

# NIOSH



## Health Hazard Evaluation Report

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USGS LABORATORY  
DORAVILLE, GEORGIA

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## I. SUMMARY

On June 22, 1984, the National Institute for Occupational Safety and Health (NIOSH) was asked by the U.S. Geological Survey (USGS), National Water Quality Laboratory (NWQL), in Doraville, Georgia, to evaluate whether physical complaints reported by many of the employees were related to exposure to chemicals used or analyzed in the laboratory; or to other workplace conditions. Several employees were seen by a rheumatologist for musculoskeletal symptoms, and had positive antinuclear antibody (ANA) tests, the first being reported in May 1984. Other medical complaints included rash, tremor, headache, fatigue, dizziness, nose bleeds, numbness and tingling in the extremities, and nausea. Subsequently there were reports of elevated liver function tests (LFT) and reticulocyte counts (RC) among employees.

On August 28-31, 1984, NIOSH personnel conducted a walk-through inspection of the facility, distributed a self-administered questionnaire, interviewed approximately 20 employees, and reviewed reports of past industrial hygiene surveys as well as the contents of personnel files. On January 8, 1985, NIOSH medical officers returned to the facility to collect blood samples for ANA determination, and to administer a second questionnaire. On August 13-14, 1985, NIOSH conducted an industrial hygiene air sampling survey.

Four interim reports were issued during the course of the investigation to inform participants and other interested parties about the progress and findings of the investigation. Questionnaire data indicated that use of certain solvents (benzene, methylene chloride, hexane, and acetone) was positively associated with certain neurological symptoms (light-headedness or dizziness, numbness or pin-and-needles sensation, unexplained muscle weakness, and unexplained muscle aching). There were slight elevations in SGPT (serum glutamic pyruvic transaminase, a liver function enzyme test) and reticulocyte (immature red blood cell) count (RC) tests among workers in the Organics Section at various times between 1983 and 1985. A significantly greater number of ANA seropositive females worked in the Organics Section.

No cause-effect relationship could be established between chemicals used or analyzed in the laboratory and ANA positivity. Exposures to individual chemicals measured by industrial hygiene air sampling were non-detectable or far below established or proposed occupational health exposure limits. The only outstanding hazardous condition found at the laboratory was a very inadequate ventilation system, virtually deplete of provisions for any outdoor air supply.

Keywords: SIC 9511 (water resource management), water quality laboratories, antinuclear antibodies, reticulocytes, analytical chemistry laboratories, solvents, poor ventilation, building-related illnesses, indoor air quality

## II. INTRODUCTION

On June 22, 1984, the Safety Officer of the U.S. Geological Survey (USGS), National Water Quality Laboratory, in Doraville, Georgia, requested a NIOSH health hazard evaluation to determine whether a variety of employee illnesses were due to exposure to occupational hazards in the laboratory. The illnesses reported in the initial request included skin rashes, headaches, respiratory illnesses, neurological disorders, and allergies. Of special concern were the building's ventilation system and the exposures associated with the analysis of water samples collected in the vicinity of hazardous waste burial sites.

Three on-site surveys were conducted during the course of the investigation. On August 28-29, 1984, NIOSH personnel conducted a walk-through inspection of the USGS Laboratory, distributed a self-administered questionnaire, interviewed approximately 20 employees, and reviewed reports of past industrial hygiene surveys as well as the contents of personnel files. Questionnaires and employee interviews revealed that several employees had been seen by a rheumatologist for musculoskeletal symptoms, and had positive antinuclear antibody (ANA) tests, the first being reported in May 1984. On January 8, 1985 NIOSH personnel returned to the USGS Laboratory to obtain blood samples for ANA determination, and to administer a second questionnaire. On August 13-14, 1985, two NIOSH industrial hygienists conducted an air sampling survey in the laboratory.

NIOSH has issued four reports since the origination of this project to keep all interested parties apprised of the progress and findings during various stages of the investigation. On September 17, 1984, an initial letter report was issued discussing the findings of NIOSH's initial site visit to the laboratory on August 28-31, 1984. In July 1985, NIOSH issued Interim Report No. 1 providing findings relating to worker symptoms and ANA seropositivity. On September 30, 1985, a letter was issued reporting a survey of liver function tests and hematological tests obtained from company medical records. The most recent report was a letter of December 10, 1985 providing the results of an air sampling survey conducted on August 13-14, 1985.

## III. BACKGROUND

### A. Facility

The laboratory is housed in a warehouse which is privately owned and leased by the General Services Administration (GSA) for USGS NWQL use. Offices and laboratory space have been provided by installing walls and suspended ceilings. Because the drains and floor traps were below the concrete floor, these systems could not be directly inspected to determine whether they were adequate to prevent sewer gases and laboratory chemicals from escaping into



the laboratory air. Some of the lab sinks drain into open floor drains. Odors from chemicals dumped in one sink have been reported to come up again in other parts of the laboratory. Most sinks are not equipped with the U-traps.

#### B. Ventilation

Laboratory hood exhaust and the building's HVAC units are all located on the building roof. The outside air dampers (for supplying outdoor air to the ventilation system) were bolted fully closed on all the units inspected by NIOSH investigators. Therefore, there are no systems in operation for supplying fresh, outdoor air to the building for ventilation purposes. The operation of the lab hoods exerts a negative pressure on the building, causing outdoor air infiltration through all available openings. In fact, air from the roof is being pulled into the building through any lab hoods not in operation. This serves to recirculate an undetermined amount of re-entrained chemical hood exhausts from the roof.

The air supply to most sections of the laboratory is recirculated air drawn from the large plenum space between the suspended ceiling and the warehouse roof. However, the Organics Section and the office area have separate return air ducts providing air recirculation to and from those areas.

Condensate collection and drainage is a potential problem. The condensate from the rooftop HVAC units drains onto the flat roof, rather than into drain pipes. Consequently, puddles of standing water, possibly stagnant at times, collect on the roof. Condensate also collects on some of the ceiling diffusers and drips into the rooms.

#### C. Hazardous Waste Water Samples

The USGS-NWQL contracted with the Environmental Protection Agency (EPA) to evaluate surface and ground water quality in the vicinity of selected hazardous waste burial sites. The Doraville USGS lab initially handled all samples from the eastern section of the nation; a similar USGS lab in Denver, Colorado, handled western area samples. Some USGS/Doraville employees associate the onset of their illnesses with the initiation of the hazardous waste water sampling program in 1982, particularly the Niagara River study in New York State. The laboratory analyzes for all the 129 EPA-designated priority pollutants. A review of the analytical results from two of the sample sets, the Niagara River Study, New York, and the Bridgeport Rental and Oil Services (BROS) site, Bridgeport, New Jersey, indicated a large variety of priority pollutants detected, in the range from 1 to 10,000,000 ug/liter (ppb), with most results falling within the 1 to 1,000 ppb range. A large array of pollutants were measured. A preliminary review of the analytical results did not show any apparent pattern of

outstanding pollutant chemicals. During the NIOSH health hazard evaluation, analysis of water samples from the vicinity of hazardous waste sites was temporarily suspended, and later transferred permanently to the USGS-NWQL in Denver.

#### D. Exposure to Laboratory Reagents

Chemical reagents are used in the lab to extract pollutants from samples, to concentrate and prepare samples for analysis, and to prepare analytical standards. The quantities of pollutants found in the water samples are very minute compared with the quantity of laboratory chemicals used in the analyses. Based upon major usage as laboratory chemicals, the most significant potential exposures appear to be the following:

##### Section 3 - Trace Metals Section

Methyl isobutyl ketone (MIBK) and mercury

##### Section 4 - Special Methods and Sample Preparation

Acid vapors and mists from the acid extraction procedure

##### Section 5 - Organic Section

Hexane, ethyl ether, methylene chloride, benzene and mercury

Exposures to most of these chemical reagents have been evaluated by industrial hygiene consultants during four previous surveys from 1979 through 1982. No overexposures were measured. Exposure levels were generally far less than exposure limits for industrial workers. Exposures that had not been adequately characterized by previous consultants included mercury in Sections 3 and 5, and acid fumes and mists in Section 4.

Due to the recirculation of air in the lab, all lab workers may receive exposure to a variety of air contaminants, particularly solvents, at low levels.

#### IV. EVALUATION METHODS

##### A. Environmental

An initial survey was conducted at the laboratory on August 28, 29, and 31, 1984 by NIOSH industrial hygienists and medical officers. An initial meeting was held with the laboratory management and safety officials, and with an employee representative chosen by the laboratory's Safety Committee. A detailed report of the initial survey was provided in our first report of September 17, 1984.

Following the meeting, a walk-through survey was conducted of the entire laboratory. Information was obtained concerning (1) types of chemical analyses performed at the laboratory, (2) quantity and frequency of use of analytical reagents, (3) work practices used, and (4) the facility's ventilation system design and operation.

NIOSH industrial hygienists reviewed reports of 4 previous industrial hygiene surveys conducted from 1979 to 1983 by consultants under contract with USGS-NWQL. The industrial hygienists also reviewed USGS analytical reports of pollutant identities and concentrations found in water samples collected in the vicinity of 2 hazardous waste burial areas; these 2 sample sets were selected because certain employees associated the onset of their illnesses with the lab's analysis of these sample sets. A visual inspection of the building's heating, ventilation, and air conditioning (HVAC) system was conducted on the roof and above the suspended ceiling.

The exposure of laboratory employees to hazardous wastes in water samples could not be adequately evaluated by the NIOSH investigators for the following reasons. A review of the analytical results of samples from two major waste site areas indicated a huge array of chemicals detected and identified, many tentatively, in the range of 1 to 10,000,000 ug/liter (ppb) in a water or sediment matrix. Most results fell within the 1 to 1,000 ppb range. There were no apparent patterns of particular outstanding pollutant chemicals in the samples, and no appropriate measure of total "hazardous waste" could be identified. Therefore, there was no particular pollutant substance or substances for which exposure could be assessed. Soon after the origination of the NIOSH project, analysis of hazardous waste water samples was discontinued at the Doraville laboratory. Therefore, it was impossible to assess any potential past exposures by conducting environmental measurements.

In response to an employee complaint, OSHA conducted an active inspection at the facility for much of 1985. NIOSH investigators reviewed OSHA's air sampling data. OSHA measured minute, if any, airborne chemical exposures.

In spite of the fact that several consultants and OSHA had never found excessive chemical exposures at the laboratory, the potential severity of some of the symptoms, and the abnormal blood test results, prodded NIOSH investigators to search for hazardous environmental conditions in the laboratory.

On August 13-14, 1985, NIOSH industrial hygienists conducted air monitoring throughout the laboratory facility. The first consideration was to evaluate exposure to specific chemical reagents which were either used frequently or which were positively associated with symptom occurrence by the questionnaire survey. To assess exposure to these targeted chemicals, employees who actually worked with the chemicals wore air sampling devices during the portion of the day when those particular chemicals were used. A second consideration was the contamination of the general laboratory air by a variety of chemicals, resulting from exhaust or ventilation deficiencies and evaporation from open floor drains. To evaluate general workroom air contamination, stationary air sampling devices were deployed through the building,

including the front office area. A third consideration was the spread of chemical contaminants through the building via the ventilation system. To evaluate the recirculation of contaminants, air samples were collected inside the outlets of ceiling air supply ducts.

In accordance with NIOSH's recommendations, USGS obtained the services of an engineering consultant to evaluate the building's heating, ventilation, and air conditioning system. The engineer's report was reviewed by NIOSH and deemed adequate to deal with ventilation issues in the facility. Therefore, a thorough ventilation assessment by NIOSH was not needed.

#### B. Medical

A self-administered questionnaire (#1) was completed by all 60 USGS workers on August 28-29, 1984. This questionnaire asked questions pertaining to use of specific chemicals, the occurrence of medical symptoms and conditions, and work practice and history. A second self-administered questionnaire (#2) was given to all 60 USGS workers on January 8, 1985. Only 51 of these individuals had completed questionnaire #1 in August, 1984. Eight of the remaining individuals represented new hires and for the other worker, information from questionnaire #1 was unavailable. Questionnaire #2 focused on medical information concerning symptoms and risk factors for disorders associated with ANA seropositivity such as: age, sex, history of hypertension, current medications, occurrence of specific illnesses associated with increased prevalence of ANA titers, ingestion of specific medications associated with increased prevalence of ANA formation, occurrence of medical symptoms associated with systemic lupus erythematosus (SLE), and a history of handling hazardous waste samples.

Serum samples were obtained from 58 employees on January 8, 1985, and 2 other employees provided samples at the Centers for Disease Control (CDC) Immunology Laboratory, Atlanta, Georgia, within the next week.

Each serum sample was analyzed using HEP-2 as substrate at the CDC Immunology Laboratory. If fluorescence was noted at a 1:16 serum dilution, the sample was also tested using a mouse liver and mouse kidney substrate. A serum sample was felt to have a positive test if either the HEP-2 or mouse liver and mouse kidney methods demonstrated fluorescence at a titer greater than 1:16. Sera demonstrating a positive ANA test were further assayed to detect anti-SM, anti-RNP, anti-SSA, anti-SSB, anti-nDNA antibodies by Ouchterlony immunodiffusion. In addition, these sera were sent to Scripps laboratory for anti-histone and anti-ssDNA antibody testing.



All laboratory blood analysis reports of USGS laboratory workers between 1983 and 1985 were obtained from the USGS laboratory contract physician. This compilation of laboratory result data did not include any blood tests obtained by private physicians unless such medical records were in our files from our prior investigation of ANA occurrence. The occurrence of abnormalities in liver enzymes, complete blood counts (CBC), and reticulocyte counts among the laboratory workers was determined. The following liver enzyme tests were reviewed:

<u>Liver Function Tests</u>	<u>Normal Range</u>
lactase dehydrogenase (LDH)	90 - 255 mU/ml
alkaline phosphatase (AP)	20 - 95 mU/ml
serum glutamic oxalacetic transaminase (SGOT)	10 - 40 mU/ml
serum glutamic pyruvic transaminase (SGPT)	5 - 40 mU/ml
total bilirubin (TB)	0.1 - 1.3 mg/dl
gamma glutamyl transpeptidase (GGTP)	0 - 60 mU/ml males
	0 - 45 mU/ml females

mU/ml=micro units/milliliter  
mg/dl=milligrams/deciliter

Any laboratory test report that indicated that a sample was hemolyzed was excluded from evaluation of liver enzyme test abnormalities. (Hemolysis occurs when some red blood cells (RBC) are ruptured during blood drawing or sample handling. Such an occurrence may spuriously elevate liver enzymes.) However, blood cell tests such as hematocrit, white cell count and reticulocyte count (the percentage of very young RBC's in the peripheral blood) were considered valid since hemolysis will have little, if any, effect on these tests.

The following blood cell tests were evaluated:

<u>Test Result</u>	<u>Range of Normal</u>
Hematocrit (Hct)	male 42 - 52% female 37 - 47%
hemoglobin (Hgb)	male 14 - 18 g/dl female 12 - 16 g/dl
mean corpuscular volume (MCV)	male 80 - 94 CU microns female 81 - 99 CU microns
white blood cells count (WBC)	4.8 - 10.8 Thou/cmm
reticulocyte count (RC)	0.5 - 1.5%

g/dl=grams/deciliter  
CU microns=cubic microns  
Thou/cmm=thousands per cubic millimeter



Telephone interviews were conducted with section chiefs of the laboratory that analyzed the liver function and blood cell tests. Blood analysis procedures were discussed as well as quality control procedures. Dates and log numbers of each blood sample were recorded to determine if test abnormalities were related to certain lot numbers. The laboratory section of all but one of the workers who had blood tests during this three year period was determined so that the possibility of geographic clustering of workers with abnormal tests could be evaluated.

#### V. EVALUATION CRITERIA

##### Environmental Criteria

As a guide to the evaluation of the hazards posed by workplace exposures, NIOSH field staff employ environmental evaluation criteria for assessment of a number of chemical and physical agents. These criteria are intended to suggest levels of exposure to which most workers may be exposed up to 10 hours per day, 40 hours per week for a working lifetime without experiencing adverse health effects. It is, however, important to note that not all workers will be protected from adverse health effects if their exposures are maintained below these levels. A small percentage may experience adverse health effects because of individual susceptibility, a pre-existing medical condition, and/or a hypersensitivity (allergy).

In addition, some hazardous substances may act in combination with other workplace exposures, the general environment, or with medications or personal habits of the worker to produce health effects even if the occupational exposures are controlled at the level set by the evaluation criterion. These combined effects are often not considered in the evaluation criteria. Also, some substances are absorbed by direct contact with the skin and mucous membranes, thus potentially increasing the overall exposure. Finally, evaluation criteria may change over the years as new information on the toxic effects of an agent becomes available.

The primary sources of environmental evaluation criteria for the workplace are: 1) NIOSH criteria documents and recommendations, 2) the American Conference of Governmental Industrial Hygienists' (ACGIH) Threshold Limit Values (TLV's), and 3) the U.S. Department of Labor (OSHA) occupational safety and health standards. Often, the NIOSH recommendations and ACGIH TLV's are lower than the corresponding OSHA standards. Both NIOSH recommendations and ACGIH TLV's usually are based on more recent information than are the OSHA standards. The OSHA standards also may be required to take into account the feasibility of controlling exposures in various industries where the agents are used; the NIOSH-recommended standards, by contrast, are based primarily on concerns relating to the prevention of occupational disease. In evaluating the exposure levels and the recommendations for

reducing these levels found in this report, it should be noted that employers are legally required to meet those levels specified by an OSHA standard.

ACGIH, OSHA, and NIOSH exposure limits were used when reviewing previous air sampling reports from private consultants. For the very few air contaminants detected by the NIOSH monitoring, the air contamination criteria are provided later in this report in the results section. Because virtually all of NIOSH's sample results were "none detected" or "trace", the exposure limit criteria for individual chemical reagents used in the laboratory are not presented or discussed here.

## VI. EVALUATION OF RESULTS AND DISCUSSION

### A. Questionnaire #1:

Table I lists symptoms reported by the laboratory's 51 workers who completed both questionnaires and had blood drawn. It also divides the occurrence of symptoms by location: non-office versus office workers (individuals who have only worked in the office over the last 2 and 1/2 years). A "yes" means the respondent had the symptom at least five times or for one week's duration in the last 2 and 1/2 years. Only rash and headache were reported significantly more often ( $p=0.0109$  and  $0.0385$ , Fisher's Exact test, two-tailed, respectively) among non-office workers. However, the number of office workers is small, and there may not be sufficient statistical power to detect a significant difference in the prevalence of other symptoms between office and non-office workers.

To determine whether symptoms were more frequent among those with longer employment at the laboratory, the frequency of symptoms was compared in individuals starting work before (49 workers) and after (11 workers) January, 1984. These data included only the original 60 respondents to questionnaire #1 on August 28-29, 1984. There were no significant differences noted in symptoms occurrence between these two groups.

### B. ANA Tests:

ANA seropositivity indicates that the body has formed antibodies to various components of cell nuclei. The formation of ANA's has been associated with various autoimmune diseases, though ANA's are also found in otherwise healthy individuals. Such antibodies are reported to occur in individuals taking certain medications, and therefore, it is possible that chemical exposure may also induce such antibody formation.

Fifty-one blood samples for ANA's were obtained in January 1985 from the original 60 employees surveyed in August 1984. Eight additional samples were obtained from workers hired since August 1984, and from one worker for whom questionnaire #1 data was unavailable. These nine individuals all tested seronegative for

ANA and have not been included in the subsequent data analysis. Five (10%) of the 51 participants had a positive ANA test. Only one of these individuals was among the five workers who had reported a previously positive ANA test between May 1984 and January 1985. Therefore, four additional positive ANA's were found. The sera drawn from the four individuals, who had a physician documented record of a positive ANA test in the past two years, but who tested negative on January 8, 1985, were retested. They were again found to be negative. Two of the previously ANA-positive workers had had positive ANA's tested on a different ANA test substrate (rat liver) and not the HEP-2 or mouse liver and mouse kidney methods. Thus, between May, 1984 and January 1985, 9 (18%) of the 51 had a positive test.

For the purposes of this report, a "case" of ANA seropositivity is defined as an individual with a positive serum ANA at any time between May 1984 and January 1985. At the time of our second survey, four cases worked in Section 5, two in Section 2, and one each in Sections 3, 4 and 7 (Figure 1). One of the cases, not currently in Section 5, had previously worked in Section 5.

Table II breaks down the number and mean ages of workers by sex and by race for the entire lab, Section 5, cases and non-cases. Seven of the nine cases (78%) were female, even though females represent only 51% of the workforce (Table II). There were only seven Blacks employed at the laboratory, but four (57%) had positive ANA tests. This was a significantly greater prevalence of positive ANA's among blacks than for employees of other races (EOR) (5/44=11%) ( $p=0.0133$ , Fisher's Exact Test). The mean age for Black cases (36 years) was significantly less than that of EOR cases (51 years) ( $t=-2.8234$ , d.f.=7,  $p=0.0256$ ). Among EOR, cases were significantly older (mean 51 years) than non-cases (mean 40 years) ( $t=-2.1259$ , d.f.=42,  $p=0.0394$ ). Other age differences listed in the table are not significantly different.

Although cases appeared to cluster among workers who had worked in Section 5 within the last two and one half years, the prevalence (5/16) of ANA positivity among individuals who had worked at least one month in Section 5 in the last 2 and 1/2 years was not significantly different than that (4/35) who had never worked in Section 5 during that time period ( $p=0.0946$ , Fisher's Exact Test, two-tailed). However, when only female cases were considered, there was a significantly higher prevalence (5/8=63%) among women who had worked in Section 5 than among those women who had not (2/18=11%) ( $p=.0382$ , Fisher's Exact Test, two-tailed).

Cases had significantly higher prevalences of several symptoms than non-cases. Table III contains many general symptoms, but the case-associated symptoms appear to cluster in three organ systems: integument (burning skin, skin sores), nervous system (dizziness, numbness, unexplained muscle weakness, problems in walking), and musculoskeletal (unexplained muscle aching). These differences remained significant when females were considered alone (Table IV).

The prevalences of various symptoms in individuals claiming they had used a particular chemical at least one hour per week were compared to those in individuals who had claimed non-use of that chemical. Fourteen chemicals were examined because they appeared to be the most frequently used: acetylene gas, hydrochloric acid, potassium permanganate, hexane, potassium dichromate, iso-octane, benzene, pesticide standards, priority pollutant standards, nitric acid, sulfuric acid and methylene chloride. Other chemicals were not analyzed because relatively few individuals indicated use of them.

Benzene use was associated with dizziness ( $p=0.0691$ ) and numbness ( $p=0.0413$ ). Methylene chloride was associated with numbness ( $p=0.0278$ ), muscle weakness ( $p=0.0167$ ) and muscle aching ( $p=0.0379$ ). Hexane was associated with muscle weakness ( $p=0.0165$ ), as was acetone ( $p=0.0065$ ). Caution must be exercised when evaluating these data. First, when individual chemical usage was examined, no single chemical was used by more than two of the cases, except acetone and benzene (each used by three of the cases). Since these chemicals are predominantly used in Section 5, our data cannot rule out that the possibility that solvents are associated with symptoms merely because the symptomatic individuals (cases) cluster there for some other, unknown reason. Second, there were 504 comparisons made altogether (occurrence of each symptom listed in Table I for each of the 14 chemicals listed above), so 6 or 7 with  $p$  values in the 0.01 to 0.05 range are not remarkable. That is, they may be occurring by chance.

The NIOSH industrial hygienist interviewed all cases with regard to their work histories. One case worked in both the organic (Section 5) and inorganic sections of the facility during the last 2 and 1/2 years, and is therefore counted in both groups. All five Section 5 cases worked in three adjacent laboratory rooms. No associations were found among Section 5 cases with regard to analytical procedures and reagent chemicals used. Two of the section 5 cases did not use solvents. The five cases in the inorganic sections of the laboratory showed no association between analytical procedures used. However, all of these cases used strong acids: four of the cases named sulfuric acid specifically. This would be expected in any inorganic chemistry lab. All non-section 5 cases probably had some exposure to mercury compounds used as preservatives in nutrient water samples. Previous industrial hygiene surveys by consultants and OSHA measured very low or non-detectable levels of airborne mercury.

The five cases which demonstrated seropositive ANA tests in January 1985 had the following additional serum analyses completed to better characterize the type of anti-nuclear antibodies which might account for the positive ANA test: anti-double stranded (nDNA), anti-SM, anti-ribonuclear protein (RNP), anti-SSA/Ro, anti-SSB/La, anti-histone and anti-single stranded DNA (ssDNA).



These tests detect antibodies to two families of antigens: DNA-containing antigens (ss- and nDNA, and RNP), and non-DNA-containing antigens (SM, SSA/Ro, SSB/La and histones).

SM, Ro and La represent the first two letters of the patient name from whom the prototype serum originated.<sup>1</sup> For cases which tested negative on the HEP-2 substrate in January, only SSA/Ro, anti-histone and anti-ssDNA were tested. All sera were negative for anti-nDNA, anti-SM, anti-RNP and anti SSB/La. One of five sera tested for anti-SSA/Ro was positive. Five of nine sera tested for anti-histone were positive as were five of nine sera tested for anti-ssDNA. Only three individuals were positive to both anti-histone and anti-ssDNA.

Antibodies to nDNA are highly specific for the clinical diagnosis of systemic lupus erythematosus (SLE) and occur in 70-75% of clinically recognizable patients,<sup>1</sup> but occasionally are seen in rheumatoid arthritis patients. Antibodies to Sm antigen occur in SLE patients. Antibodies to SSA/Ro occur in patients with Sjogren's syndrome, with SLE, and at a lower frequency and titer in scleroderma and mixed connective tissue disease. Antibodies to SSB/La occur in patients with Sjogren's syndrome and with SLE. Antibodies to RNP occur in patients with mixed connective tissue disease, with SLE, and at lower frequency and titer with scleroderma. Antibodies to histones occur in 60% of SLE patients, 95% of drug-induced SLE and 20% of rheumatoid arthritis patients.<sup>2</sup>

#### C. Questionnaire #2:

To determine whether individuals who had a positive ANA test possessed other characteristics which might increase their likelihood of having a positive ANA, we compared the occurrence of hypertension, use of medications and illnesses associated with a high prevalence of ANA for cases and non-cases. No significant differences were found. Similarly, no significant difference was found with respect to length of employment at the lab (greater versus less than 2 and 1/2 years) or having ever handled hazardous waste samples. (The question regarding hours per week of handling hazardous waste samples was inconsistently answered, so no meaningful analysis of exposure duration could be made).

#### D. Review of Employee Medical Records

Blood test analysis and quality control procedures were deemed to be adequate. The dates and log numbers of blood samples indicated that these tests were analyzed on different days, thus minimizing the possibility of laboratory error occurring in one particular lot of samples.

### 1. Liver Function Tests

The majority of the liver enzyme abnormalities were in the SGPT test. This test is fairly specific for liver abnormalities as is the GGTP test. LDH, AP, TB and SGOT may be elevated by non-liver processes. Therefore, the analysis centered on elevations in SGPT because it is more specific for liver abnormalities, and there were very few GGPT, LDH, AP, TB and SGOT elevations.

In 1983, 16 workers had liver analysis panels. Eight workers were from section 5 and eight were workers from other laboratory sections. Two employees had slightly increased SGPT's (range: 70 - 90 mU/ml). Investigation of their records indicated the presence of non-occupational health conditions that would account for these elevations.

In 1984, 19 workers had specimens for liver enzyme panels drawn; one of the specimens was hemolyzed. Of the 18 non-hemolyzed specimens (12 from Section 5), two had slightly elevated SGPT's (both were 43 mU/ml), but all of their other LFT's were in the normal range. One SGPT returned to normal range when retested 7 months later. The other showed a minimal elevation when retested 7 months later, that returned to normal in the following month. Both of these individuals were from section 5.

In 1985, 30 workers had specimens for liver enzyme panels drawn; two of the specimens were hemolyzed. Of the 28 non-hemolyzed specimens (15 from workers in section 5), specimens from two workers had moderately elevated SGPT levels. These individuals were felt to have non-occupational health conditions that could cause these SGPT elevations. Seven had slight SGPT elevations (range: 42 - 55 mU/ml). Of these seven individuals with slightly elevated SGPT tests, five were from section 5. Five of the seven had SGPT's redrawn in the next two months, and their SGPT levels returned to the normal range. Laboratory results for repeat SGPT's were not available for the other two individuals with slightly elevated SGPT's. These seven individuals did not have elevations in other liver function tests.

In 1985, two individuals had isolated, slight elevations in LDH (range 270 - 284 mU/ml), and one individual had a slight elevation in LDH (258 mU/ml) as well as AP (97 mU/ml). The LDH and AP returned to normal on retesting. Another individual had a slight elevation in LDH (284 mU/ml) and SGOT (49 mU/ml), but no retest data was present in the available records. Another individual had an isolated, slight increase in SGOT (49 mU/ml). The increases in LDH were found in individuals from three different sections of the laboratory.

## 2. Blood Count Analysis

The following blood indices included in the CBC were evaluated: Hct, Hgb, MCHC, MCV, WBC. Reticulocyte counts were not necessarily included with each CBC, so these totals will be discussed separately.

In 1983, 15 CBC's were analyzed. No abnormalities were found. A total of seven blood samples for reticulocyte count (RC) were drawn (five from Section 5 workers) and one was elevated (2.1% in a Section 5 worker).

In 1984, 20 CBC's were tested. Two low WBC counts were found (3.6 and 4.6 thou/ccm). These individuals were not from Section 5. Fourteen blood samples for RC's were obtained. Six were slightly elevated (1.6 - 3.0%; median=2.0%). One individual was known to have medical conditions that could explain an elevated RC. Insufficient data was available for such determinations on the other five. Nine of the 14 samples were from Section 5 employees. Five Section 5 employees had elevated RC's (range: 1.8-3.0%).

In 1985, 30 CBC's were tested. Two individuals (both from sections other than section 5) had low WBC's (range 3.3 - 3.6 th/ccm). One of these individuals had a medical condition which could account for such results. Three individuals had slightly elevated Hct's (46.4 - 51.8%). One individual had a low Hct with other indices that suggested iron deficiency anemia. Five workers (three male and two female) had increased RC's (one was from a Section 5 worker). The other four employees were from two other sections.

## E. Air Sampling Results

On August 13 and 14, 1985, industrial hygienists from the NIOSH regional office conducted an industrial hygiene survey in the laboratories and collected air samples to measure for chemical contaminants.

To determine the types of organic chemicals in the laboratory air, air samples were collected on benchtops and in air supply ducts throughout the building, with special emphasis on Section V (Organics). Organic compounds were collected on activated charcoal, desorbed with carbon disulfide, and analyzed by gas chromatography and mass spectrometry. No organic airborne chemicals were detected.

To determine the types and concentrations of airborne acids, air samples were collected on Orbo 53 silica gel tubes, and analyzed for sulfate, nitrate, chloride, and phosphate by ion chromatography. Samples were collected in the inorganic sections of the lab where inorganic acids are frequently used. No airborne acids were detected.

Ethyl ether was sampled in the Extraction Room in Section V (Organics). The chemist who extracted herbicides from water samples using ethyl ether, wore a personal sampling device to measure his personal exposure during the workday. His average measured exposure was 0.21 ppm of airborne ethyl ether vapor; the OSHA exposure limit is 400 ppm. An area sample collected on a benchtop or desktop in the Extraction Room measured 0.17 ppm as an average level for the day.

Hexane and other organic vapors were also sampled in the Extraction Room. A general desktop area sample was collected to evaluate general room air contamination. Two chemists who performed pesticide extractions or column cleanup work using hexane and other solvents wore personal air sampling devices throughout the day. Only a trace of hexane vapor was detected in the general room sample. No hexane was detected in the sample from the column cleanup operator. The pesticide extraction chemist's average daily exposure was 0.3 ppm; the NIOSH recommended exposure limit is 500 ppm, as is the OSHA limit. No other organic vapors were detected in the Extraction Room air.

The exposure of the chemist in Section III (Trace Metals) who uses methyl isobutyl ketone (MIBK) was also sampled. No MIBK was detected in the air sample.

Methylene chloride use had generally been discontinued at the laboratory by the time of the NIOSH air sampling survey. Therefore, air sampling for this substance was not performed.

In summary, the NIOSH air sampling survey did not detect any significant air contamination in the laboratory.

#### F. Ventilation

The ventilation system was evaluated by an engineering firm. The report concluded that the ventilation as designed was not suitable for a laboratory facility. The most significant problem was the lack of a fresh, outdoor air supply system for the building. Although laboratory hoods were operating to exhaust 40,000 cubic feet of air per minute (cfm), there was virtually no outside make-up air provided. The intake air ports were located on the roof in close proximity to the exhaust stacks. However, all outdoor air louvers on air conditioning units were sealed shut to avoid re-entry of contaminated hood exhaust into the building.

### VII. DISCUSSION

The laboratory workers, in general, complained of a number of general physical symptoms which were irritative (rash, sore throat, nose or sinus irritation), neurological (numbness, muscle weakness) and nonspecific (dizziness, headache, emotional swings,



insomnia, muscle aching, fatigue). Though only rash and headache were significantly more frequent among non-office than among office workers, there was a general trend for non-office personnel to report higher prevalences of symptoms. When interpreting this data it is important to acknowledge that the small numbers of individuals in each group may obscure other significant associations. Many of these general complaints are similar to those noted by investigators in office buildings with inadequate ventilation.

The results of the January 8, 1985 blood sampling survey showed that five (10%) of the fifty-one workers in the study population had antinuclear antibodies detected in their blood. The medical literature contains population studies which examine the point prevalence of positive ANA tests among healthy, asymptomatic people,<sup>2-5</sup> as well as among individuals with non-collagen vascular diseases that may increase the likelihood of ANA occurrence.<sup>6-12</sup> The point prevalence of ANA's is higher in older individuals, females,<sup>2,4,5</sup> and Blacks.<sup>13</sup> According to these published studies, the 10% point prevalence of ANA's found in January 1985 was within the limits of what could be expected to occur in a survey of 25 males and 26 females in the general population of similar age. However, the reported point prevalence studies used methods of determining ANA titers which may not be comparable to those used in testing the USGS employees. Although the 10% point prevalence of positive ANA tests on January 8, 1985 does not seem abnormally high for this laboratory population, the fact that, between May 1984 and January 1985 nine employees, including the five identified by NIOSH testing, have been found to have antinuclear antibodies present on at least one occasion, may be cause for concern. Unfortunately the available ANA prevalence studies have not looked at the same populations over time to assess the natural history of ANA titers and thus there are no population based data to determine the expected incidence rate for ANA positivity over the nine-month period in question. It is also possible that other lab workers may have intermittantly had ANA present in their blood over the same nine month period (ANA titers may fluctuate), but the lab employees, as a group, have not been surveyed with periodic ANA blood testing. Of the nine known ANA positives, two were male and seven were female. Five of the women had worked in Section 5 during the last 2 and 1/2 years. In total, only eight of the 26 women in the study population had ever worked in Section 5 during that period, and one of the eight had worked there only one month. The fact that five out of eight women who ever worked in Section 5 (70%) developed the presence of ANA's suggests that some chemical exposure present in Section 5 may have influenced the development of such antibodies.

When cases were compared to non-cases with regard to the presence of known ANA risk factors. It was found that Blacks were more likely than EOR's to have had positive ANA tests. Fifty-seven percent of Blacks (4 of 7) employed in the lab have had positive

ANA's in the last two years. The medical literature indicates that Blacks, in general, are more likely than Whites to develop ANA positivity.<sup>13</sup> However, without comparable prevalence data for Black populations it is difficult to determine what excess this 57% point prevalence might represent. It did not appear that the cases differed significantly from non-cases with regard to known ANA risk factors except for race and sex.

Because of the number of employees with reported positive ANA tests, there was understandable concern that some chemical exposure in the laboratory might be causing the workers to form ANA's. No reports could be located in the indexed medical literature that discussed any chemical exposures having caused the formation of ANA's but numerous medicinal drugs have been shown to cause the formation of ANA's and the appearance of a drug-induced SLE syndrome in some exposed people.<sup>14-15</sup> Studies of drug-induced SLE suggest that an offending drug must be given continuously for a period ranging from three weeks to two years before ANA's develop.<sup>16</sup> Many workers felt that the handling of hazardous waste samples might have been associated with the development of their symptoms and ANA positivity. Reportedly, the lab began to analyze hazardous waste samples in mid-1982. This time course is compatible with the first reports of positive ANA's in 1984, but no significant association was found between exposure to the hazardous waste samples or other chemicals and the development of ANA's. However, it is still conceivable that an exposure to the hazardous waste samples or to some other chemical or combination of chemicals used in the laboratory caused ANA positivity. It is also possible that a reduction in exposures in the lab to the hazardous waste samples or to some other putative causative chemical agent may have contributed to subsequently negative ANA tests among four of the five original cases. It is of interest that the five cases who worked in section 5 were located in three contiguous rooms. There are many chemicals commonly used in this section, and the ventilation system has been shown to be inadequate.<sup>17</sup> However, no overt overexposures to chemicals have been measured, and airborne concentrations are quite low in comparison to existing or proposed occupational health limits.

To pursue this chemical causation hypothesis, sera of cases were further analyzed for the presence of additional classes of anti-nuclear antibodies that are associated with specific connective tissue diseases to determine if the group of workers with positive ANA's demonstrated similar patterns of ANA antibodies which might suggest a drug (or chemical)-induced SLE picture. This testing did not demonstrate any common pattern which might suggest a drug (chemical)-induced etiology.

The occurrence of certain symptoms reported more frequently by cases than non-cases can be categorized into dermatological, neurological and nonspecific. While they do not specifically

delineate a SLE-like syndrome, the skin problems and myalgias are complaints commonly experienced by individuals with a collagen vascular disease.

Interestingly, exposure to solvents was associated with symptoms that were biologically plausible, disregarding the issue of ANA positivity. The neurological complaints of dizziness or lightheadedness, muscle weakness and numbness can be associated with certain solvent exposures at sufficiently high exposure levels.<sup>18</sup> Analysis of available industrial hygiene data from the USGS lab has not demonstrated such exposures.

In 1985, all but two section 5 workers had valid, non-hemolyzed liver function testing on at least one occasion. Discounting two individuals with non-occupational medical conditions that would account for their liver enzyme elevations, five Section 5 employees had isolated, slight SGPT elevations. All of these returned to the normal range upon retesting within two months. While an episode of exposure to a liver toxic agent cannot be ruled out, such low level elevations in SGPT without concomitant elevations in other liver enzymes may be due to biological and/or analytical variability.

There were no geographic patterns found in the occurrence of abnormalities in WBC, Hct, HGB, or MCV among the workers tested. Of the six employees that had increased RC's in 1984, records of 1985 testing were available for three. Of these three (all in section 5) one maintained a slightly elevated RC (1.6%), and two returned to normal. Of the three not retested, one left employment at USGS and for the remaining two, no records were received. The 1984 RC data suggested that Section 5 employees might tend to run slightly elevated RC's. However, in 1985, of the 14 RC's obtained from Section 5 workers (a total of 15 workers were assigned to section 5 in 1985) only one had an elevated RC (1.6%).

It has been reported that workers occupationally exposed to benzene, toluene, and xylene have shown an elevation in their reticulocyte counts.<sup>19</sup> Thus, it might be possible that an occupational chemical exposure received at the laboratory may have caused the slight increase in reticulocyte counts seen in some of the workers. While the slight increases found may be of no clinical significance, it was suggested in the NIOSH medical report of September 30, 1985 that the laboratory workers be medically followed to be sure no ill effects occur and to attempt to determine if a chemical exposure may be affecting the reticulocyte count of laboratory workers.

VIII. CONCLUSIONS

1. Female USGS employees were more likely than males employees to have had a positive serum ANA test. It has been reported in the medical literature that females are more likely than males to develop a positive ANA. However, among female workers, a female in Section 5 was significantly more likely to have had a positive ANA test than females working in other sections of the laboratory.
2. Black workers were more likely than EOR workers to have had a positive ANA test. There is no comparable data in the medical literature to assess whether this is an abnormally high point prevalence of ANA positivity (57%) among black workers. The affected black workers were generally younger than affected EOR workers.
3. No cause-effect relationship could be established between a chemical or group of chemicals in the laboratory and ANA positivity. However, there appears to be an association between ANA test positivity and symptoms among five of the cases that were first reported to NIOSH (May 1984 - September 1984). Cases were more likely than non-cases to report the following symptoms: burning skin, skin sores, light-headedness or dizziness, numbness or pins-and-needles sensation, unexplained muscle weakness, problems walking and unexplained muscle aching.
4. Reported exposure to certain solvents (benzene, methylene chloride, hexane and acetone) were positively associated with certain neurological symptoms (light-headedness or dizziness, numbness or pins-&-needles sensation, unexplained muscle weakness and unexplained muscle aching).
5. There were slight elevations in SGPT and RC tests among section 5 workers at various times between 1983 and 1985. While the number of tests done, and the selection procedures for who was tested make a statistical determination of significance impossible, there was enough evidence to advise that the laboratory conduct medical follow-up of section 5 workers and other individuals with abnormal tests.
6. Industrial hygiene air sampling has not demonstrated any remarkable exposure to chemical contaminants. However, the building's ventilation system has been shown to have many inadequacies, including re-entry of lab hood exhaust and lack of outdoor air supply.<sup>17</sup>



IX. RECOMMENDATIONS:

1. Black and female workers, as well as all those individuals working in Section 5, should be informed of a possible increased risk of developing ANA's. Even though Blacks and females are generally at greater risk than white males of developing a positive ANA, the prevalence of ANA seropositivity among these workers at USGS may be higher than expected. If any worker develops persistent physical complaints, such as muscle or joint aching, excessive fatigue, unexplained rashes, chest pains, excessive, unexplained hair loss or unexplained numbness or tingling in extremities, medical evaluation, including an ANA test would be advisable.
2. To evaluate the significance of mild elevations in SGPT and reticulocyte counts among laboratory workers, it is recommended that the laboratory conduct medical follow-up of Section 5 workers and other individuals with abnormal tests as outlined in Interim Letter #2 dated September 30, 1985.
3. An engineering firm has evaluated the heating, ventilating, and air conditioning (HVAC) system. The engineers provided a thorough and detailed report with a large number of recommendations for HVAC improvements. The engineering report should be used as a guide for this and similar laboratory facilities. The following recommendations from the HVAC report are deemed especially important:
  - a. Remove rain caps and install new zero static high velocity vertical cap protection, and extend stacks above building wake cavity.
  - b. The existing building air handling units do not have sufficient capacity for outdoor air supply, and several new 100% outdoor make up air units should be installed to serve the laboratory. The location and design of these systems should consider laboratory heating loads, cooling loads, present air exhaust requirements, future exhaust air requirements with addition of new hoods, exhaust stack locations, and direction of prevailing winds.
  - c. Roof penetrations should be sealed, especially where duct penetrations are not used, such as abandoned ducts. This will help reduce the uncontrolled flow of air and recirculation of exhaust air.
  - d. The existing waste disposal of chemicals to open sanitary sewer drains in the floor is poor. Consideration should be given to installation of a new system.

**X. AUTHORSHIP AND ACKNOWLEDGEMENT**

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**XI. DISTRIBUTION AND AVAILABILITY OF REPORT**

Copies of this report are currently available upon request from NIOSH, Division of Standards Development and Technology Transfer, Publications Dissemination Section, 4676 Columbia Parkway, Cincinnati, Ohio 45226. After 90 days, the report will be available through the National Technical Information Service (NTIS), 5285 Port Royal, Springfield, Virginia 22161. Information regarding its availability through NTIS can be obtained from NIOSH Publications Office at the Cincinnati address. Copies of this report have been sent to:

1. Director, USGS-NWQL-Atlanta
2. Safety Officer, USGS-NWQL-Atlanta
3. Employee representative, Safety Committee, USGS-NWQL-ATL
4. Eastern Regional Safety Officer, USGS, Reston, Virginia
5. NIOSH, Region IV
6. OSHA, Region IV
7. GSA, Region IV
8. Appropriate safety and health agencies of the State of Georgia

In view of the proposed closing of this facility prior to the anticipated completion date of this report, it is recommended that the employer make copies available to all employees, or former employees.

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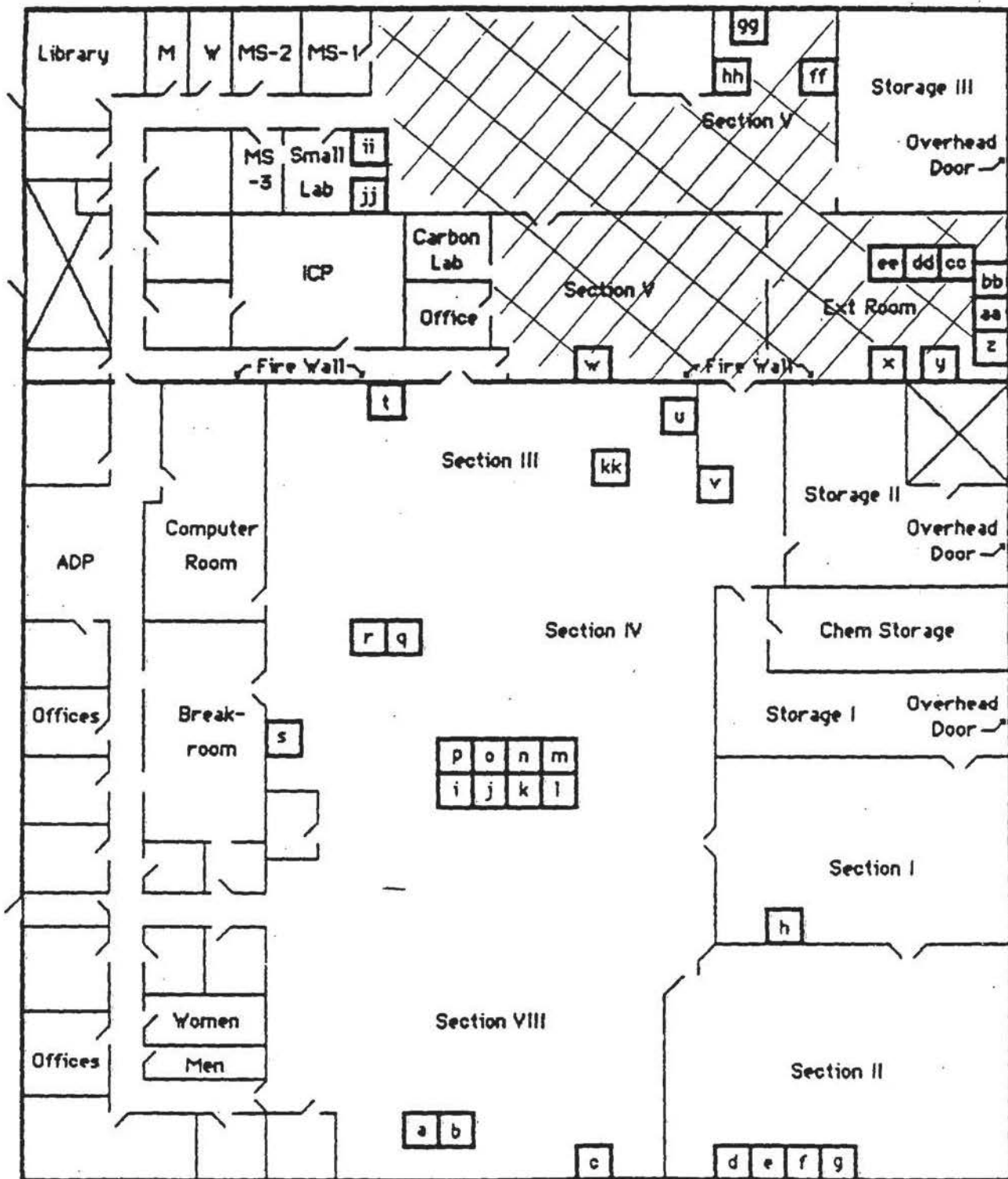


Figure 1. Hatched marking depicts areas in Section 5 where cases have worked.

TABLE I

Questionnaire # 1 - Symptoms of  
51 Laboratory Workers

Symptom	percentage of entire lab (n=51)	percentage among non-office workers (n=41)	percentage among office workers (n=10)	p-value (Fisher's Exact Test) (two-tailed)
rash	49	59	10	0.0109
burning skin	24	29	0	0.0920
sore throat	39	44	20	0.2801
hives	12	12	10	1.0000
eye irritation	37	44	10	0.0695
skin sensitivity to light	20	22	10	0.6635
nose or sinus irritation	51	54	40	0.4986
skin sores	14	17	0	0.3203
shortness of breath	25	27	20	1.0000
nose bleeds	12	12	10	1.0000
chest tightness	16	15	20	0.6469
diarrhea	29	32	20	0.7027
nausea/ vomiting	20	22	10	0.6635
palpitation	6	5	10	0.4881
chronic cough	10	10	10	1.0000
wheeze	6	7	0	1.0000
light-headed- ness or dizzi- ness	31	37	10	0.1421
stomach pain	22	22	20	1.0000
headache	51	59	20	0.0385
loss of libido or interest in sex	18	22	0	0.1760
nervous/ anxiety	29	32	20	0.7027
loss of appetite	22	24	10	0.4282
unexplained numbness or pins-&-needles sensation in arm, leg, face	27	32	10	0.2496
weight loss	10	10	10	1.0000
weakness in an arm or leg	20	20	0	0.1782
blurred vision	14	12	20	0.6116
problems walking	22	24	10	0.4282
tremor	12	15	0	0.3308
emotional swings or irritability	33	39	10	0.1352

TABLE I Continued

Symptom	percentage of entire lab (n=51)	percentage among non-office workers (n=41)	percentage among office workers (n=10)	p-value (Fisher's Exact Test) (two-tailed)
problems with hand- writing	20	22	10	0.6635
trouble fall- ing asleep	27	32	10	0.2496
memory problems	20	22	10	0.6635
concentration problems	20	22	10	0.6635
depression	24	22	30	0.6822
unexplained muscle aching	20	24	0	0.1782
fatigue	41	46	20	0.1666

**TABLE II****Demographic Characteristics of the Work Force**

	entire lab	Section 5	cases	non-cases
number of employees	51	15	9	42
mean age	41	41	44	40
number of female employees	26	7	7	19
mean age	40	39	43	39
number of male employees	25	8	2	23
mean age	42	41	51	42
number of Black employees	7		4	3
mean age	38		36	44
number employees of other races*	44		5	39
mean age	42		51	40

\*41 caucasian, 2 asian, 1 hispanic



TABLE III

Symptoms Among ANA Seropositive  
Cases and Non-Cases

All employees (n=51)

Symptom	% positive ANA cases (n=9)	% positive non-cases (n=42)	p-value (Fisher's Exact Test) (two-tailed)
rash	7 (78)	18 (43)	0.0751
burning skin	5 (56)	4 (17)	0.0244
hives	2 (22)	4 (10)	0.2836
skin sensitivity to light	4 (44)	6 (14)	0.0609
sore throat	6 (67)	14 (33)	0.1289
eye irritation	6 (67)	13 (31)	0.0625
nose or sinus irritation	5 (56)	21 (50)	1.0000
nose bleed	0 (0)	6 (14)	0.5749
skin sores	4 (44)	3 (7)	0.0135
chest tightness	2 (22)	6 (14)	0.6187
light-headedness or dizziness	7 (78)	9 (21)	0.0024
shortness of breath	4 (44)	9 (21)	0.2079
unexplained numbness or pin-&-needles sensation in arm, leg, face	6 (67)	8 (9)	0.0085
wheezing	0 (0)	3 (7)	1.0000
unexplained muscle weakness	5 (56)	5 (12)	0.0092
cough	1 (11)	4 (10)	1.0000
problems walking	5 (56)	6 (14)	0.0155
palpitations	1 (11)	2 (5)	0.4487
unexplained muscle aching	6 (67)	4 (10)	0.0008
nausea/vomiting	3 (33)	7 (17)	0.3534
diarrhea	5 (56)	10 (24)	0.1022
stomach pain	3 (33)	8 (19)	0.3849
headache	6 (67)	20 (48)	0.4654
loss of libido or interest in sex	1 (11)	8 (19)	1.0000
loss of appetite	4 (44)	7 (17)	0.0868
weight loss	2 (22)	3 (7)	0.2090
vision blurring	2 (22)	5 (12)	0.5922
depression	4 (44)	8 (19)	0.1877
trouble falling asleep or staying asleep	3 (33)	11 (26)	0.6920
concentration problems	3 (33)	7 (17)	0.3534
memory problems	3 (33)	7 (17)	0.3534

TABLE IV

Symptoms Among Female ANA Seropositive  
Cases and Non-Cases

Women employees (n=26)

Symptom	% positive ANA cases (n=7)	% positive non-cases (n=19)	p-value (Fisher's Exact Test)
problems with handwriting	4 (44)	6 (14)	0.0609
emotional swings	6 (67)	11 (26)	0.0454
nervousness/ anxiety	4 (44)	11 (26)	0.4206
tremor	3 (33)	3 (7)	0.0599
fatigue	6 (67)	15 (34)	0.1362
burning skin	5 (71)	5 (26)	0.0138
skin sores	4 (57)	2 (11)	0.0278
light-headedness or dizziness	6 (85)	5 (26)	0.0208
unexplained numbness or pin-&-needles sensation in arm, leg face	6 (85)	4 (21)	0.0053
unexplained muscle weakness	5 (71)	3 (16)	0.0138
problems walking	5 (71)	4 (21)	0.0283
unexplained muscle aching	5 (71)	2 (11)	0.0057

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