type of product was made. We are especially interested in previous work exposure to dust, gases, fumes, or chemicals and to their types, if known. If you worked where you did not have exposure to these substances, the details are not as important in this section.

4. Section four deals with your present work history as to the company you are working with now, how long you have been with that company, and what your present job is. Then there is a detailed section of the different types of work that you may have done at your current place of employment.

5. Section five lists the hospitalization you have had and asks for the year of hospitalization and how long you stayed. This is for your last four hospitalizations, if you have had that many.

6. Section six is a set of questions about your lungs as to cough, wheezing, phlegm, and shortness of breath.

7. Section seven asks about some of the major illnesses that you and your immediate family have or may have had, and asks in your case for details as to age of onset, and length of illnesses, and whether medication is being taken for any of the illnesses you may list.

8. Section eight is a history of your smoking habits, if you are or have been a smoker.

9. Section nine asks about the use of a respirator at your job.

In the same general area where the questionnaire is being completed, your height, weight, and blood pressure will be recorded.

Depending on the order of scheduling, the following additional procedures will be done in specified areas:

1. A breathing test which will measure how well you breathe and which will show how much air you can hold in your lungs and how rapidly you move it out of your lungs. You will simply be asked to take in a deep breath and blast the air

out into the machine as fast as you can and empty all the breath you can into the machine. This will be repeated five times to get your best effort.

2. A breathing test which will measure how much gas you remove from you lungs, especially through the passages in the deepest part of your lung. First, you will simply hold some oxygen gas in your lungs, and then slowly breathe out into a machine for a short period while we measure the gases in your breath.

3. X-rays of your chest will be made. Proper shielding will be given you to protect you from the radiation.

4. A sample of blood will be drawn from you arm under sterile conditions.

5. A sample of your sputum (spit from your lungs) will be collected. To assist you we will have a fine mist for you to inhale; this mist is harmless but helps you bring up sputum.

In the event that you cannot have these things all accomplished at one time, you may be rescheduled for a later time.

In all these procedures there appears to be minimal or no risk in accomplishing them.

You will be given the opportunity to have any questions you may have about this study answered by the investigators. It is important for you to realize that you are entering this study entirely voluntarily and are free to withdraw without any penalty at any time.

It is also important to note that the data collected in this research study will be kept as confidential data shared only among the various investigators and your personal physician if you have designated him to receive the information. The investigators are as follows:

Principal Investigator: David P. Discher, M.D.

Principal Co-investigators: Miles O. Colwell, M.D., William J. Bovard, M.D., Bertram D. Dinman, M.D., Sherman Williamson, M.D., James P. Hughes, M.D., Frank B. Metting, M.D., and Bryce D. Breitenstein, M.D.

Associate Investigators: Abraham I. Schweid, M.D., Donovan Thompson, Ph.D., Peter Breysse, M.P.H.

Appendix C

WRITTEN CONSENT

DEPARTMENT OF ENVIRONMENTAL HEALTH
UNIVERSITY OF WASHINGTON
SEATTLE, WASHINGTON 98195

OCCUPATIONAL HEALTH STUDY

Section 1

_____
Questionnaire Number

ASSURANCE OF CONFIDENTIALITY

The University of Washington and the National Institute for Occupational Safety and Health give their assurance that your identity and relationship to any information obtained by reason of your participation in the study will be kept confidential and will not otherwise be disclosed except as authorized below. Specifically, only the Study Team will have access to this information and it will not be available to any agency or employer. Your individual findings will be released only to you and to the personal physician you may designate below.

David P. Discher, M.D.
Associate Professor
Department of Environmental Health

Marcus M. Key, M.D.
Assistant Surgeon General, Director
National Institute for Occupational Safety and Health

CONSENT AND AUTHORIZATION TO RELEASE MEDICAL INFORMATION

I hereby voluntarily agree to participate in the study which will be conducted by the University of Washington. I understand that in addition to my answering the questionnaire, blood, urine, and sputum specimens will be collected, and X-rays and breathing tests will be done.

_____ _____
Date Signature

I hereby request the University of Washington to inform my personal physician should there be any significant medical findings from this study.

_____ _____
Date Signature

Name and Address of Personal Physician

_____

_____

_____

Witnessed by_____

Preceding page blank

Appendix D

IDENTIFICATION CARD

ALUMINUM OCCUPATIONAL HEALTH STUDY

Name:

Study number:

1. Spirometry_____ 4. X-ray_____

2. Closing volume_____ 5. Blood_____

3. Sputum_____ 6. Questionnaire_____

Ht.	Wt.	Age	B.P.	Comments
in.	lb.			

Identification Card

Appendix E

QUESTIONNAIRE

INTERVIEWER INSTRUCTIONS

Introduction

The purpose of the questionnaire is to obtain a work and medical history which can be used along with the laboratory tests to determine the effects, if any, of effluents in the aluminum industry on those workers in the immediate vicinity of the reduction pots.

The data from the records will be placed on computer cards, so it will be necessary to be as accurate as possible with the realization that many of the answers are only estimates and that rounding off of times and durations will be necessary.

The questionnaire has been broken down into sections for ease of identification. These sections are as follows:

Section 1 - Consent and Confidentiality Form

Section 2 - Identification Data

Section 3 - Past Work History

Section 4 - Present Work History and Respirator usage

Section 5 - Hospitalizations

Section 6 - Current Respiratory History

Section 7 - Medical Illnesses

Section 8 - Smoking History.

The questions have been selected on the basis of literature review of effects of aluminum reduction effluents and from questions used in other industrial surveys.

Part of Section 4 will be filled out by our data clerical staff from company personnel records, a copy of which is attached to the questionnaire,

but it will be necessary to review this information for accuracy with the subject and note any variance in writing.

Pretesting of the questionnaire showed that about 10-20 minutes were usually required to complete the interview depending on the number of positive answers.

It is intended that the interviewer will ask each of the questions and record the answers and observations, giving any additional explanation that seems necessary to clarify for the respondent.

Section 1

In most cases, the consent form will be signed in advance, but check it for completeness. If not previously signed, ask interviewee to read and sign consent form, giving any explanation needed. Also be sure to obtain the name and address of interviewee's personal physician on bottom of page.

Sections 2, 3, 4, and 5

Fill in the answer to the questions by direct interview. If the answer does not fit precoded format, please write in the margin the necessary information for evaluation at the time of review prior to keypunching.

Section 6

Question 47--observe if subject has an apparent cold or acute respiratory symptoms. Ask questions as outlined in 48 through 56, and make observation on subject as requested in question 55.

Section 7

In obtaining the medical illness portion, tell the subject you will be asking him if he has any of the illness listed and also if any of his immediate relatives listed have had the disorder. It is possible that some disorders may have occurred more than once (e.g., acute bronchitis). In this case there is enough room to record more than one number (i.e., age of onset). It would probably be best to make an average for duration of illness if more than one. In recording blood relatives in the last column, more than one can be recorded for an illness.

At end of this question, it would be well to ask again if any of the relatives listed had any of these types of illnesses and scan over the illness again, especially if respondent has named only a few or no relatives.

Some of the medical terms might not be understood by the subject. It is probably best to not record an answer unless you can be reasonably sure that the respondent understands it is not making an unwarranted self diagnosis. A method of confirmation would be to ask if a physician has told him that he has had this particular problem--e.g., "coronary insufficiency." Usually if a subject has been told he has a given diagnosis, he will remember it as such.

Section 8

Smoking History--This is generally self-explanatory. Please use the number of cigarettes rather than packs (there are 20 in an average package). A pipe tabacco can contains 2 oz of tabacco.

For current smokers, the section beginning with question 70 should be filled out; for former smokers the section beginning with question 76. For smokers who are current smokers and have changed their smoking habits both sections will have to be completed.

It will be necessary to fill in all answers that are not applicable with 9s or Xs if special not applicable code is provided. This will aid in reducing keypunch errors and will assume quality reviewers that the questions were all asked.

OMB-68-R-1353 PC
Expires 7/1/75

ALUMINUM OCCUPATIONAL HEALTH STUDY
QUESTIONNAIRE
JANUARY 1974

SECTION 2 - IDENTIFICATION DATA

CARD # 1 (1-2) QUESTIONNAIRE # (3-6)

1. Date ___ (7-11)

2. Interviewer ___ (12)

3. Name _____ (13-37)

4. Address _____ (38-63)

City _____ (64-72) Dose category ___ (73-74)

Zip code _____ (75-79) SURVEY 1 (80)

CARD # 0 2 (1-2) QUESTIONNAIRE # (3-6)

5. Home telephone _____

6. Age ___ (7-8)

7. Sex ___ (9)

8. Race: Black 1 Chicano 7

Oriental 4 White 6 Other 5 _____ (10)
specify

9. Marital status: Single 1 Married 2

Widowed 3 Separated 4 Divorced 5 (11)

10. Education, years ___ (12-13)

11. Height ___ (14-17)
inches

12. Weight ___ (18-20)
pounds

13. Blood pressure ___/___ (21-26)

SECTION 3 - RELEVANT PAST WORK HISTORY

			Years at this job (if greater than ½ year raise to next whole year
Have you ever worked in a dusty job:			
14. At a coal mine?	Yes ☐ No ☐ (27)		years ☐☐ NA ☐ (28-29)
15. At any other mine? _____ specify	Yes ☐ No ☐ (30)		years ☐☐ NA ☐ (31-32)
16. At a quarry?	Yes ☐ No ☐ (33)		years ☐☐ NA ☐ (34-35)
17. At a foundry?	Yes ☐ No ☐ (36)		years ☐☐ NA ☐ (37-38)
18. At a pottery?	Yes ☐ No ☐ (39)		years ☐☐ NA ☐ (40-41)
19. At a cotton, flax, or hemp mill?	Yes ☐ No ☐ (42)		years ☐☐ NA ☐ (43-44)
20. At any other dusty job? _____ specify	Yes ☐ No ☐ (45)		years ☐☐ NA ☐ (46-47)
Have you ever worked in an area where you encountered:			
21. Welding and soldering fumes?	Yes ☐ No ☐ (48)		years ☐☐ NA ☐ (49-50)
Have you ever worked with:			
22. Asbestos?	Yes ☐ No ☐ (51)		years ☐☐ NA ☐ (52-53)
23. Beryllium?	Yes ☐ No ☐ (54)		years ☐☐ NA ☐ (55-56)
24. Cadmium or its compounds?	Yes ☐ No ☐ (57)		years ☐☐ NA ☐ (58-59)
25. Ceramic acid dust?	Yes ☐ No ☐ (60)		years ☐☐ NA ☐ (61-62)
26. Epoxy resins?	Yes ☐ No ☐ (63)		years ☐☐ NA ☐ (64-65)
27. Fiber glass?	Yes ☐ No ☐ (66)		years ☐☐ NA ☐ (67-68)
28. Other chemicals, gases, fluids or metals that you or your employer considered to be dangerous or hazardous? _____ specify	Yes ☐ No ☐ (69)		years ☐☐ NA ☐ (70-71)
29. Verified:	Yes ☐ No ☐ (72)		

SKIP (73-79)

SURVEY ☐ (80)

NOTES OR COMMENTS:

SECTION 4 - PRESENT WORK HISTORY AND RESPIRATOR HISTORY

CARD # 01 (1-2) QUESTIONNAIRE # (3-6)

Job - Dose	Total Duration
30. ___ (7-8)	years ___ NA 99 (9-10)
31. ___ (11-12)	years ___ NA 99 (13-14)
32. ___ (15-16)	years ___ NA 99 (17-18)
33. ___ (19-20)	years ___ NA 99 (21-22)
34. Verified: Yes __ No__ (23)	SKIP (24-59)

IF "NO", NOTE ANY DISCREPANCIES OR COMMENTS BELOW:

INTERVIEWER: If where the respirator was worn was other than at an aluminum reduction plant, write details under NOTES AND COMMENTS below.

35. Have you ever worn a respirator on the job? Yes 1 No 0 (60)

If "yes", what type did you wear?

36. Cartridge type	Percent time worn ___ NA 99 (61-62)
37. Cloth or paper type	Percent time worn ___ NA 99 (63-64)
38. Other _____	Percent time worn ___ NA 99 (65-66)

Approximately how long did you wear the respirator? (Use only whole number of years, raise ½ year or more to next whole number of years.)

39. Cartridge type	years ___ NA 99 (67-68)
40. Cloth or paper type	years ___ NA 99 (69-70)
41. Other _____	years ___ NA 99 (71-72)
SKIP (73-79)	SURVEY 1 (80)

NOTES AND COMMENTS:

SECTION 5 - HOSPITALIZATIONS

CARD # ___ (1-2) QUESTIONNAIRE # (3-6)

42. Have you been hospitalized more than four times during the past ten years? Yes 1 No 0 (7)

List last four hospitalizations:

	Year	Reason (specify)	Code	Length of Stay-Days	
43.					(8-16)
44.					(17-25)
45.					(26-34)
46.					(35-43)

SKIP (44-79) SURVEY 1 (80)

SECTION 6 - CURRENT RESPIRATORY HISTORY

CARD # ___ (1-2) QUESTIONNAIRE # (3-6)

47. INTERVIEWER: Does the subject have a cold or acute respiratory symptoms? Yes 1 No 0 (7)

PREAMBLE: I am going to ask you some questions about your chest. Please answer "yes" or "no" whenever possible.

48. Do you cough first thing in the morning (when you get up) on more than 50 days in a year? Yes 1 No 0 (8)

IF "YES" TO # 48 ASK: How many years have you coughed like this? years ___ NA 99 (9-10)

49. Do you bring up any phlegm from your chest first thing in the morning (when you get up) on more than 50 days in a year? Yes 1 No 0 (11)

50. Do you bring up any phlegm from your chest later in the day on more than 50 days in the year? Yes 1 No 0 (12)

51. IF "YES" TO EITHER # 48, 49, OR 50 ASK: Does most of this coughing (and phelgm) come during just one season of the year? No 0 Winter 1 Spring 4 Summer 3 Fall 5 NA 9 (13)

52. In the past three years have you had a period of INCREASED cough and phlegm lasting for three weeks or more? Yes 1 No 0 (14)

IF "YES" TO # 52 ASK: Have you had more than one such period? Yes 1 No 0 NA 9 (15)

53. Do you ever have wheezing noises in your chest? Yes 1 No 0 (16)

IF "YES" TO # 53 ASK: On how many days did this happen during the past year? days ___ NA 999 (17-19)

54. Do you suddenly become short of breath when taking it easy (not exercising)? Yes 1 No 0 (20)

IF "YES" TO #54 ASK: On how many days did this happen during the past year? days ___ NA 999 (21-23)

55. INTERVIEWER: Does subject appear to be disabled (crippled) by reason other than shortness of breath? _____ _____ reason Yes 1 No 0 (24)

56. Are you troubled by shortness of breath when hurrying on level ground or walking up a slight hill? Yes 1 No 0 (25)

IF "YES" TO # 56 ASK: Do you get short of breath walking with other people your own age on level ground? Yes 1 No 0 NA 9 (26)

IF "YES" TO ABOVE QUESTION ASK: Do you have to stop for breath when walking at your own pace on level ground? Yes 1 No 0 NA 9 (27)

SKIP (28-79) SURVEY 1 (80)

SECTION 7 - MEDICAL ILLNESSES

PREAMBLE: "I am going to ask you some questions about medical illnesses you may have or have had and whether any of your immediate family have had these illnesses. The family members I am interested in knowing about are your parents, brothers, sisters, spouse and your children. If you have or had any of these illnesses, I will ask you additional questions. Have you had _____ (asthma, etc.)."

For any illnesses that the respondent indicates he has had or has ask: "At what age did the _____ (e.g. asthma) start? How long did it last? Is it still present? Are you taking medication for it now?" Please record the answers in the spaces provided. Please record a 9 in each unused space for questions 57 through 67.

Key to blood relatives: 1. Father 2. Mother 3. Sibling 4. Spouse
5. Children 6. All 9. None

CARD # ___ (1-2) QUESTIONNAIRE # (3-6)

	Illness	?	Age Onset	Duration	Still Present	Currently Medicated	Blood Relatives Who Had This	
57.	Asthma	Yes			Yes	Yes		
		No		years	No	No		(7-17)
58.	Emphysema	Yes			Yes	Yes		
		No		years	No	No		(18-28)
59.	Acute bronchitis	Yes			Yes	Yes		
		No		days	No	No		(29-39)
60.	Chronic bronchitis	Yes			Yes	Yes		
		No		years	No	No		(40-50)
61.	Pneumonia	Yes			Yes	Yes		
		No		days	No	No		(51-61)
62.	Pulmonary tuberculosis	Yes			Yes	Yes		
		No		months	No	No		(62-72)

SKIP (73-79) SURVEY ___ (80)

CARD # ___ (1-2) QUESTIONNAIRE # (3-6)

63.	Sinusitis	Yes			Yes	Yes		
		No		days	No	No		(7-17)
64.	Lung tumor	Yes			Yes	Yes		
		No		years	No	No		(18-28)
65.	Cancer or tumor of an other organ ____ specify	Yes			Yes	Yes		
		No		years	No	No		(29-39)

	Illness	?	Age Onset	Duration	Still Present	Currently Medicated	Blood Relatives Who Had This
66.	Heart attack	Yes 1			Yes 1	Yes 1	
		No 0		days	No 0	No 0	(40-50)
67.	High blood pressure	Yes 1			Yes 1	Yes 1	
		No 0		years	No 0	No 0	(51-61)

SKIP (62-79) SURVEY 1 (80)

NOTES AND COMMENTS:

SECTION 8 - SMOKING HISTORY

CARD # 5 (1-2) QUESTIONNAIRE # (3-6)

68. Have you ever smoked? (Record NO if subject never smoked as much as 1 cigarette a day, or 1 ounce of tobacco a month for as long as 1 year, or 20 packs or 12 ounces in a life time.) Yes 1 No 0 NA 9 (7)

INTERVIEWER: If response is "no," disregard remaining questions.

69. Do you smoke now? (CHECK ONLY ONE BOX BELOW) Yes 1 No 0 (8)

If "no," did you:

a. Smoke cigarettes only? (IF "YES" GO TO QUESTION 76) Yes 1 No 0 NA 9 (9)

b. Smoke cigars or pipe only? (IF "YES" GO TO QUESTION 76) Yes 1 No 0 NA 9 (10)

c. Smoke both or all three? (IF "YES" GO TO QUESTION 76) Yes 1 No 0 NA 9 (11)

If "yes," have you:

a. Smoked only cigarettes? Yes 1 No 0 NA 9 (12)

b. Smoked only cigars or pipe? Yes 1 No 0 NA 9 (13)

c. Smoked cigarettes but are smoking cigars or pipe? Yes 1 No 0 NA 9 (14)

d. Currently smoking both cigarettes and cigars or pipe? Yes 1 No 0 NA 9 (15)

70. Current smoking activities:

How many cigarettes do you usually smoke in a week? ___ NA 999 (16-18)

How many cigars do you usually smoke in a week? ___ NA 99 (19-20)

How many ounces of pipe tobacco do you usually smoke in a week? ___ NA 99 (21-22)

How many ounces of handrolled tobacco do you usually smoke in a week? ___ NA 99 (23-24)

71. Approximately how many years have you been smoking the above amounts per week?

Cigarettes years ___ NA 99 (25-26)

Cigars years ___ NA 99 (27-28)

Pipe tobacco years ___ NA 99 (29-30)

Handrolled tobacco years ___ NA 99 (31-32)

72. Are you currently smoking filter tip cigarettes?

No 0; Less than 1/2 of the time 1; 1/2 of the time 2; All the time 3; NA 9 (33)

73. Do you usually inhale the cigarette smoke into your chest?

Not at all 0; Slightly 1; Moderately 2; Deeply 3; NA 9 (34)

74. Do you usually inhale the pipe/cigar smoke into your chest? Yes 1 No 0 NA 9 (35)

75. From the time you started smoking regularly have your smoking habits changed? Yes 1 No 0 NA 9 (36)

INTERVIEWER: If "no" in question 75, skip remaining questions.

76. Past smoking activities: From the time that you started to smoke-- up to the time you quit or began smoking at your present level questions 70 and 71-- how much smoking would you say that you averaged per week?

Average cigarettes smoked per week ___ NA 9999 (37-39)

Average cigars smoked per week ___ NA 99 (40-41)

Average ounces of pipe tobacco smoked per week ___ NA 99 (42-43)

Average ounces of handrolled tobacco smoked per week ___ NA 99 (44-45)

77. Approximately how many years did you smoke the above amounts per week? (Exclude the number of years that you have been smoking at your current level as stated in questions 70 and 71)

Cigarette years ___ NA 99 (46-47)

Cigars years ___ NA 99 (48-49)

Pipe tobacco years ___ NA 99 (50-51)

Handrolled tobacco years ___ NA 99 (52-53)

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Expires 7/1/75

78. At what age did you start smoking cigarettes regularly? age __ NA 99 (54-55)

79. How old were you when you stopped smoking cigarettes regularly? age __ NA 99 (56-57)

80. Did you smoke filter tip cigarettes?

No 0; Less than 1/2 of the time 1; 1/2 of the time 2; All the time 3; NA 9 (58)

81. Did you usually inhale the cigarette smoke into your chest?

Not at all 0; Slightly 1; Moderately 2; Deeply 3; NA 9 (59)

82. At what age did you start smoking pipe/cigars regularly? age __ NA 99 (60-61)

83. How old were you when you stopped smoking pipe/cigars regularly? age __ NA 99 (62-63)

84. Do (did) you usually inhale the pipe/cigar smoke into your chest? Yes 1 No 0 NA 9 (64)

SKIP (65-79) SURVEY 1 (80)

NOTES AND COMMENTS:

UNIVERSITY OF WASHINGTON

OCCUPATIONAL HEALTH SURVEY
SMOKING QUESTIONNAIRE

INSTRUCTIONS: Below your name, please fill in your staff employee number, the department where you work, and your age in years. Then answer the questions regarding your smoking habits.

CARD # 3 0 (1-2) SHOP ☐ 1 CUSTODIAN ☐ 2 (3)

Name _____ (4-28)

University Staff Employee # _____ (29-33)

Physical Plant Department _____

Age _____ years (34-35)

PLEASE PUT AN "X" IN THE BOX THAT BEST ANSWERS THE QUESTION

1. Have you ever smoked cigars or a pipe? (Mark "No" if you have smoked less than 12 cigars and/or 12 pipefuls of tobacco in your life) Yes ☐ 1 No ☐ 2 (36)

2. Have you ever smoked cigarettes? (Mark "No" if you have smoked less than 20 packages of cigarettes or 12 ounces of tobacco in your life) Yes ☐ 1 No ☐ 2 (37)

SKIP THE REST OF THE QUESTIONS IF YOU ANSWERED QUESTION 2 "No"

3. Do you smoke cigarettes now? Yes ☐ 1 No ☐ 2 (38)

4. How many packages of cigarettes (average) do you or did you smoke and for how many years? (Please write in the numbers)

_____ packages of cigarettes a day (average*) (39-42)

for _____ years. (43-44)

SKIP (45-79) SURVEY 3 (80)

*If you cannot easily make this determination please write in the space provided above, your cigarette consumption and the years that you smoked these amounts, beginning when you first started smoking and proceeding up to the present (e.g., 1 package a day for first 3 years, then 2 packages a day for next 5 years, etc.). If you roll your own cigarettes consider 20 of these cigarettes equal to one package.

Appendix F

HOSPITALIZATION DIAGNOSTIC CATEGORIES

ALUMINUM OCCUPATIONAL HEALTH STUDY

HOSPITALIZATION
DIAGNOSTIC CATEGORIES
January 29, 1974

0100 Infective and parasitic diseases
- 0120 Diseases attributable to viruses
- 0130 All other infective and parasitic diseases

0200 Neoplasms
- 0210 Malignant neoplasm of large intestine and rectum
- 0220 Malignant neoplasm of other digestive organs and peritoneum
- 0230 Malignant neoplasm of thoracic organs
- 0240 Malignant neoplasm of prostate
- 0250 Malignant neoplasm of urinary organs
- 0260 Neoplasms of lymphatic and hematopoietic tissues
- 0270 Malignant neoplasm of other and unspecified sites
- 0280 Benign neoplasms of skin
- 0290 Benign neoplasm of other and unspecified organs and tissues and neoplasms of unspecified nature

0300 Allergic, endocrine system, metabolic, and nutritional diseases
- 0310 Hay fever and asthma
- 0320 Diseases of thyroid gland
- 0330 Diabetes mellitus
- 0340 All other allergic, endocrine, metabolic, and nutritional diseases

0400 Diseases of blood-forming organs

0500 Mental, psychoneurotic, and personality disorders
- 0510 Acute brain disorders
- 0520 Chronic brain disorders
- 0530 Psychotic disorders
- 0540 Depressive reaction
- 0550 Other psychoneurotic disorders
- 0560 All other mental, psychoneurotic and personality disorders

0600 Diseases of the nervous system and sense organs

- 0610 Vascular lesions affecting central nervous system
- 0620 Other diseases of central nervous system
- 0630 Diseases of nerves and peripheral ganglia
- 0640 Cataract
- 0650 Other diseases and conditions of eye
- 0660 Diseases of ear and mastoid process

0700 Diseases of the circulatory system

- 0710 Rheumatic fever and chronic rheumatic heart disease
- 0720 Arteriosclerotic heart disease so described
- 0730 Acute coronary occlusion
- 0740 Other arteriosclerotic heart disease
- 0750 Congestive heart failure
- 0760 Hypertensive heart disease
- 0770 Other and unspecified diseases of heart
- 0780 Other hypertensive disease
- 0790 General arteriosclerosis
- 0791 Varicose veins of lower extremities
- 0792 Hemorrhoids (with or without ulcer)
- 0793 All other diseases of circulatory system

0800 Diseases of the respiratory system

- 0810 Acute upper respiratory infections
- 0820 Hypertrophy of tonsils and adenoids
- 0830 Influenza
- 0840 Bronchopneumonia
- 0850 Primary atypical pneumonia
- 0860 Pneumonia, other and unspecified
- 0870 Acute bronchitis (or subacute)
- 0880 Bronchitis, unqualified and chronic without emphysema
- 0890 Emphysema (with or without bronchitis)
- 0891 All other diseases of respiratory system

0900 Diseases of the digestive system

- 0910 Diseases of buccal cavity and esophagus
- 0920 Ulcer of stomach, duodenum, and gastrojejunal ulcer
- 0930 Gastritis and duodenitis
- 0940 Appendicitis
- 0950 Inguinal hernia
- 0960 Other hernia of abdominal cavity
- 0970 Intestinal obstruction without mention of hernia
- 0980 Gastroenteritis and colitis, except ulcerative
- 0990 Chronic enteritis and ulcerative colitis
- 0991 Cholelithiasis
- 0992 Cholecystitis and cholangitis without emention of calculi
- 0993 Diseases of liver, gallbladder, and pancreas, except cholelithiasis and cholecystitis
- 0994 All other diseases of digestive system

1000 Diseases of the genitourinary system

- 1010 Infections of kidney
- 1020 Calculi of kidney and ureter
- 1030 Other diseases of kidney and ureter
- 1040 Cystitis
- 1050 All other deseases of urinary system
- 1060 Hyperplasia of prostate
- 1070 Other diseases of male genital organs

1200 Diseases of the skin and cellular tissue

- 1210 Infections of skin and subcutaneous tissue
- 1220 All other diseases of skin and cellular tissue

1300 Diseases of the bones and organs of movement

- 1310 Osteoarthritis (arthrosis) and allied conditions
- 1320 Other and unspecified froms of arthritis and rheumatism except rheumatic fever
- 1330 Displacement of intervertebral disc
- 1340 Synovitis, bursitis and tenosynovitis
- 1350 All other diseases of bones and organs of movement

1400 Congenital malformations

1500 Certain diseases of early infancy

1600 Symptoms, senility, ill-defined conditions and special admissions

- 1610 Symptoms referable to respiratory system
- 1620 Symptoms referable to abdomen and gastrointestinal system
- 1630 All other symptoms
- 1640 Observation, examinations and aftercare
- 1650 Undiagnosed disease and diagnosis not codable

1700 Injuries and adverse effects of chemical and other external causes

- 1710 Fracture of skull and face bones
- 1720 Fracture of radius and ulna (either or both)
- 1730 Fracture of neck of femur
- 1740 Fracture of other and multiple sites
- 1750 Dislocation without fracture
- 1760 Sprains and strains of back (including neck)
- 1770 Head injury (excluding skull fracture)
- 1780 Open wound of eye, ear and face
- 1790 Laceration and open wound of other and multiple sites
- 1791 Burns
- 1792 All other injuries
- 1793 Complications of surgical procedures
- 1794 All other adverse effects of chemical and other external causes

Appendix G

SPUTUM CYTOLOGY PROCESSING AND CLASSIFICATION

Appendix G

SPUTUM CYTOLOGY PROCESSING AND CLASSIFICATION

Sputum production was induced by inhalation of 5% propylene glycol aqueous mist. The specimen, preserved in a 2% propylene glycol and 50% ethanol solution, was transmitted to the laboratory where smears were prepared by the Saccomanno concentration method.[24] The smears were stained by the Papanicolaou method and screened by registered cytotechnologists under the supervision of one of the authors (AIS). Sputa were categorized as:

Negative	No abnormal cells and/or regular metaplasia.
Atypical	Mild and moderate atypical squamous metaplasia.
Suspicious	Severe atypical squamous metaplasia and/or cells suggestive but not diagnostic of malignancy.
Positive	Cells diagnostic of squamous carcinoma in situ or invasive carcinoma.

The criteria for the various grades of metaplasia, carcinoma in situ, and invasive carcinoma were those of Saccomanno.[25,26]

Appendix H

SERUM TESTS FOR ALPHA$_1$ ANTITRYPSIN

Appendix H

SERUM TESTS FOR ALPHA$_1$ ANTITRYPSIN

Serum Trypsin Inhibitory Capacity (STIC)

Serum samples were sent to the City of Hope where a spectrographic method[27] was used that is an adaptation of two previous methods (Schwert and Takanaka, and Homer, Katchman, and Zipf). The method has been shown to be reliable for repeated analysis with serum at room temperature for over two weeks. Activity was measured using benzoyl-L-arginine ethyl ester as a substrate. The number of milligrams of trypsin inhibited by 1 milliliter of serum was determined by plotting the trypsin activity as a function of undiluted serum added, extrapolating the early linear portion of the curve to obtain the quantity of serum causing 100% inhibition.

Acid Starch Gel Electrophoresis (Phenotyping)

Serum samples sent to the City of Hope were also processed for phenotyping.[28] All samples with low STIC values were phenotyped, and a large portion of the remaining or "normal" samples were also phenotyped. The method used was modified from Fagerhol. Electrophoresis of serum on acid-starch gels causes the alpha$_1$ antitrypsin protein to migrate to the anode, similar to serum haptoglobin. The latter can be prevented by adding hemoglobin to the serum. Protein bands of the alpha$_1$ antrypsin proteins can be distinguished for various phenotypes. Since this method has difficulty in the recognition of heterozygous Z variants, confirmation of such results was obtained using the antigen-antibody crossed electrophoresis. At the City of Hope a modification of the Laurell method is used.

Radial Immunodiffusion (RID)

The serum samples were also processed at the University of Washington using another screening test method. RID was performed according to a method of Dietyz, Rubinstein, and Hodges[29] with data obtained using techniques shown by Berne[30] to increase reliability. The basic principal is that an antibody to the serum protein is incorporated in agar. Sera are placed in wells in the agar and the precipitin ring diameter can be measured after movement is stable.

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Appendix I

SERUM FLUORIDE AND URINE FLUORIDE DETERMINATIONS

Appendix I

SERUM FLUORIDE AND URINE FLUORIDE DETERMINATIONS

Serum Fluoride Determination

The serum unbound fluoride determination was made using the technique of Fry and Taves [31] with an anion fluoride electrode in conjunction with a pH meter, results being expressed in parts per million. Normal values are 0.1-0.2 mg% in communities with fluoridated water.[32]

Urine Fluoride Determination

Urine fluoride determination were made using a Fluoride Specific ion electrode in conjunction with a pH meter. The results were expressed in mg/liter, corrected to a specific gravity of 1.024.

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Appendix J

SPIROMETRY CLASSIFICATION SCHEME

Appendix J

SPIROMETRY CLASSIFICATION SCHEME

The electronic spirometer used in this study required calibration and computer processing of the digital volume signals on magnetic tape. Two basic computer programs were used, CALIB and SPIRO. The former gives to each electronic voltage signal a corresponding liter value; the latter processes this calibration factor and a temperature and barometric pressure correction factor (BTPS), and calculates the various ventilatory parameters in relationship to regression equations for nonsmoking normals.

CALIB deals with a sine wave electronic signal generated by pumping air in and out using a mechanical calibrator. The observed mean electronic signal from repeated pumping is used as a ratio of the known volume of 5 liters, thus establishing a liter to signal factor.

SPIRO deals with signals from repeated inputs of air from subjects tested. The electronic signal after baseline has been exceeded plus 500 digits is the voltage for the FEV_1. It is converted to liters by subtracing the baseline voltage from this voltage at the 500th digit above baseline and multiplying this by a calibration factor and a BTPS correction factor. To convert this liter value to deviation units two steps were taken:

- Calculate predicted value using the equation

  FEVPRE = - 1.6789 + (- 0.0263 × age) + (0.1326 × height) .

- Subtract the predicted liter value from the observed value and divide by the deviation value

  DEV(2) = 0.5274 .

The following example serves to illustrate this process:

Subject code number 2102

Age = 43 years

Height = 68 inches

Calibration factor = 1.11

BTPS correction factor = 1.0964 (21° C at 760 mm)

$$\text{Predicted } FEV_{1.0} = -1.6789 + (-0.0262 \times 43) + (0.1326 \times 68)$$
$$= 3.66$$

$$\text{Observed } FEV^{*}_{1.0} = 4.388 \times 1.11 \times 1.0964$$
$$= 5.34 \text{ liters}$$

$$\text{Deviations from predicted} = \frac{5.34 - 3.66}{0.5274} = 3.17^{\dagger}$$

SPIRO also processes 53 other ventilatory measurements for each trial, calculates a prediction for six parameters, categorizes the best observed value in relation to the predicted, and establishes the reliability of the test by comparing the best value with the second best value. The final outputs are tape images for all calculations and an 80 column data card for each subject which is the key data from five trials. The following sheets are detailed documentation for CALIB and SPIRO.

---

*This was trial number two out of five, and it was the best $FEV_{1.0}$ value. The 4.388 was the 500th (1-second) signal in excess of baseline.

†This value is well above predicted; i.e., 3.17 deviation units better than a male of age 43 who is 68 inches tall.

Program CALIB

Purpose

CALIB computes a calibration factor for each data tape from information on it, in order to relate the numbers recorded on tape to those registered mechanically on the spirometer.

Procedure

CALIB reads through all records on the data tape and finds those that are recordings of the mechanical spirometer calibration procedure. All data records have an 18-digit header; these particular records are identified by 14999999999999 in digits 5-18.

For each such record, CALIB finds the first "trough" and then the first subsequent "peak" in the calibration values and prints the difference as the "calibration mean." If the volumes recorded electronically were exactly the same as those registered mechanically, the calibration mean would be 5.000 liters and the calibration factor would be 1.00; otherwise, the mean should be within half a liter or so of 5, and the factor is 5.000/mean.

A trough is defined as the point at which the change from the preceding volume sample is zero or negative, and the change to the following volume is positive. In other words, given three subsequent volume samples, X_1, X_2, and X_3, point X_2 is a "trough" if $(X_2 - X_1) \leq 0$ and $(X_3 - X_2) > 0$.

Similarly, a peak is defined as the point at which the change from the preceding volume sample is zero or positive, and the change to the following sample is negative. That is, for some three points X_1, X_2, and X_3, point X_2 is a "peak" if $(X_2 - X_1) \geq 0$ and $(X_3 - X_2) < 0$.

Program SPIRO

Purpose

SPIRO processes spirometry data recorded on nine-track magnetic tape with a Beckman digicorder, for which the calibration factor is known (computed by program CALIB).

Procedure

To hand reproduce the output of SPIRO, "beginning of person" is marked by a 0 record for each trial for that person, on Channel 13 or 14.

The array printed by KELLER (100 samples/second, with each sample an average of five samples from the original 500 samples/second input) is the same as array OUT in SPIRO; it is the raw volume in liters registered in the spirometer. The instantaneous flow at the time of any of the printed samples is taken as the difference in volume between that sample and the next; since the samples are 0.01 seconds apart, this difference gives a flow in liters per hundredth of a second, which is multiplied by 100 to attain liters/second.

The data record (the array) hopefully begins before the actual start of trial (beginning of exhalation) and ends after the end of trial, so that you can see several samples of the electronic background (baseline) at the beginning and end of the record. The program currently requires five samples of background before beginning of trial, which it defines as an increase of at least 0.01 liters from one sample to the next; the sample just before the one showing the increase is taken as beginning of trial, but this must be no earlier than sample five for the trial to be accepted. If the first 0.01 liter increase occurs before that point the trial is declared invalid, with no stable baseline. End of trial is said to occur at the last sample before a decrease in volume, which occurs when

the subject inhales. If that sample is one of a whole string of samples with the same value, end of trial is taken as the first sample of the string.

All samples included in the trial have to be multiplied by the BTPS correction, computed once for each person by SPIRO, and the calibration factor for the entire tape, computed by CALIB.

To get the actual volume in liters at any sample, the background reading must be subtracted. To allow for electronic drift, the background level is taken as a weighted average of all samples before beginning of trial, with the weight greatest on the samples closest to beginning of trial. To compute the background reading at beginning of trial:

(1) Average the first two samples of the record together.

(2) Consider the result as a sample, and average it together with the next sample.

(3) Continue with step 2 up to the beginning of trial. The last sample before beginning of trial should be the last sample included, and the average taken including it gives the background reading.

The FVC is the volume expired by end of trial; to get it, subtract the background reading just computed from the value of the sample defined as end of trial.

Most times (in seconds) quoted in SPIRO output are measured from beginning of trial, not beginning of record. To get the "time" of any sample, count to get its sample number, taking beginning of trial as sample number 0, and multiply its sample number by 0.01, since samples are 0.01 seconds apart.

SPIRO output for each trial is organized into three sections. One section gives times and flow rates where particular volumes were attained; another gives volumes and flow rates at particular time intervals from

start of trial; and the third gives the time and volume at the moment of peak flow, and other volumes and flow rates at certain time intervals after peak flow.

The volume oriented section gives the time (from start of trial) and instantaneous flow rate at the samples where 0.2, 1.0, 1.2, 2.0, 3.0, 4.0, 5.0, and 6.0 liters were attained or exceeded; if a particular volume is not attained before the defined end of trial, its time is given as 99.99 and its flow rate as 0.00. Times and flow rates are also given for the samples at which the person attained FVC, 1/4 FVC, 1/2 FVC, and 3/4 FVC.

The output section concerned with specific intervals measured from start of trial gives volumes and instantaneous flow rates at 1/4, 1/2, 3/4, 1, 2, 3, and 4 seconds after start of trial; if a certain time greater than 1 second occurred after end of trial, the volume there is given as 99.99 and the flow rate at 0.00. If 1/4 second, 1/2 second, 3/4 second, or 1 second occurs after end of trial, the volume given is FVC and the flow is zero or negative.

The peak-flow-related section of output gives the time from beginning of trial and the expired volume at the sample where the subject attained peak expiratory flow, and the volumes and instantaneous flow rates at 0.10, 0.50, 1, 2, 3, and 4 seconds after he attained peak flow. If end of trial occurred before a particular interval had elapsed, the volume there is given as 99.99 and the flow rate as 0.00.

Two additional parameters are also computed. The MEFR is the average flow rate over the period from attainment of 0.2 liters expired through attainment of 1.2 liters expired; the times involved are given in the volume-oriented section. The MMEF is the average flow rate over the period beginning with the sample at which 1/4 FVC was reached or exceeded

and ending with the sample at which 3/4 FVC was reached or exceeded; these times and volumes are also available from the volume-oriented output section.

As the computations are being done for each trial, various checks are also made on the trial's reliability; the trial's output includes a reliability code, which is cause for concern if anything other than 0. The reliability codes are:

0 = SATISFACTORY TRIAL
1 = PEAK FLOW WAS MORE THAN 3.10 DEVIATION UNITS ABOVE PREDICTED
EXTREME ABNORMALITY, PROBABLE VENTURI EFFECT
2 = NO FLOW OVER 1.0 L/S IN ANY 0.01 SECOND INTERVAL
3 = FEV1.0 IS LESS THAN 1.04*FEV0.5
OR FEV2.0 IS LESS THAN 1.04*FEV1.0
4 = APPARENT INHALATION OCCURRED

When all the trials for a person have been processed, a summary of his performance with respect to six of the above parameters is published. The best value he attained in any trial is given for volume 1/2 second after start of trial ($FEV_{0.5}$), volume 1 second after start of trial ($FEV_{1.0}$), volume at end of trial (FVC), peak flow rate, flow rate when 1/2 of FVC was attained (0.50 FVC flow), and flow rate when 3/4 of FVC was attained (0.75 FVC flow). No best value given need be from the same trial as any other best value. The deviation of each best value from what was predicted as normal for the person's age, height, and sex is given in both deviation units and percentage of predicted value. The predictions are made from the results of a linear regression analysis done on performance of certain people receiving Breathmobile screening tests in Los Angeles County over several years, as published in "Development of a New Motivational Spirometer--Rationale for Hardware and Software" by Discher and Palmer, JOM, Vol. 14, No. 9 (September 1972). A person's performance is categorized on the basis of the deviation (in deviation units) of his $FEV_{1.0}$ and FVC from predicted. A deviation of not more

than 1.645 units below predicted (any amount above predicted is fine) is considered to be within normal limits. A deviation of 1.646 to 2.326 units below predicted is classed as borderline; a deviation of more than 2.326 units below predicted is considered abnormal. (Deviation in units is (best value--prediction)/standard error of estimate; see the aforementioned article.)

The spirometry categories are:

10 = FVC AND FEV1 WITHIN NORMAL LIMITS
21 = FEV1 NORMAL, FVC BORDERLINE
22 = FEV1 BORDERLINE, FVC NORMAL
23 = FEV1 AND FVC BORDERLINE
31 = FEV1 NORMAL, FVC ABNORMAL
32 = FEV1 ABNORMAL, FVC NORMAL
33 = FEV1 BORDERLINE, FVC ABNORMAL
34 = FEV1 ABNORMAL, FVC BORDERLINE
35 = FEV1 AND FVC ABNORMAL
40 = NO USABLE TRIALS

Finally, a check is made on the consistency of the person's trials and the result given as a "data category":

0 = SATISFACTORY
1 = OVER 10% DIFFERENCE IN TWO BEST FVC
2 = OVER 10% DIFFERENCE IN TWO BEST FEV1
3 = OVER 10% DIFFERENCE IN TWO BEST FVC AND FEV1
4 = ONLY ONE OR NO RELIABLE TRIAL

Annex to Appendix J

CALCULATIONS

Calculations to Get Temperature, Barometric Pressure, and BTPS Factor

```
ISTNDI=NDSTR(13)*10
ISTND=ISTNDI+NDSTR(14)
ITECH=NDSTR(9)*10+NDSTR(10)
ITEMP=NDSTR(11)+20
IF(ITEMP.GE.28) ITEMP=ITEMP-10

IBP=NDSTR(12)*10+700
IF(IBP.GE.770) IBP=IBP-100
IF(ITEMP.LE.18) PSL=15.48
IF(ITEMP.EQ.19) PSL=16.48
IF(ITEMP.EQ.20) PSL=17.54
IF(ITEMP.EQ.21) PSL=18.65
IF(ITEMP.EQ.22) PSL=19.83
IF(ITEMP.EQ.23) PSL=21.07
IF(ITEMP.EQ.24) PSL=22.38
IF(ITEMP.EQ.25) PSL=23.76
IF(ITEMP.EQ.26) PSL=25.21
IF(ITEMP.EQ.27) PSL=26.74
IF(ITEMP.EQ.28) PSL=28.35
IF(ITEMP.GE.29) PSL=30.04
TEMP=FLOAT(ITEMP)+273.16
TEMP=310.16/TEMP
PB=FLOAT(IBP)
XNUM2=PB-PSL
DENOM=PB-47.067
XPB=XNUM2/DENOM
BTPS=TEMP*XBP
```

NDSTR is the 18-word array in which each word contains the corresponding one-digit number in the header record printed by KELLER.

Calculations to Make Predictions and Define Standard Error for Men and Women

```
41      IF(ISEX.EQ.2) GO TO 42
        BASE=2.171
        FVCPRE=-3.5263+(-0.0262*AGE)+(0.1326*HT)
        FEVPRE=-1.6789+(-0.0263*AGE)+(0.0952*HT)
        PRE(1)=-0.9731+(-0.0166*AGE)+(0.0662*HT)
        PRE(4)=-1.0628+(-0.0474*AGE)+(0.2150*HT)
        PRE(5)=+2.0249+(-0.0234*AGE)+(0.0662*HT)
Men     PRE(6)=+1.2390+(-0.0249*AGE)+(0.0373*HT)
        DEV(1)=0.4125
        DEV(2)=0.5274
        DEV(3)=0.6763
        DEV(4)=1.9585
        DEV(5)=1.5306
        DEV(6)=1.1504
        GO TO 43

42      BASE=1.393
        FVCPRE=-2.1963+(-0.0195*AGE)+(0.0966*HT)
        FEVPRE=-1.0358+(-0.0212*AGE)+(0.0724*HT)
        PRE(1)=+0.0208+(-0.0138*AGE)+(0.0417*HT)
        PRE(4)=-0.5532+(-0.0331*AGE)+(0.1493*HT)
        PRE(5)=+3.2939+(-0.0244*AGE)+(0.0325*HT)
Women   PRE(6)=+1.3303+(-0.0238*AGE)+(0.0284*HT)
        DEV(1)=0.3494
        DEV(2)=0.3730
        DEV(3)=0.4719
        DEV(4)=1.3321
        DEV(5)=1.1369
        DEV(6)=0.9162
```

```
PRE(1) = prediction of FEV at 1/2 second
PRE(2) = prediction of FEV at 1 second
PRE(3) = prediction of FVC
PRE(4) = prediction of peak flow
PRE(5) = prediction of flow at 1/2 FVC
PRE(6) = prediction of flow at 3/4 FVC
```

where

```
HT=DSTR(7)*10.+DSTR(8)
WT=DSTR(9)*100.+DSTR(10)*10.+DSTR(11)
AGE=DSTR(12)*10.+DSTR(13)
```

For both sexes, DSTR is the floating point version of NDSTR, and DEV(1) is the standard error for PRE(1), and so on.

Sample Outputs

On the following pages are results of computer calculations. Sample Output, Type 1, shows a summary of the calculations on 13 people. Sample Output, Type 0, shows the detailed results of calculations for one person.

SAMPLE OUTPUT, TYPE 1

CALIBRATION FACTOR= 1.11 OUTPUT TYPE=1

PROGRAM WILL SKIP 0 RECORDS AND PROCESS THE NEXT 9999 RECORDS IF POSSIBLE.

ID	AGE	HT	WT	FEV.5	PRE	DEV	FEV1.	PRE	DEV	FVC	PRE	DEV	FEFPK	PRE	DEV	FEF50	PRE	DEV	FEF75	PRE	DEV	S	D	MT	SX
2102	43.	68.	179.	4.14	2.81	3.22	5.34	3.66	3.17	6.46	4.36	3.10	21.18	11.52	4.93	7.06	5.52	1.01	2.43	2.70	-0.24	10	0	5	1
2227	33.	74.	242.	4.30	3.38	2.24	5.24	4.50	1.41	6.28	5.42	1.25	21.18	13.28	4.03	7.06	6.15	0.59	3.16	3.18	-0.01	10	0	5	1
2232	46.	72.	170.	4.04	3.03	2.45	5.10	3.97	2.16	5.75	4.82	1.38	14.60	12.24	1.21	8.76	5.71	1.99	3.16	2.78	0.33	10	4	1	1
2224	19.	69.	150.	3.19	3.28	-0.21	4.16	4.39	-0.43	4.93	5.13	-0.29	18.99	12.87	3.12	6.32	6.15	0.44	2.92	3.34	-0.36	10	0	5	1
2197	32.	70.	175.	3.94	3.13	1.96	5.68	4.14	2.92	6.91	4.92	2.95	14.12	12.47	0.84	6.82	5.91	0.59	3.65	3.05	0.52	10	3	4	1
2 95	23.	67.	136.	3.89	3.08	1.95	5.17	4.09	2.04	6.22	4.76	2.16	13.39	12.25	0.58	6.09	5.92	0.11	3.16	3.17	-0.00	10	0	5	1
2 79	51.	72.	232.	3.35	2.95	0.97	4.43	3.83	1.13	5.95	4.68	1.87	14.60	12.00	1.33	4.38	5.60	-0.79	1.46	2.65	-1.04	10	9	3	1
2 78	22.	75.	223.	4.74	3.63	2.71	6.35	4.88	2.70	7.40	5.84	2.30	15.09	14.02	0.59	9.01	6.48	1.65	4.14	3.49	0.56	10	0	5	1
2150	28.	71.	168.	3.83	3.26	1.38	4.95	4.34	1.15	5.68	5.15	0.78	14.92	12.87	1.04	6.12	6.07	0.03	2.20	3.19	-0.86	10	2	3	1
2168	34.	68.	147.	2.15	3.63	-2.13	3.07	4.00	-1.75	5.04	4.73	0.45	7.79	12.16	-2.23	2.43	5.80	-2.20	1.46	2.97	-1.31	22	2	2	1
2226	37.	71.	181.	2.99	3.11	-0.29	3.80	4.11	-0.58	4.89	4.92	-0.05	16.79	12.45	2.22	5.60	5.86	-0.17	1.95	2.97	-0.89	10	0	4	1
2175	33.	69.	177.	4.01	3.65	2.33	5.74	4.02	3.26	7.52	4.76	4.05	17.04	12.21	2.47	5.84	5.82	0.01	2.43	2.93	-0.45	10	0	5	1
2171	28.	72.	204.	4.29	3.33	2.33	5.41	4.44	1.84	6.40	5.29	1.65	16.55	13.09	1.77	7.79	6.14	1.08	3.16	3.23	-0.05	10	3	5	1

SAMPLE OUTPUT, TYPE 0

CALIBRATION FACTOR= 1.11 OUTPUT TYPE=0

PROGRAM WILL SKIP 0 RECORD AND PROCESS THE NEXT 9999 RECORDS IF POSSIBLE.

SUBJECT NUMBER 3-103 SEX MALE AGE=43.YEARS HEIGHT=68.INCHES WEIGHT=175.LBS. TEMP. NO. 3 3

PREDICTED VALUES: FEV0.5= 2.91 FEV1.0= 3.65 FVC= 4.35 PEAK FLOW=11.52 0.50FVC FLOW= 5.52 0.75FVC FLOW= 8.79

TRIAL	*	VOLUME(L)	TIME(SEC)	FLOW(L/S)	*	TIME(SEC)	VOLUME(L)	FLOW(L/S)	*	TIME(SEC)	VOLUME(L)	FLOW(L/S)	*
	*	0.2	0.05	11.44	*	1/4	2.63	7.06	*PEAK	0.09	0.76	15.09	*
	*	1.0	0.11	14.12	*	1/2	3.92	3.89	*	+.10	2.09	9.93	*
	*	1.2	0.13	13.87	*	3/4	4.70	2.19	*	+.50	4.35	3.65	*
	*	2.0	0.15	9.53	*	1.0	5.13	1.45	*	+1.0	5.24	1.13	*
	*	3.0	0.31	5.84	*	2.0	5.83	0.50	*	+2.0	5.85	0.19	*
1	*	4.0	0.52	3.09	*	3.0	6.03	0.73	*	+3.0	6.08	1.09	*
(14)	*	5.0	0.82	1.22	*	4.0	99.99	0.00	*	+4.0	99.99	0.00	*
	*	6.0	2.68	0.45	*								
	*	.25FVC	0.15	12.50	*								
	*	.50FVC	0.33	4.87	*	- FVC= 6.19 AT 3.69 SEC		MEFR=13.50		MMEF= 3.05		RELIABILITY CODE= 0	
	*	.75FVC	0.73	2.15	*								

TRIAL	*	VOLUME(L)	TIME(SEC)	FLOW(L/S)	*	TIME(SEC)	VOLUME(L)	FLOW(L/S)	*	TIME(SEC)	VOLUME(L)	FLOW(L/S)	*
	*	0.2	0.08	18.25	*	1/4	2.60	8.76	*PEAK	0.03	0.50	21.18	*
	*	1.0	0.12	16.79	*	1/2	4.14	3.65	*	+.10	1.99	8.98	*
	*	1.2	0.13	16.79	*	3/4	4.88	2.19	*	+.50	4.46	2.52	*
	*	2.0	0.20	9.25	*	1.0	5.34	1.22	*	+1.0	5.47	1.22	*
	*	3.0	0.38	8.76	*	2.0	6.11	0.49	*	+2.0	6.15	0.09	*
2	*	4.0	0.47	5.86	*	3.0	6.32	0.00	*	+3.0	6.33	0.49	*
(14)	*	5.0	0.91	2.43	*	4.0	99.99	0.00	*	+4.0	99.99	0.00	*
	*	6.0	1.77	6.24	*								
	*	.25FVC	0.19	19.71	*								
	*	.50FVC	0.33	7.86	*	- FVC= 6.46 AT 3.50 SEC		MEFR=18.99		MMEF= 3.15		RELIABILITY CODE= 0	
	*	.75FVC	0.74	2.43	*								

SAMPLE OUTPUT, TYPE 0 (Concluded)

	*	0.2	0.05	13.39	*	1/4	2.87	7.30	*PEAK	0.07	0.53	19.23	*
	*	1.0	0.10	17.04	*	1/2	4.06	3.65	*	+.10	2.14	9.74	*
	*	1.2	0.11	17.53	*	3/4	4.71	2.19	*	+.50	4.26	3.16	*
	*	2.0	0.15	9.76	*	1.0	5.12	1.70	*	+1.0	5.23	1.70	*
	*	3.0	0.27	6.82	*	2.0	5.83	0.24	*	+2.0	5.87	0.00	*
4	*	4.0	0.49	3.41	*	3.0	6.12	0.00	*	+3.0	6.15	0.00	*
(14)	*	5.3	0.91	1.46	*	4.0	99.99	0.00	*	+4.0	99.99	0.00	*
	*	6.0	2.51	0.00									
	*	.25FVC	0.13	15.06	-								
	*	.50FVC	0.29	4.87	- FVC= 6.28 AT 3.87 SEC			MEFR=17.24		MMEF= 3.11		RELIABILITY CODE= 0	
	*	.75FVC	0.76	2.19	-								
	*	0.2	0.06	15.82	*	1/4	2.55	6.09	*PEAK	0.09	0.83	17.77	*
	*	1.0	0.10	16.31	*	1/2	3.77	3.89	*	+.10	2.10	6.82	*
	*	1.2	0.12	14.85	*	3/4	4.46	1.55	*	+.50	4.07	2.68	*
	*	1.0	0.19	6.82	*	1.0	4.87	1.46	*	+1.0	5.00	1.46	*
	*	2.0	0.33	5.11	*	2.0	5.09	0.97	*	+2.0	5.64	1.22	*
5	*	4.3	0.57	3.65	*	3.0	5.56	0.00	*	+3.0	5.87	0.49	*
(14)	*	5.0	1.10	1.22	*	4.0	6.00	0.00	*	+4.0	6.02	0.00	*
	*	6.0	3.91	0.24									
	*	.25FVC	0.14	10.47	-								
	*	.50FVC	0.34	4.62	- FVC= 6.09 AT 4.94 SEC			MEFR=16.71		MMEF= 3.99		RELIABILITY CODE= 0	
	*	.75FVC	0.81	1.70	-								

BEST TRIAL RESULTS:	FEV0.5	FEV1.0	FVC	PEAK FLOW	.50FVC FLOW	.75FVC FLOW
BEST RECORDED VALUE	4.14	5.34	6.46	21.18	7.06	2.43
DEVIATION FROM PREDICTED (UNITS)	3.22	3.17	3.10	4.93	1.01	-0.24
DEVIATION FROM PREDICTED (PERCENT)	47.18	45.63	48.09	83.84	27.87	-10.61

Appendix K

CLOSING VOLUME CLASSIFICATION SCHEME

Appendix K

CLOSING VOLUME CLASSIFICATION SCHEME

The following formulas[23] were used to calculate the predicted values for Type 1 and Type 2 parameters:

$$\text{Type 1 } (CC/TLC \times 100) = (0.525 \times \text{age}) + 14.348$$

$$\text{Type 2 } (CV/VC \times 100) = (0.318 \times \text{age}) + 1.919$$

The deviations from predicted values were calculated by subtracting the observed value from the predicted value and dividing by the standard deviation value for each (Type 1 = 4.61% and Type 2 = 4.34%).

A typical calculation for Type 2 is given below:

$$\text{PRED}(2) = (0.318 \times 46) + 1.919$$

$$= 16.547$$

$$\text{DEV}(2) = \frac{7.623^{*} - 16.547}{4.34}$$

$$= 2.06$$

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Appendix L

CHEST X-RAY CRITERIA FOR OBSTRUCTIVE EMPHYSEMA

Appendix L

CHEST X-RAY CRITERIA FOR OBSTRUCTIVE EMPHYSEMA

There are three criteria that have been validated for use by readers of chest x-rays (P-A views). These three are as follows:

(1) Flat diaphragms

(2) Relatively small heart size

(3) Blood vessel diminution of lung fields (hyperlucent lungs).

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Appendix M

TEXT OF PRESENTATION AT THE NEW YORK
ACADEMY OF SCIENCE, NEW YORK CITY, MARCH 27, 1975

SPUTUM CYTOLOGY AMONG ALUMINUM POTROOM WORKERS

by David P. Discher, M.D., Bryce D. Breitenstein, M.D.,
and Abraham I. Schweid, M.D.,
University of Washington, Seattle, Washington

Potroom employees of the aluminum reduction industry are exposed to a variety of airborne fumes, gases, and vapors. The two specific agents of greatest concern are fluorides in the form of hydrogen fluoride and particulate fluoride, and coal tar pitch volatiles. Most pertinent reports deal with the possible chronic systemic and respiratory effects of fluoride inhalants. These (Evang[1], Hjort[2], Midttun[3], Rybicki[4], and Kaltreider[5]) come to no clear conclusions regarding the risk of chronic respiratory diseases among aluminum potroom workers.

An excellent epidemiologic study of the steel industry has implicated coal tar pitch volatiles in the excess lung cancer risk among men working on coke ovens[6]. A mortality study of the aluminum industry is presently being undertaken. Two poorly documented reports from the USSR[7,8] represent the only available evidence that aluminum workers suffer an increased risk of cancer or that the aluminum industry contributes to the risk of cancer or the morbidity of bronchitis or pneumonia in the community.

PROCEDURE

The present study was primarily designed to detect at a high level of probability, a two-fold or greater risk of chronic respiratory disease in aluminum workers in comparison to a group of match controls.

The study included:

1. A questionnaire addressed to major and minor respiratory symptoms (cough, phlegm, wheeze, and dyspnea), as well as smoking history and other personal data, including work history.
2. Pulmonary function studies including spirometry and single-breath oxygen, providing: Forced Expiratory Volume in one second, Forced Vital Capacity, Closing Capacity/Total Lung Capacity, and Closing Volume/Vital Capacity.
3. Postero-Anterior Chest X-ray.
4. Sputum cytology.
5. $Alpha_1$ antitypsin screening tests and phenotyping of borderline and positives.

The subjects were aluminum potroom workers in the Pacific Northwest located at 3 plants - 1 with the Soderberg Process and the other 2 with the PreBake Process. A National Institute for Occupational Safety and Health study of the two processes suggests that the PreBake method presents a negligible risk of exposure to the polycylic aromatics. The anodes are thoroughly heated at about 950°C for 36-48 hours in sealed ovens during which time essentially all the polycylic aromatics are removed.

Controls, matched for age and smoking history, were obtained from shop personnel and other manual workers in the Physical Plant Department at the University of Washington and the General Telephone Company in Kirkland, Washington.

This report will be limited to the cytopathologic findings in the sputum specimens obtained from the aluminum workers and the matched controls.

Sputum production was induced by inhalation of 5% propylene glycol aqueous mist. The specimen, preserved in a 2% propylene glycol and 50% ethanol solution, was transmitted to the laboratory where smears were prepared by the Saccomanno concentration method.[9] The smears were stained by the Papanicolaou method and screened by registered cytotechnologists under the supervision of one of the authors (AIS).

Sputa were categorized as:

Negative: No abnormal cells and/or regular metaplasia.

Atypical: Mild and moderate atypical squamous metaplasia.

Suspicious: Severe atypical squamous metaplasia and/or cells suggestive but not diagnostic of malignancy.

Positive: Cells diagnostic of squamous carcinoma in situ or invasive carcinoma.

The criteria for the various grades of metaplasia, carcinoma in situ and invasive carcinoma were those of Saccomanno.[10]

RESULTS

The cytopathologic findings are given in Tables I and II. Table I depicts the number of satisfactory, unsatisfactory, and unknown specimens and their proportion in percent. Table II enumerates the classification of the satisfactory specimens. The yield of satisfactory specimens compares favorably with that of Saccomanno's mining population.[11]

TABLE I

Cytopathologic Findings

	Study Group	Controls
Satisfactory	390 (85.4)	193 (84.4)
Unsatisfactory	62 (13.6)	31 (13.6)
Unknown	5 (1.0)	4 (2.0)
Total Groups	457 (100%)	228 (100%)

TABLE II

Cytopathologic Findings

Classification	Study Group	Controls
Negative	266 (68.2)	159 (82)
Atypical	118 (30.3)	34 (18)
Suspicious	5 (1.3)	0 (0)
Positive	1 (0.2)	0 (0)
Total Satisfactory	390 (100%)	193 (100%)

TABLE II-A

Cytopathologic Findings

Classification	Study Group	Controls
Negative	266 (68.2)	159 (82.4)
Atypical	118 (30.3)	34 (17.6)
Mild	94 (24.1)	29 (15.0)
Moderate	24 (6.2)	5 (2.6)
Suspicious	5 (1.3)	0 (0)
Positive	1 (0.2)	0 (0)
Total Satisfactory	390 (100%)	193 (100%)

DISCUSSION

It was recognized from the outset that the sample size was not adequate to estimate the prevalence of cancer in an industrial group. It, therefore, comes as no surprise that the finding of one squamous cancer in the study group was not statistically significant. Combining Positive with Suspicious cases results in non-significance (P=.25). The findings with respect to Atypical smears were statistically significant (P<.01).

Several cautions in interpretation are important:

(1) The significance of mild and moderate atypical squamous metaplasia must be weighed against the assumption that only a small proportion if any of these will necessarily progress to outspoken cancer. Some will regress, and some will persist. In fact, the atypical epithelium may result from inflammatory agents, rather than carcinogens. It is impossible to say that a proportionately larger number of the Study Group than of the Controls will progress. Follow-up studies to date show no evidence of progression.

(2) The prevalence of atypical smears in the Study Group is strikingly lower than in a comparable population. Taking into account the smoking risk in our Study Group, one might have expected 260 Atypicals, 25 Suspicious, 4 Positives, using Saccomanno's non-mining group males of comparable mean age.[10] In our Study Group we observed 118 Atypicals, 5 Suspicious, and 1 Positive. It should be pointed out that repeated sputum studies in our group would be necessary for valid comparison; however, no other data from a large group of controls were available.

(3) Our non-response in the Study and the Control groups was 20%, and Satisfactory sputum samples were obtained on 85% of the respondents. Therefore, we are reporting results on less than 70% of the two populations sampled. We see no particular reasons why more abnormal sputa should be found in the respondents, or in the Satisfactory cases, but such a bias is a possibility.

(4) The Controls were matched on the basis of 1 Control for each 2 Study Group workers by age and by smoking history. A large group of 160 men not matched with Study Group workers in the Aluminum industry were also tested. Two Suspicious sputum samples were reported in these unmatched subjects, which corresponds to the frequency of Suspicious smears in the Study Group; i.e., 2 in 160 is approximately equal to 5 in 390.

(5) Several weeks to months after the first sampling, we tried to repeat the 5 Suspicious cases in the Study Group and the 2 among the unmatched subjects. Of the 7, 6 agreed to be retested; 4 were classed as Atypical and 2 as Negative. Moreover a stratified random sample of our smears will be reviewed by Dr. Saccomanno.

(6) Only 1 of the 5 Study Group workers with a Suspicious sputum worked in the Soderberg Process. He was a 19 year old potroom worker who had been employed in the Aluminum industry for 1 year, and he was an ex-smoker who had worked for an undetermined short time with asbestos. The 1 Positive was a 58 year old PreBake Process worker who was also a heavy smoker with chronic obstructive lung disease. A lobectomy revealed a small (2 cm.) squamous cell carcinoma in the left supper lobe.

SUMMARY

1. The cytopathologic findings in sputum from aluminum potroom workers in the Pacific Northwest were compared with a group of matched controls.

2. In view of the above-mentioned considerations, the meaning of the difference between the Study Group and the Controls remains doubtful.

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