

U.S. Department of Energy

**A COMPARISON OF AUTOIMMUNE DISEASE OCCURRENCE AT
IDAHO NATIONAL LABORATORY AND OTHER SITES
IN THE ILLNESS AND INJURY SURVEILLANCE PROGRAM**

Conducted by the staff of the Office of Epidemiology and Health Surveillance (EH-53)

Report issued September 2005

*This report contains an evaluation of health concerns raised by employees of the Radiological and Environmental Sciences Laboratory at Idaho National Laboratory. Any evaluations and recommendations made in the report are for the specific facility evaluated and may not be universally applicable. Recommendations made are not to be considered as final statements of DOE policy or of any other agency or individual involved. When finalized, this report will be made available on our web site at <http://www.eh.doe.gov/health/epi/surv/index.html>.

PREFACE

The Office of Epidemiology and Health Surveillance conducts field investigations of potential health hazards in the Department of Energy (DOE) workplace upon management or worker request. The office also provides, upon request, technical assistance and epidemiologic consultation to DOE Headquarters, Field Elements, and DOE contractors to facilitate the control of occupational health hazards, reduce risks to worker health and safety, and help to identify emerging occupational health issues through the conduct of health surveillance of the workforce.

ACKNOWLEDGMENTS AND AVAILABILITY OF REPORT

This report was prepared by Dr. Clifton Strader with assistance from Dr. Bonnie Richter and Ms. Jasmine Kenney of U.S. Department of Energy Headquarters, and Dr. Betsy Dupree-Ellis and Mr. Phil Wallace of Oak Ridge Institute for Science and Education. Invaluable field assistance was provided by the data coordinators of the sites participating in the Illness and Injury Surveillance Program.

Copies of this report have been sent to employee and management representatives of the Idaho National Laboratory and the Radiological and Environmental Sciences Laboratory. The report is also available on our Web site at <http://www.eh.doe.gov/health/epi/surv/index.html>.

SUMMARY

On August 16, 2004, an employee health concern at the Idaho National Laboratory's (INL) Radiological and Environmental Sciences Laboratory (RESL) was brought to the attention of the Office of Epidemiology and Health Surveillance (EH-53) by a member of the Office of Quality Assurance Programs (EH-31) who had just returned from a site visit at INL. RESL management had briefed him concerning an employee who had contracted an as yet undiagnosed autoimmune related disease that appeared to be neurological. The employee noted that he knew several other former and current RESL employees with similar types of illnesses and questioned whether the illnesses might be occupational in origin.

In follow-up discussions we conveyed to RESL management that the diseases grouped together by the employee were different enough that they could not reasonably be classified as a disease cluster, and that the lack of clinical diagnoses was a concern. Further, the cases were diagnosed over a period of approximately six years, and no specific occupational exposure was suspected. Independently of our initiative, INL bargaining unit officials asked the National Institute for Occupational Safety and Health (NIOSH) to investigate worker health concerns regarding autoimmune disease at INL. The NIOSH review concluded that there was insufficient evidence of a disease cluster to warrant detailed investigation.

We used the Department of Energy's (DOE) Illness and Injury Surveillance Program (IISP) data to assess whether the occurrence of autoimmune diseases at INL changed over time and to compare rates with other sites participating in the program between 1995 and 2002. The IISP does not include Federal employees and lacks information on a worker's specific work site, limitations that precluded evaluating RESL specifically. However, our more general evaluation of contractor workers focused on a broad array of autoimmune diagnoses with particular emphasis on diagnoses identified as being of special concern to RESL employees. The evaluation covered the period 1995-2002, years for which complete data are available. We found that INL workers had lower overall rates of autoimmune disease than did other sites in the program and showed little evidence of any consistent change in rates over time at the site. Recommendations were made for future actions to enhance protection of worker health at the facility.

INTRODUCTION

RESL is a government owned and operated laboratory currently employing 18 Federal workers and a few contractor workers at the INL. Another smaller contractor program shares the same building. The Office of Environment, Safety and Health (ESH) assumed landlord responsibilities for RESL from the Office of Environmental Management (EM) in 2004. RESL's work supports DOE primarily through its role as a reference laboratory for complex-wide measurement and calibration quality assurance programs. These programs include the DOE Laboratory Accreditation Program for worker radiation protection programs in dosimetry and radio-bioassay, and the Mixed Analyte Performance Evaluation Program for work performed by analytical laboratories. In support of this work, RESL employees prepare performance test materials such as samples for radiological and chemical analysis, phantoms for counting in whole body counting vaults, and irradiated dosimeters. RESL also operates radiation sources at a nearby facility. The lab is approximately 40 years old.

A health concern at RESL was initially brought to the attention of an Office of Epidemiology and Health Surveillance (EH-53) staff member on August 16, 2004 by a staff member of the Office of Quality Assurance Programs (EH-31), who had visited INL the prior week. During that visit, RESL management briefed him regarding an employee with what appeared to be an autoimmune related disease, although the employee had not been given a specific diagnosis. This Federal employee indicated that his symptoms appeared to be neurological, and that he knew several other former and current RESL employees with similar types of illnesses. He questioned whether these conditions could be occupationally related.

In an August 26 telephone discussion with Dr. Roy Carlson, RESL's director, concerning the worker's health concern, we expressed a number of reservations about moving forward with an investigation, including the following:

1. the diseases grouped by the employee as autoimmune disorders were so disparate that they could not reasonably be classified as a disease cluster,
2. no clinical diagnoses were available,

3. no specific reputed occupational exposures were cited,
4. the time frame in which the diagnoses were made or diseases identified appeared to span six or more years,
5. the latency period (the time between the reputed exposure and disease identification) did not fit the pattern of a disease cluster, and
6. the number of individuals involved was very small.

Independently, the President of the International Federation of Professional and Technical Employees, Local 94, requested that NIOSH conduct a Health Hazard Evaluation to investigate a possible cluster of autoimmune disease among RESL employees. NIOSH representatives discussed the concern with union officials, learning that the requesting worker had identified three cases of autoimmune disease among 40 currently employed RESL workers. The cases included one person with multiple sclerosis (MS), one with inflammatory arthritis, and a third with fibromyalgia (FM). One other employee had symptoms consistent with MS but had not been diagnosed with that disease. The affected workers did not share job exposures. Based on this information, the NIOSH officials concluded that an investigation was not warranted, and the Health Hazard Evaluation was closed out with a memorandum to file (Appendix A). Office of Epidemiology and Health Surveillance staff conferred with NIOSH concerning their findings.

We discussed the health concern with Dr. Paul Creighton, INL's Site Occupational Medical Director (SOMD). Dr. Creighton had reviewed the limited records available to him and did not find sufficient similarity of the diagnoses to suspect a cluster of autoimmune disease. Some records had no specific diagnosis and others indicated diagnoses he did not consider to be autoimmune. He also noted that the potential exposures at RESL did not appear to present a hazard for these diseases, based on his review of the medical literature.

Given the considerations listed above, we informed Dr. Carlson that the available evidence was not sufficient to warrant an investigation by NIOSH. However, our IISP contained data that would permit a more general evaluation of autoimmune disease occurrence at INL compared with that of other sites in our program, and we agreed to conduct this more general evaluation using the IISP data.

BACKGROUND

The immune system is the defense system of the body, defending it against a broad spectrum of potentially harmful bacterial and viral pathogens. Despite this essential function, the same immune reactions can also be harmful. Autoimmune disease occurs when the body cannot distinguish itself from foreign material and attacks its own tissues (Rose, 2001). Recent research suggests that autoimmune disease is a significant source of morbidity within the U.S., with an estimated three percent of the American population affected by autoimmune disorders. The majority of those affected are women, representing 75 percent of all cases between 15 and 44 years of age (Jacobson 1997, Dooley and Hogan 2003; Olson and O'Connell 2001). Complete consensus does not exist concerning which diseases are autoimmune. Some conditions clearly involve autoimmunity, examples being systemic lupus erythematosus (SLE) and Type 1

diabetes. Other entities such as FM are less clearly characterized and not universally recognized as a clinically specific diagnosis.

A number of factors contribute to an individual's susceptibility to autoimmune disease. Genetics has been found to be an important contributor in various epidemiologic studies, but it appears that a trigger is required to initiate autoreactivity and that these trigger factors may be environmental. Investigators have found that genetically similar populations in different locations vary in the incidence of Type 1 diabetes and MS. Microbial or infectious agents and certain drugs and compounds have been found to initiate an autoreactive response. However, the identification of trigger factors involved in most autoimmune diseases remains elusive (Davidson and Diamond, 2001; Dooley and Hogan, 2003). Although the induction of autoimmune disease in the presence of predisposing genes may be initiated by exposures such as drugs, bacteria, or occupational hazards such as silica, Powell et al. (1999) emphasize that it is unlikely that autoimmune diseases are characterized by a "one inducer, one disease" etiology.

Diseases that are of particular interest in the current report include FM, MS, and SLE. Both FM and SLE affect the musculoskeletal system. FM, as a specific clinical disease, remains contested. Many researchers prefer to classify it under the broad category of Chronic Widespread Pain and suspect that it may be psychological in origin (White and Harth, 2001). The symptoms of FM include pain, sleep disturbance, mood disturbance, and fatigue. The condition is predominantly diagnosed among women (Olsen and O'Connell, 2001).

MS involves the neuromuscular system and has been reported as "the most common chronic neurologic disease of adults between the ages of 20 and 50" (Olsen and O'Connell, 2001). No consensus exists regarding its cause or causes. The disease is characterized by a variety of symptoms including disturbances of vision, balance, sensation, bowel and bladder function, and tremor and weakness (Olsen and O'Connell, 2001). Individuals affected by SLE frequently exhibit arthritis, photosensitivity, and facial rashes (D'Cruz 2000). Similar to many other autoimmune diseases, SLE primarily affects young women (D'Cruz, 2000).

Groups with high occupational exposure to silica have shown increased rates of autoimmune disease compared with the general population. An association between silica exposure and SLE has been reported (Loveren, Vos, Germolec, Simeonova, Eijkemanns, McMichael, 2001). A study conducted with 15,000 uranium workers found the prevalence of SLE to be ten times higher than the prevalence expected in other men (D'Cruz, 2000). Ultraviolet light also appears to be an environmental trigger factor in the development of SLE, and approximately 70 drugs have been found to be linked to the variant drug-induced lupus.

Some evidence exists suggesting that high levels of fluoride ingestion over an extended period of time can suppress the immune system, either through inactivation or outright destruction of developing immune cells. To date, evidence for this hypothesis has been indirect, coming from studies comparing populations living in areas with fluoridated water supplies versus populations living in areas without fluoridation (Sutton 1987). Occupationally, continuing and potentially high level exposure to fluoride containing compounds would appear necessary to induce an

effect on the immune system. According to the SOMD, the potable water supplies to INL have been checked and do not contain high levels of fluoride.

Scleroderma, a progressive disease characterized by the deposition of fibrous connective tissue in the skin and internal organs, or a scleroderma-like illness has also been linked to occupational or environmental exposure to silica. As with SLE, scleroderma may be drug induced (D’Cruz, 2000). Vinyl chloride and solvents such as benzene, toluene, perchloroethylene, trichloroethylene, and epoxy resin are among the chemicals that can produce symptoms and illnesses that are like autoimmune diseases such as SLE, scleroderma, and rheumatoid arthritis (D’Cruz, 2000; Olson and O’Connell, 2001). Hexachlorobenzene exposure has been demonstrated to induce immune dysfunction in animal studies, but its potential effects in man have not been established.

Ultraviolet radiation (UV) has been found to suppress the immune system, although measurement of the effect of UV on the risk of autoimmune disease has not yet been reported. Recent studies have documented that UV can initiate a skin lesion reaction in those who already suffer from SLE (Loveren, Vos, Germolec, Simeonova, Eijkemanns, McMichael, 2001; D’Cruz 2001). A study is currently being conducted in Idaho to test a hypothesized link between nuclear testing in Nevada decades ago and current cases of MS. The study will attempt to determine whether Idaho has a higher rate of MS compared with the rate of MS in other western states (Seattle Post Intelligencer, Feb. 10, 2005).

Additional research is needed to clarify the relationship between occupational exposures and autoimmune disease. Other factors such as lifestyle and genetics complicate efforts to identify and characterize these relationships. Nonetheless, numerous studies suggest that silica, certain drugs, and ultraviolet radiation can produce autoimmune disease or similar effects in susceptible individuals. Future research must better characterize these exposure-disease relationships and improve our understanding of the mechanisms that underlie their expression.

METHODS

EH-53 staff held discussions with both the worker who submitted a health concern to management and with RESL management. These discussions determined that the focus of concern was on autoimmune conditions, particularly neurological or musculoskeletal conditions. There was sufficient breadth in the anecdotal reports of illness and the concern expressed by the worker to suggest that a broad, nonspecific ascertainment of autoimmune diseases and conditions would be most appropriate for an initial comparison, with additional evaluation of more specific diagnostic categories. For this review, we used a broad definition of autoimmune disease based on information from the American Autoimmune Related Diseases Association, conditions recognized by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (see Dunkin 2002), and supplemented these diagnoses with a list published in Shomon (2002). Additional potentially autoimmune diseases were identified in *Introduction: Possibly Autoimmune Diseases* (2005). Appendix B contains a list of the specific diseases and conditions we included.

INL's SOMD was familiar with the employee's concern, although he had not met with the employee. INL's federal employees are not generally served by contractor medical services. The SOMD had reviewed the occupational medical records of several of the individuals and had some information regarding their diagnoses or tentative diagnoses, which included: 1) "an autoimmune deficiency disorder", 2) rheumatoid arthritis, 3) MS (diagnosed in 1996), 4) FM, and 5) chronic fatigue syndrome. No private medical records were available to confirm the workers' diagnoses. The SOMD indicated that the diagnoses were made over several years and that most of the individuals were no longer employed at the site. He suggested that the symptoms, e.g., joint pain and neuropathy, could suggest fluoridosis (fluoride toxicity), but the fluoride levels in nearby wells were low. No evidence pointed to an occupational exposure. The worker had reported that his neurologic examination was negative. The SOMD had suggested that the worker be tested for Lyme Disease, which can exhibit similar symptoms.

In discussions with Dr. Carlson, we determined that the building housing the RESL is approximately 40 years old. The building has a history of ventilation (HVAC) deficiencies. Cooling water is now treated routinely to prevent the growth of mold and bacteria that could enter the ventilation system. RESL's chemical exposure information and industrial hygiene records are limited. Although a variety of activities take place in the building including fabrication and machining operations, various materials analyses, and calibration processes, there is no particular chemical exposure that dominates in the work conducted in the building. Most of these processes are designed to produce a one-off product rather than sustained manufacturing.

The IISP's data base contained relevant data for 13 participating sites, each site contributing one or more years of information covering all or a portion of the period 1995-2002. The IISP data base did not provide sufficient detail to permit a specific analysis of RESL, considering that the Federal workers employed at the lab do not routinely report through the site's occupational medical clinic when returning to work after sick leave. However, the data could be used to evaluate the overall occurrence of autoimmune diseases at INL compared with the occurrence at other DOE sites in the IISP data base. Comparisons were conducted for INL versus the other sites, with particular emphasis given to neurological and musculoskeletal autoimmune diagnoses, the categories of autoimmune disease of greatest interest to the RESL worker who initiated the request.

The objectives of the assessment were:

- To describe the occurrence of autoimmune conditions among INL workers and compare their patterns of occurrence with those of other sites participating in the IISP.
- To evaluate whether any occupational groups or the workforce as a whole at INL are at increased risk of various autoimmune diseases and conditions compared with other sites in the IISP, and
- To interpret the findings of these analyses in terms of their relevance to the health concern expressed at RESL.

EVALUATION CRITERIA

This assessment relied upon data collected routinely from a number of DOE sites participating in the IISP. The data included both annual rosters of each site's contractor workforce and self-reported diagnoses of workers who return through their site's medical clinic for a return to work clearance following an absence of five or more consecutive workdays. Health event and roster data were available for most sites for the years 1995 through 2002, with some sites entering or leaving the surveillance program during that period while others participated throughout the full eight years. Federal employees were excluded from this assessment because they are not required to use site occupational medicine clinics for their occupational health care needs.

Most autoimmune diseases do not prove fatal, hence the number of people with disease in a population can accumulate over time. The analysis focused on the first report of a specific disease rather than the total number of absences related to the disease. This approach more specifically addressed the question of how many workers were being diagnosed with an autoimmune disease rather than how often they were ill enough to be absent for five or more consecutive workdays.

Statistical testing was conducted to assess whether differences in absence or diagnosis rates differed significantly between INL and the other sites included in the review. Much of the analysis focused on an assessment of trends over time comparing INL with other sites. The effects of age, gender, and occupation were also evaluated in comparing health event rates between INL and other sites. A number of analyses evaluated the first absence reported by an individual as a surrogate for the "diagnosis" of the condition; other analyses assessed overall absence rates which included the total number of absences attributable to an autoimmune disease. The IISP does not collect industrial hygiene (IH) exposure data; hence no directly measured IH data were included in this survey. The evaluation considered both the rates of health event diagnosis at the various sites and the absolute number of health events on which the rates were based.

RESULTS

Demographics

Figure 1 is an overview of various characteristics of the INL workers and those from other sites. The INL workforce had a slightly higher percentage of men but was quite similar to other sites in its age distribution. INL's occupational distribution was comparable to that of other sites with a few notable departures, including a smaller percentage of Field Professionals and Line Operators. Most notably, almost 24 percent of INL's workforce has been characterized by site surveillance program staff as having an "Unknown" occupational status, at least in part attributable to the classified nature of work conducted by many workers at the site. Their occupations are not reported to the Occupational Medical Department in sufficient detail to

permit job categorization. About five percent of the workers at other sites had an unknown occupational status. We excluded 110 Hanford records due to missing dates of birth which prevented calculation of these workers' ages.

Figure 1. Characteristics of workers from INL and other IISP sites

Worker Characteristic	INL*	Other Sites*
Gender:		
Male	76%	71%
Female	24%	29%
Age Group		
16-29	06%	08%
30-39	24%	24%
40-49	37%	37%
50+	33%	31%
Average (Mean) Age:	45 years	44 years
Median Age:	45 years	44 years
Occupational Group:		
Administrative	20.0%	24.5%
Biohazard	0.3%	0.4%
Crafts	8.2%	7.7%
Security/Fire Protection	4.2%	2.6%
Field Professionals	4.3%	15.3%
Guests	0.0%	2.4%
In-House Professionals	13.9%	11.4%
Management	9.7%	9.5%
Line Operators	2.9%	5.8%
Service	3.9%	5.7%
Technical Support	9.0%	9.9%
Unknown	23.8%	5.1%

**Percentages may not add up to 100 percent due to rounding. A person-year = one worker counted as employed for one year. Each site's person-years contribution was summed over all years in which the site participated in IISP.*

Our analyses evaluated autoimmune disease rates from 1995 through 2002, a time period for which completed health event and roster data were available for most sites. The majority of the sites included in this review participated in the IISP for the full eight year period, but some sites joined after 1995 (Figure 2).

Figure 2. Site person-year contribution and years of participation in the IISP

Site	Years of Participation in IISP	*Person-Years Contributed Percent (%)
Brookhaven National Laboratory	1995-2002	5.2
East Tennessee Technology Park (K-25)	1999-2002	0.6
Fernald	1995-2002	3.2
Hanford Site	1995-2002	23.6
Idaho National Laboratory	1995-2002	13.9
Kansas City Plant	2002	0.6
Lawrence Livermore National Laboratory	2002	1.7
Oak Ridge National Laboratory (X-10)	1999-2002	3.7
Pantex Plant	1995-2002	4.9
Rocky Flats Environmental Technology Site	1995-2000	5.1
Sandia National Laboratory	1995-2002	12.3
Savannah River Site	1995-2002	20.6
Y-12 Site (Oak Ridge)	1998-2002	4.7

Autoimmune Disease Occurrence

Overall, 828 contractor workers reported 1268 separate absences involving autoimmune disease over the eight years. Counting only the first time a worker reported a specific diagnosis, 911 “first reports” occurred during the eight years. The distribution of these first reported diagnoses by category (Figure 3) emphasizes the preponderance of conditions affecting musculoskeletal and connective tissue, almost 35 percent of the total. Neurological conditions (13 percent); those affecting the digestive tract (12 percent); and diagnoses involving the endocrine, metabolic, and immune systems (12 percent) were also common. National statistics are unavailable for many autoimmune diseases, but the distribution among DOE contractor workers is similar to that observed in hospital discharge data published by the Connecticut Department of Public Health (Olson and O’Connell, 2001). The Connecticut data identified diagnoses involving the musculoskeletal and connective tissue, digestive tract, neurological, and endocrine systems as the more common organ systems affected among patients discharged from hospitals during 1993 through 1997 with an autoimmune disease diagnosis.

The distribution of autoimmune disease diagnoses differed between INL and other sites

(Figure 4). INL workers reported fewer neurological and musculoskeletal diagnoses than did workers at other sites, but they reported a greater percentage of digestive and genitourinary diagnoses involving autoimmunity.

FIGURE 3. FREQUENCY OF AUTOIMMUNE DISEASES BY DIAGNOSIS CATEGORY, 1995-2002, EIGHT YEAR TOTAL REPORTED BY DOE CONTRACTOR WORKERS IN IISP

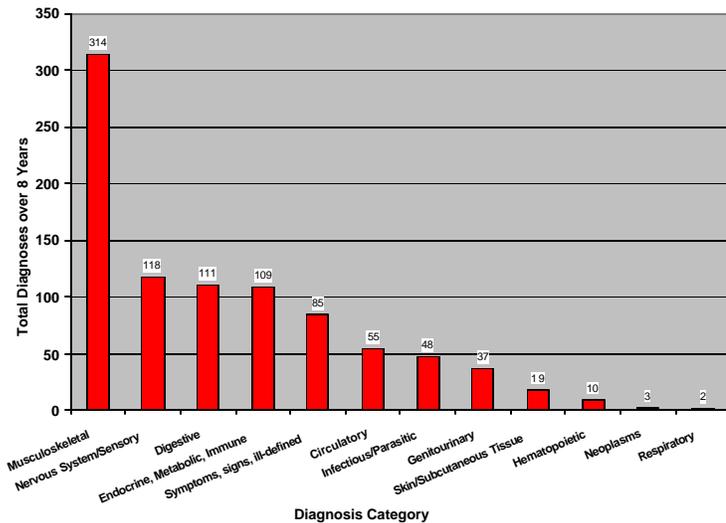
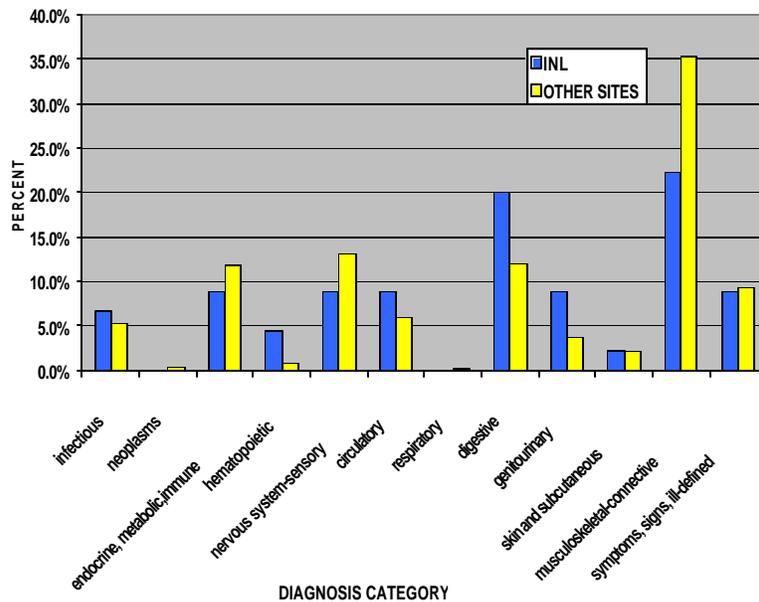


FIGURE 4. PERCENT DISTRIBUTION OF AUTOIMMUNE DIAGNOSES, INL VERSUS OTHER SITES, 1995-2002

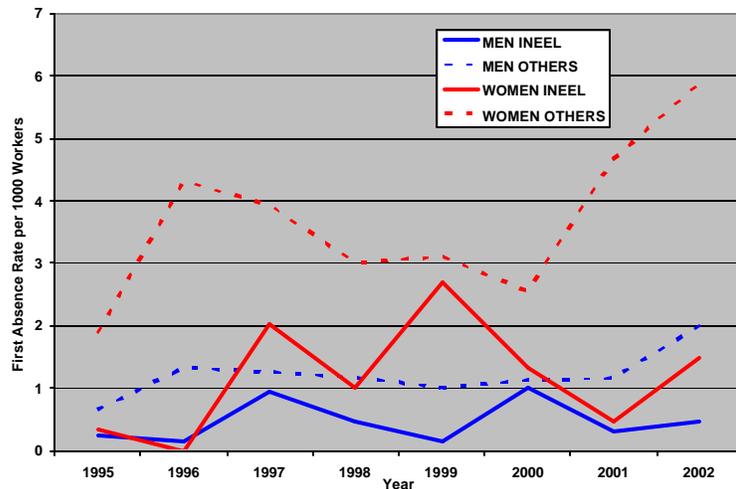


The overall rates of *first absence* for men and women in the INL contractor workforce are compared with rates for workers at other sites in Figure 5. The figure represents the 828 individual workers who reported at least one autoimmune disease over the eight year period. Six individuals reported three different autoimmune diagnoses during this period, 71 others reported two different diagnoses, and the remaining 751 reported one diagnosis. These rates, based only on the *first reported absence*, more closely approximate rates of initial diagnosis. One diagnosis can lead to several absences, depending on the severity of the disease, thus overall absence rates are higher than those examining only the first absence.

Gender

Rates of first absence for autoimmune disease were higher among women than men at both INL and other sites (Figure 5). National rates suggest that about three-fourths of autoimmune disease diagnoses occur among women. At INL, the difference in rates between men and women was greatest during 1997 through 2000, narrowing more recently. At other sites, the difference between genders was considerably broader. We saw no consistent trend over the eight years for either gender at INL or at other sites. The rates among women at other sites increased substantially from 2000 to 2002, an increase that was much less evident among women at INL or among men at INL or elsewhere.

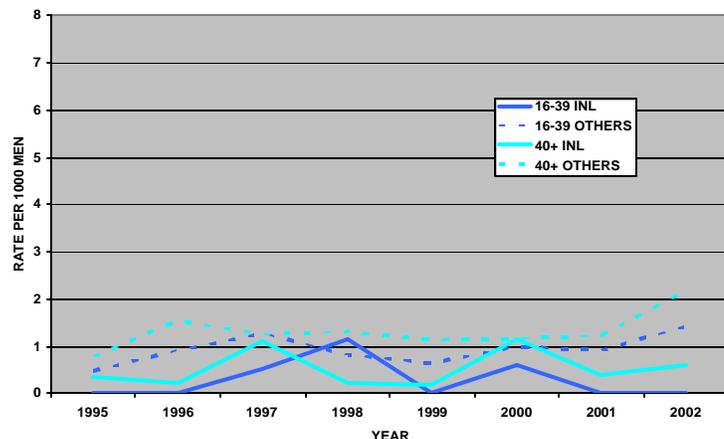
FIGURE 5. AUTOIMMUNE DISEASE FIRST ABSENCE RATES AMONG MALE AND FEMALE WORKERS, INL VERSUS OTHER SITES, 1995-2002



Age

Autoimmune diseases vary by age at onset; some diseases such as MS, SLE, and FM tend to occur among younger individuals, with peak incidence in the 40s and 50s. Other syndromes such as scleroderma and Sjogren’s syndrome occur with increasing incidence into the 70s. In our review, the rate of first reports of autoimmune disease among men showed no evidence of consistent change with age at either INL or other sites (Figure 6a).

FIGURE 6a. ANNUAL AGE SPECIFIC RATE FOR FIRST REPORTED AUTOIMMUNE DISEASE AMONG MEN, INL VERSUS OTHER SITES, 1995-2002



Rates among men in comparable age groups at other sites tended to be somewhat higher than those at INL. Among women, rates were more variable than those of men (Figure 6b). As with men, INL women generally had lower rates than did women in comparable age groups at other sites (Figure 6b). Rates among women of age 16-39 at other sites were lower than those of older women, but both groups showed somewhat increased rates from 2000 through 2002. Men tended to have lower rates than did women at both INL and at other sites. Men and women in comparable age groups shared a similar pattern of rising and falling rates over the eight year period. Over the surveillance period, the rate of first reports rose consistently and rapidly with age among women at other sites, but this trend was not apparent at INL (Figure 6c). The rate rose less dramatically with age among men at other sites and at INL. In general, we noted somewhat less of a “gender gap” in the rate of initially reported autoimmune disease at INL than among workers at other sites. We saw no evidence of an increasing trend in the overall rate of autoimmune diseases among either women or men at INL over the eight years. Rates of first reported diagnosis were generally lower among INL workers than among workers at other sites.

Occupation

Most epidemiologic studies examining occupational exposures and the occurrence of autoimmune disease have focused on exposures rather than particular occupations. An exception is the well documented association of silica dust exposure with rheumatoid arthritis, scleroderma, Sjogren’s syndrome, and SLE.

FIGURE 6b. ANNUAL AGE SPECIFIC RATE OF FIRST REPORTED AUTOIMMUNE DISEASE AMONG WOMEN, INL VERSUS OTHER SITES, 1995-2002

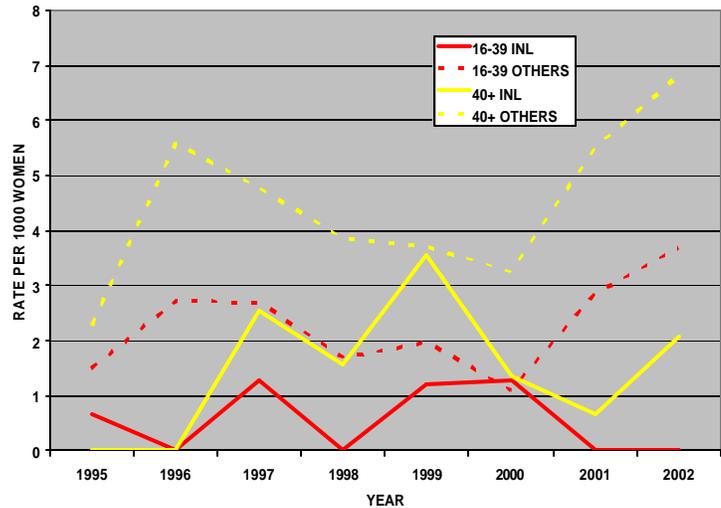
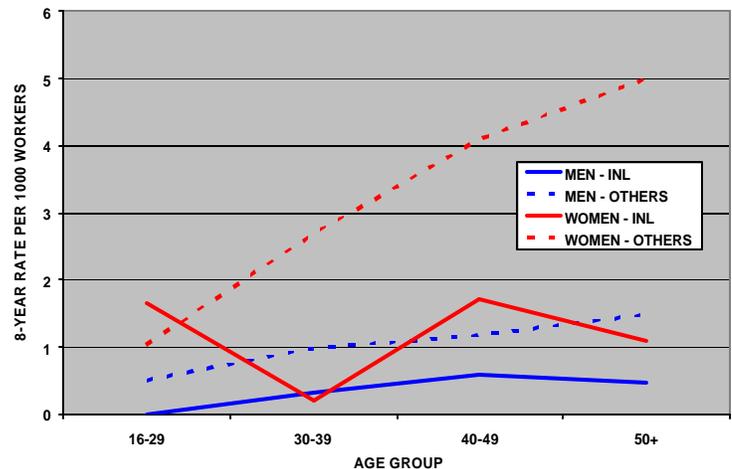


FIGURE 6c. OCTENNIAL AGE SPECIFIC AUTOIMMUNE DISEASE RATES OF FIRST ABSENCE, INL VERSUS OTHER SITES, 1995-2002



By implication, sandblasters and workers likely to receive significant incidental exposure to silica dust are at potentially increased risk for these diseases. Other exposures identified in the literature include ultraviolet light; various solvents such as benzene, trichloroethylene, vinyl chloride, and epoxy resins; a number of pharmaceuticals that induce drug-related lupus and other autoimmune syndromes; estrogenic compounds; and certain pesticides (Hess 1999, D’Cruz 2000). The breadth of these exposures suggests that a variety of occupations could involve increased risk for one or more autoimmune syndromes. Our data contained no specific occupational exposure information. Job titles, sorted into categories, are used as a general surrogate for exposure information. We reviewed rates of autoimmune disease in various job categories defined by data coordinators for the sites participating in the IISP. Category definitions are presented in Appendix C. The Biohazard and Service occupational groups are not included among the figures because they had no reported autoimmune disease diagnoses during the eight year period. Similarly, guests were not included because at INL, they had no reported autoimmune diagnoses.

At INL, only one diagnosis of autoimmune disease was reported by men and one by women in Management from 1995 to 2002. Thus the rates shown for INL managers in Figure 7 cannot be considered reliable due to the small number of diagnoses. Rates among managers at other sites show considerable variability over the eight years but no consistent change over time. Rates are higher among women than among men at sites other than INL.

Administrative Support workers at INL reported 47 initial absences related to autoimmune disease over the eight year period; 238 diagnoses were recorded at other sites. Rates among women at both INL and other sites fluctuated substantially over this period and, as shown in Figure 8, rates for women at other sites have been increasing since 2000. There is little evidence of any consistent change among women at INL.

FIGURE 7. FIRST REPORTED AUTOIMMUNE DISEASE RATES AMONG MANAGERS, INL VERSUS OTHER SITES, 1995-2002

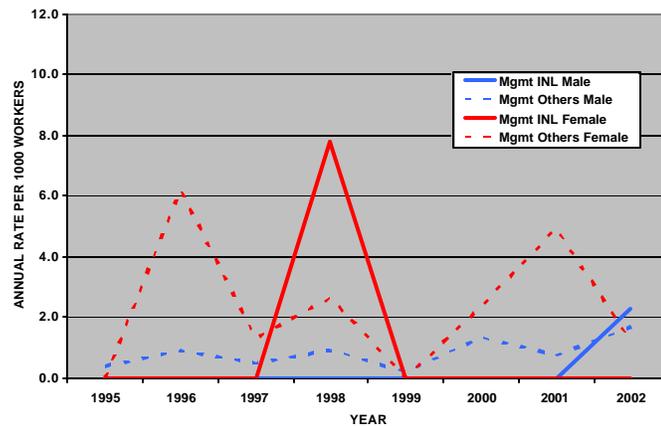
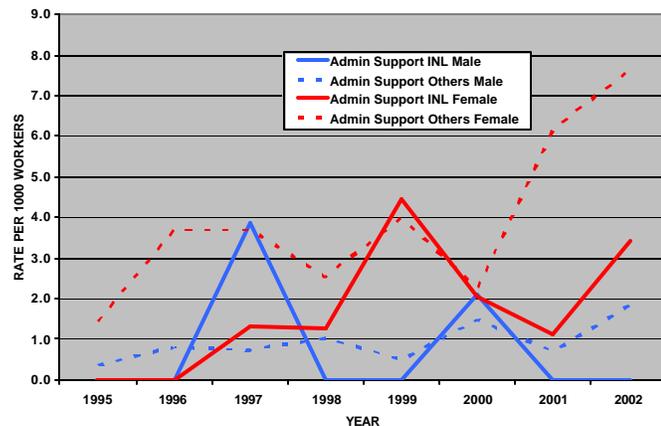
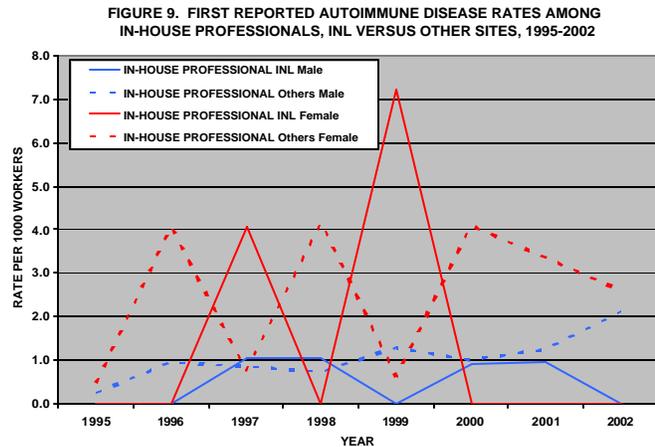


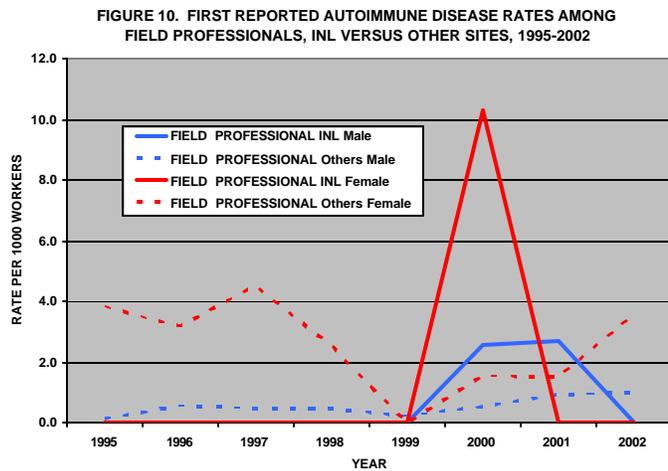
FIGURE 8. FIRST REPORTED AUTOIMMUNE DISEASE RATE AMONG ADMINISTRATIVE SUPPORT WORKERS, INL VERSUS OTHER SITES, 1995-2002



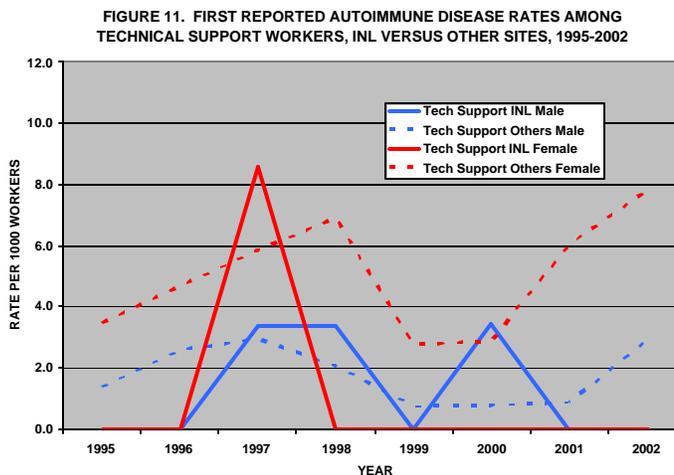
Despite considerable fluctuation in rates of first reported autoimmune disease over the eight years, In-House Professionals (Figure 9) showed no evidence of consistent change. The variation reflects very small numbers of cases, hence broader fluctuation at INL than among other sites as a group. Males had more stable but generally lower rates than did women.



The same observations apply to Field Professionals (Figure 10). A peak was noted among women at INL in 2000, one year later than a similar peak among INL’s female In-House Professionals. Rates varied among Field Professionals at other sites but neither men nor women demonstrated a consistent trend.

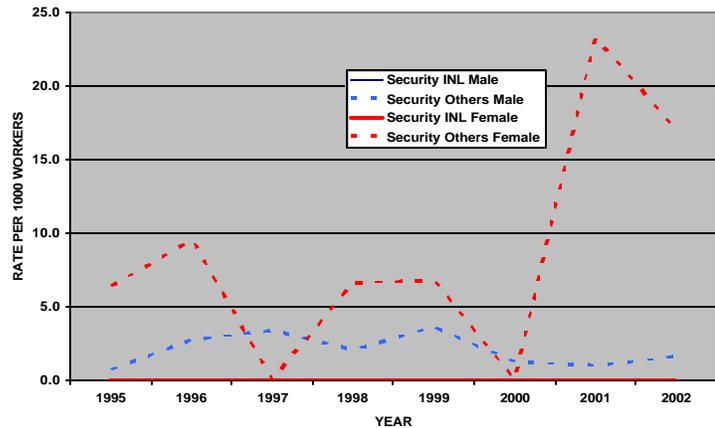


The most noteworthy observation associated with Technical Support workers was the manner in which rates among men and women at sites other than INL varied in a similar manner over time (Figure 11). Rates of reported autoimmune disease among men remained consistently lower than those of women. INL rates, by contrast, show consistency over time only among women, who reported no new cases from 1998 through 2002.



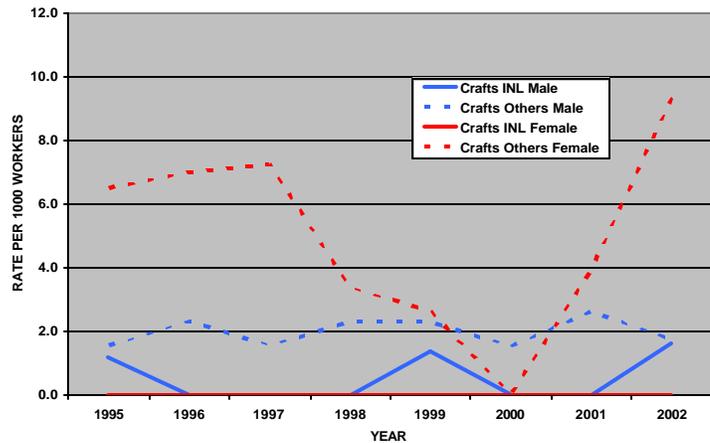
We noted a similar pattern among Security workers (Figure 12). Rates among women at other sites were generally higher than those of men and fluctuated more widely. An extreme increase in the rate among women at other sites was noted in 2001, but decreased in 2002. Additional years of data will help to clarify whether the increase is sustained. No autoimmune disease diagnoses were reported among Security workers of either gender at INL over the eight year period.

FIGURE 12. FIRST REPORTED AUTOIMMUNE DISEASE RATES AMONG SECURITY WORKERS, INL VERSUS OTHER SITES, 1995-2002



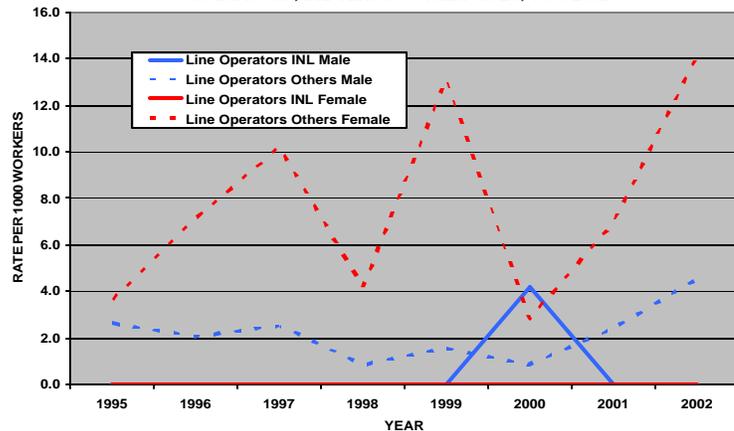
No new autoimmune disease diagnoses were reported by women in Crafts at INL during the eight year period (Figure 13). Men in Crafts at INL also had very low rates. Rates among men at other sites were somewhat higher and quite consistent, fluctuating very little from approximately 2 cases per 1000 workers annually. By contrast, rates among women in Crafts at other sites showed considerable instability. After a rapid decrease from 1997 to 2000, the rate among women increased above its 1997 level in 2002. Other than the vagaries of rates based on small numbers, we found no obvious explanation for such a rapid decline and reversal in the rate of autoimmune diseases among women, particularly when rates among men at these sites were comparatively stable.

FIGURE 13. FIRST REPORTED AUTOIMMUNE DISEASE RATES AMONG CRAFTS WORKERS, INL VERSUS OTHER SITES, 1995-2002



No new diagnoses of autoimmune disease were reported among INL female Line Operators during the eight years (Figure 14). Men in this occupational group at INL also reported no new cases in most years. As among Crafts workers, male Line Operators at other sites had a relatively consistent rate throughout most of the period, not exceeding about four initial diagnoses per 1000 workers over the period. By

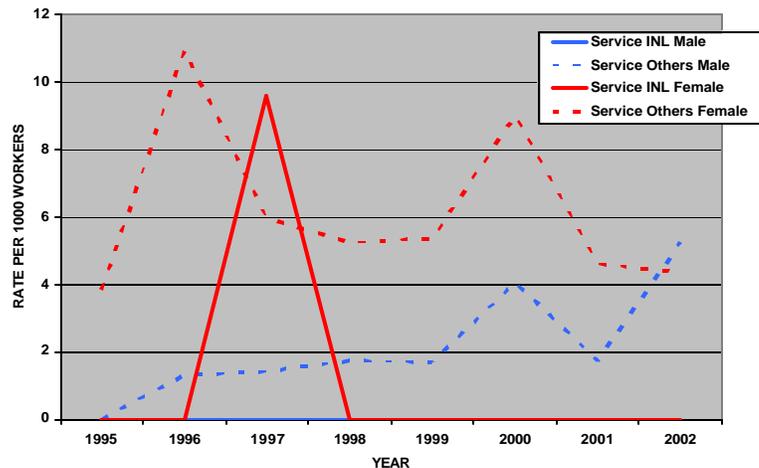
FIGURE 14. FIRST REPORTED AUTOIMMUNE DISEASE RATES AMONG LINE OPERATORS, INL VERSUS OTHER SITES, 1995-2002



contrast, rates among women at other sites were extremely unstable, at least in part due to the relatively small number of women in this occupational group. INL averaged fewer than 50 female Line Operators over the eight year period. Small changes in the number of diagnoses made in a given year in such a small group lead to large swings in rates.

Male Service workers at other sites showed a small, almost steady increase in the rate of initial reports of autoimmune disease over the eight years (Figure 15). Women in Service occupations at other sites showed much wider fluctuations but no evidence of a consistent change in the rate. At INL, no new initial diagnoses of autoimmune disease were reported by men at INL and only one initial diagnosis among women in Service occupations was reported during the period. On average, INL's workforce included about 240 male and 110 female Service workers over the eight year period, a relatively small number of workers.

FIGURE 15. FIRST REPORTED AUTOIMMUNE DISEASE RATES AMONG SERVICE WORKERS, INL VERSUS OTHER SITES, 1995-2002



We saw no evidence of an overall consistent trend in the reporting of autoimmune diseases among either men or women at INL during 1995-2002. The rate of initially reported diagnoses was marked by considerable variability at other sites as well. The rate among female In-house Professionals decreased through the first half of the eight year period, then stabilized. Rates among workers in the Administrative Support and Technical Support occupational groups showed remarkable consistency between genders, but the reasons for this consistency are not apparent. Considered collectively, men and women in Administrative Support occupations at other sites showed an increased rate of first reported disease from 2000 to 2002. Over the eight year period, their rate increased from approximately 1 report per 1000 workers to 5 reports per 1000 workers. No comparable trend was noted among Administrative Support workers at INL, whose rate varied but did not increase over the eight year period.

Diagnoses

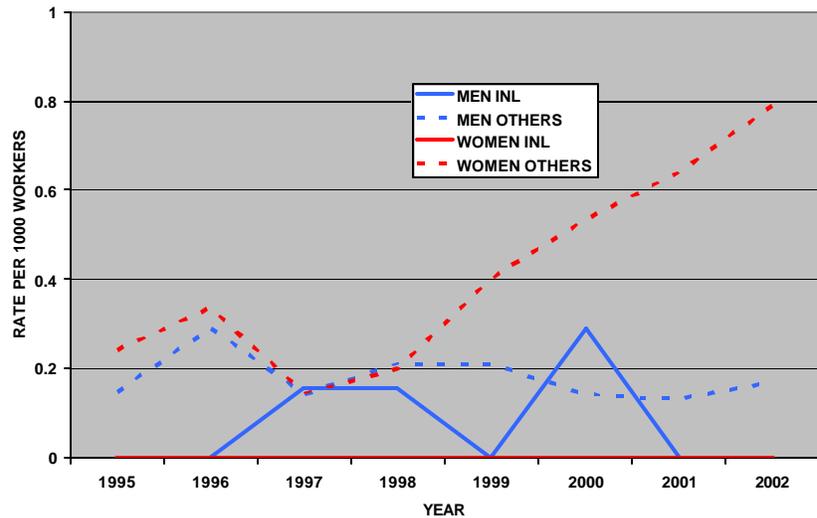
An analysis of overall trends in autoimmune disease occurrence is of value, but the differences in occurrence by gender, age, and physical expression of various types of disease indicate a need to evaluate particular diagnoses more specifically. At RESL, particular concerns were voiced concerning MS, FM, and neurologic autoimmune diseases. Some caveats should be kept in mind in considering the assessments presented below. Although some diseases such as MS are relatively well characterized clinically, others such as FM have yet to be agreed upon as a distinct clinical entity. Moreover, to say that an autoimmune disease is neurologic or musculoskeletal may only reflect its primary physical expression. Many autoimmune diseases

affect more than one organ system, suggesting that the primary expression of an autoimmune disease is often part of a continuum of physical response to a challenge posed by environmental and genetic factors. Autoimmune diseases are found in a variety of physical expressions, the musculoskeletal system being the most frequently reported in the IISP data. The nervous system and sensory organs, digestive system, and a variety of endocrine, metabolic, and immune system responses followed in frequency of occurrence (see Figure 3).

Nervous system diseases include diagnoses such as MS, Guillain-Barre syndrome, and myasthenia gravis. No female workers at INL reported autoimmune disease diagnoses affecting the nervous and sensory systems from 1995 to 2002 (Figure 16). By contrast, the rate among women at other sites rose

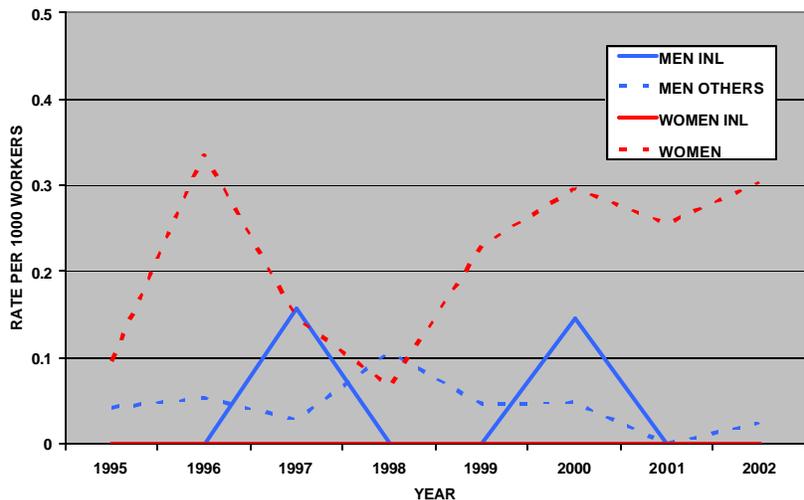
steadily from 1997, although at a peak of about 0.8 diagnoses per 1000 workers in 2002, the absolute number of affected workers remained quite small. Women of all age groups showed an increase, but women under 50 years of age had a more consistent increase over the eight years. Men at INL and at other sites showed no evidence of an increase. During the period 1997 to 2002, male workers at other sites had an essentially flat rate of nervous and sensory system autoimmune disease.

FIGURE 16. FIRST REPORTED NERVOUS SYSTEM AND SENSORY AUTOIMMUNE DISEASE BY GENDER, INL VERSUS OTHER SITES, 1995-2002



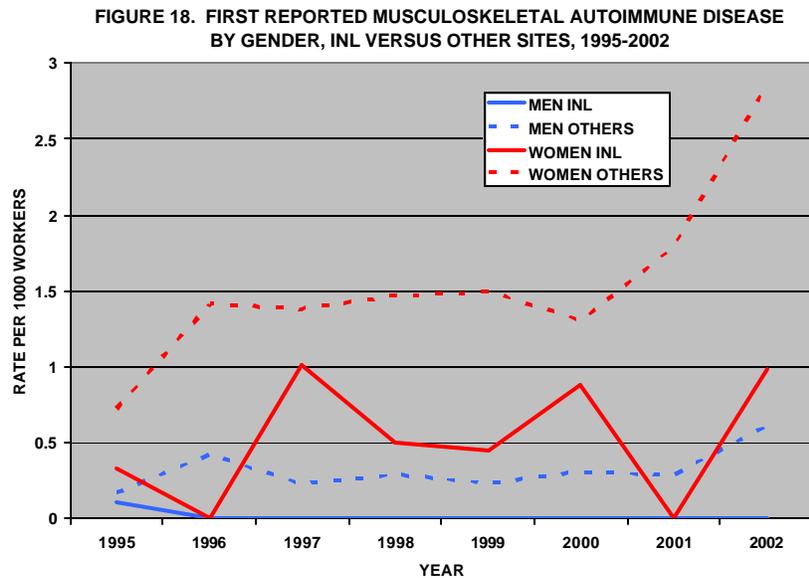
MS (Figure 17) involves the destruction of the myelin sheath that normally covers nerves and is marked by areas of hardened tissue in the brain or spinal cord. The disease may ultimately lead to partial or complete paralysis. We saw no evidence of a consistent change in rates over time for either men or women at INL or the other sites. The increasing rate since 1998 among women at other sites may only reflect wide

FIGURE 17. FIRST REPORTED MULTIPLE SCLEROSIS RATES BY GENDER, INL VERSUS OTHER SITES, 1995-2002

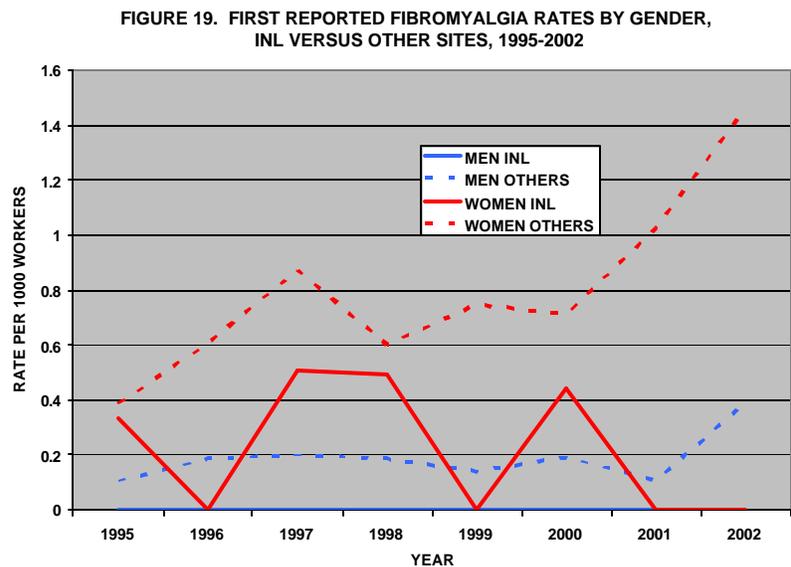


variations from year to year.

Musculoskeletal diseases affect the muscles and skeleton. Examples include SLE, rheumatoid arthritis, and FM. Our overall evaluation of autoimmune conditions in this diagnosis category (Figure 18) indicated that the rate has been increasing sporadically among women at other sites during the eight year period, from an initial rate of about 0.7 diagnoses per 1000 women in 1995 to almost 3 diagnoses per 1000 women in 2002. At other sites, higher rates were seen among women aged 50 and above than among younger women, but both age groups' rates tended to increase over time. Women at INL showed no evidence of an increase, nor did men at either INL or other sites. In general, rates were higher among women than among men.



FM (Figure 19) is characterized by chronic or recurring widespread pain, musculoskeletal stiffness, paresthesia (a sense of tingling or prickling on the skin without apparent cause), fatigue, and areas of tenderness. About 90 percent of FM patients are women. The estimated prevalence of the disorder in the United States is about 3.4 percent in women and 0.5 percent in men, and increases with age. FM is often found among individuals who have other



rheumatic disorders, chronic viral infections, or other systemic diseases such as SLE. Relatives of FM patients also appear to be at higher risk for the condition (Neumann and Buskila 2003, Harrison's 2005). Among the workers we assessed, the rate of first reports of FM increased relatively steadily from 1995 through 2002 among women at other sites, but no similar trend was

observed among men. Rates among INL women were lower than those of women at other sites throughout the period but did not display a consistent trend. No diagnoses were reported among INL men during the eight years. At other sites, rates among men were much lower than those of women.

Endocrine and Metabolic diseases (Figure 20) include a diverse spectrum of conditions affecting the endocrine system, the body's metabolic balance, and the immune system itself. The category includes such diagnoses as

insulin dependent, or Type I diabetes mellitus; Grave's disease (a disorder involving an overactive thyroid gland which affects women about seven times more often than men); and Cushing's syndrome (a relatively rare hormonal disorder caused by prolonged exposure of the body to high levels of the hormone cortisol, most commonly affecting adults of age 20 to 50). In our data, four of the 109 initially reported diagnoses in this

category were at INL. The diagnoses at INL included two cases of diabetes mellitus and two cases of chronic thyroiditis. The diagnoses at INL and at other sites were divided equally by gender. Three of the four reports at INL occurred among In-house Professionals, as did 10 of the 105 first reports at other sites, a significantly different occupational distribution (Chi-square = 15.73, DF=1, $p \leq .001$). Rates of initially reported diagnoses in the endocrine and metabolic disease category showed no evidence of a consistent trend among women at INL nor at other sites. The rate increased over time among men at other sites, but still remained quite low throughout the period, reaching

a high of about one case per 3000 men in year 2000. The overall rate of initial reports was quite low, estimated at about 5.5 cases per 100,000 workers in eight years at INL and, at other sites, 23 cases per 100,000 workers in eight years.

Type 1 diabetes mellitus (Figure 21) is an inflammatory autoimmune disease involving the pancreas, results in the destruction of insulin

FIGURE 20. FIRST REPORTED ENDOCRINE AND METABOLIC AUTOIMMUNE DISEASE BY GENDER, INL VERSUS OTHER SITES, 1995-2002

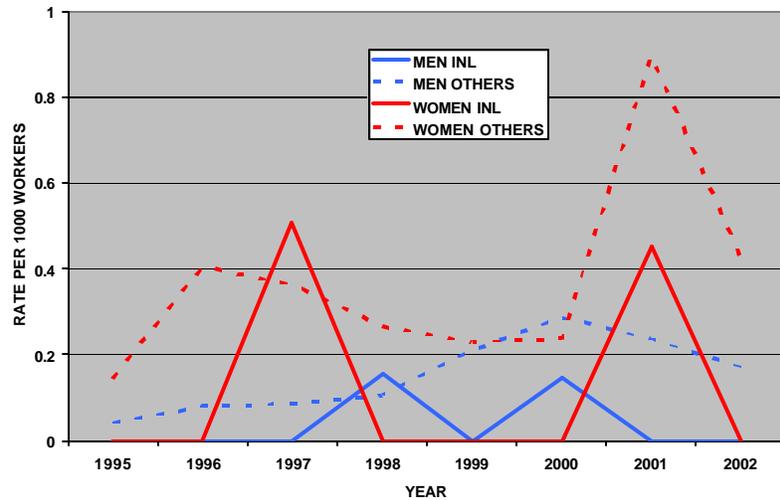
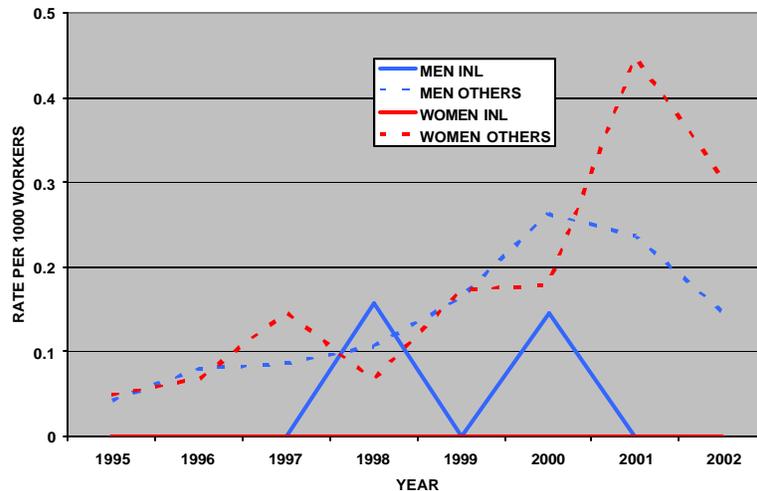
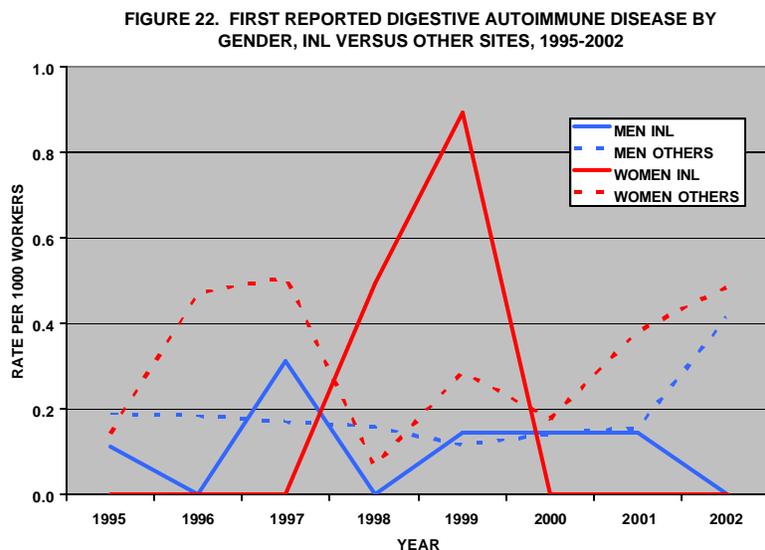


FIGURE 21. FIRST REPORTED DIABETES MELLITUS BY GENDER, INL VERSUS OTHER SITES, 1995-2002



producing cells and, consequently, results in chronic insulin deficiency. It occurs primarily in children and adolescents. As yet unidentified environmental triggers are suspected of playing a role in the expression of Type 1 disease in susceptible individuals. A variation of Type 1 diabetes called autoimmune diabetes of adulthood does occur in adults. Type 2 diabetes, in contrast, is the more common type, occurring primarily in adults. Until recently it was not considered to have an autoimmune component, but recent research has opened the possibility that Type 2 diabetes might involve an autoimmune response, based on the detection of markers of such a response among adults diagnosed with the Type 2 form of the disease (Hathout et al. 2001). Nonetheless, Type 2 diabetes is considered predominantly a disease of lifestyle, with diet, obesity, and lack of exercise being major risk factors. Our data did not permit a clear distinction between the types of diabetes, hence we examined them collectively. We found a noteworthy increase in the rate of diabetes among women at other sites from 1998 to 2001 and a similar increase among men from 1995 to 2000. Of the 72 reports of diabetes in our analysis, only two were reported by male INL workers and none by women at INL.

Digestive tract diseases (Figure 22) known to be or suspected of being autoimmune diseases include such conditions as Crohn's disease (a form of chronic inflammation of the lower small intestine), ulcerative colitis (an inflammatory condition of the large intestine), and regional enteritis (an inflammatory condition of certain areas of the small intestine). Our data contained 111 diagnoses involving potentially autoimmune digestive tract diseases, nine of which were reported by INL workers. Slightly more than half of the diagnoses at INL and at other sites involved regional enteritis; almost all of the remainder were ulcerative colitis. We saw no evidence of



any systematic trend in digestive disease rates among INL workers. A large spike in the rate among INL women during 1997 to 2000 peaked in 1999, but returned to zero by year 2000. Among women at other sites, a decline in the rate from 1996 to 1998 has been followed by a somewhat steady increase. In similar fashion, men's rates increased from year 2000 to 2002 after an earlier, modest decline. Rates of enteritis increased recently among both men and women at other sites, but we found no evidence of any systematic change among INL workers. We also examined rates of ulcerative colitis in these populations but found no evidence of a systematic change over time among workers at INL or the other sites.

DISCUSSION AND CONCLUSIONS

Limitations

The primary limitation of this assessment is that it could not determine specifically whether RESL employees experience an increased risk of various autoimmune diseases, compared with other workers. IISP data lacked a designation for the specific place of work or a history of former work sites for individuals at INL or at other sites. The overall purpose of this assessment was to evaluate whether indications exist that INL workers are at increased risk for autoimmune disease, and to determine if additional health assessment activities are warranted or feasible. Federal workers are not required to use site occupational medicine facilities, therefore they are not included in the IISP.

No absolute consensus exists on which diseases are autoimmune in origin. Our review adopted a broad approach, including a number of diagnoses (e.g., chronic fatigue syndrome) for which autoimmune status is currently debated. We applied the same definition of eligible diagnoses uniformly for all sites in the review (Appendix B).

The lack of precise diagnoses for some of the RESL employees was of concern. Dr. Creighton, the SOMD, reviewed the available medical and industrial hygiene data for the individuals and found no potential exposures of concern. He pointed out that high levels of fluoride exposure could produce a number of the symptoms reported by the RESL workers, but a source of high fluoride levels was not found. The water sources for the laboratory had been tested and found to have normal concentrations of fluoride. Our preliminary review of chemicals used at RESL identified no potential exposures having a known association with autoimmune disease.

We also discussed the employee health concern with NIOSH officials who investigated the health concern at the request of INL bargaining unit officials. They found insufficient evidence of a disease cluster to pursue a full health hazard evaluation. We concur with their conclusion that the available information did not indicate a cluster of specific autoimmune disease at RESL.

Health events are reported to site occupational medicine clinics by workers returning to work following absences equivalent to five or more consecutive workdays' duration. This approach inevitably fails to capture many diagnoses which result in shorter absences. As a result, the autoimmune diseases that appear to be more common may simply be those more likely to involve *absences* of five or more workdays, not necessarily those that *occur* more frequently. Moreover, the diagnoses we analyzed were self-reported by returning workers, subject to their understanding of their diagnosis, and not necessarily supported by a documented physician's diagnosis. Clinical documentation is not always required of or provided by a returning worker.

Discussion

Figure 23 summarizes our assessment of autoimmune disease trends at INL and a number of other sites in the IISP. Diagnostic categories for which trends of increasing rates appear systematic or large increases are evident are highlighted in red; decreasing trends or rates in blue. In general, the number of reported diagnoses at INL was too small to permit a thorough assessment of whether trends were statistically significant. In total, only 46 of the 911 “first reports” came from INL workers over eight years.

FIGURE 23. SUMMARY OF TRENDS BY DIAGNOSIS CATEGORY AND GENDER, INL VERSUS OTHER SITES, 1995-2002				
Diagnosis Category	INL Men (Diagnoses)	Other Sites Men (Diagnoses)	INL Women (Diagnoses)	Other Sites Women (Diagnoses)
<i>Endocrine, Metabolic, and Immune</i>	No overall change (2)	Possible small increase since 1998 (50)	Increase beginning in 2001 (2)	Increase beginning in 2001 (51)
<i>Hematopoietic (blood and blood forming tissues)</i>	No overall change (1)	No overall change (5)	No overall change (1)	No overall change (2)
<i>Nervous System and Sensory Organs</i>	No overall change (4)	No overall change (58)	No cases reported (0)	Steady increase since 1997 (54)
<i>--Multiple Sclerosis</i>	No overall change (2)	Slight decrease (15)	No cases reported (0)	No overall change (34)
<i>Digestive System</i>	No overall change (6)	Increase in 2002 (62)	Decrease since 1999 (3)	No overall change (40)
<i>--Regional Enteritis</i>	No overall change (2)	Increase since 1999 (29)	No overall change (3)	Increase since 2001 (23)
<i>--Ulcerative Colitis</i>	No overall change (4)	No overall change (32)	No cases reported (0)	No overall change (14)
<i>Musculoskeletal System</i>	No overall change (1)	No overall change (102)	No overall change (9)	Sporadic increase (200)
<i>--Fibromyalgia</i>	No overall change (1)	No overall change (56)	No overall change (4)	Increasing (126)

Examining rates in the various diagnosis categories, we saw no apparent, broad trend of increasing rates of any autoimmune disease category among the sites included in this assessment. In general, rates tended to be higher among women than among men at both INL and at other sites. In this respect, rates at DOE sites parallel those of other populations. Overall rates among women and men at other sites were generally higher than those of like-gendered INL workers

throughout the eight years, and a tendency of the overall rates to increase with age among both genders at INL and other sites was evident. No changes of consequence among INL men were seen; most changes were noted among women at sites other than INL.

Women at other sites had the greatest number of increased rates in various diagnosis categories. We noted increased rates in endocrine and metabolic diseases, nervous system diagnoses, regional enteritis, musculoskeletal conditions, and specifically, FM. The rate of nervous system and sensory organ diagnoses increased steadily among women at other sites, but no other group displayed evidence of a similarly consistent trend. Women at INL had recently increasing rates of endocrine and metabolic diagnoses but a declining rate of diagnoses affecting the digestive system.

An increase in the rate of musculoskeletal diagnoses was observed among women at other sites beginning in calendar 2000, but not among any other group. The rate of FM has been increasing from the same year among women at other sites, but no other group showed a noteworthy change. The predominance of FM among women is consistent with other reports (Olson 2001, White 2001). It is possible that the observed increase reflects growing acceptance of FM as a specific clinical diagnosis among physicians, increasing health insurance compensability for this diagnosis, a true increase in the condition, or some combination of these factors.

Among men, other sites had an increasing rate of endocrine and metabolic diseases and a recent increase in digestive system diagnoses including regional enteritis. Men at INL showed no evidence of a systematic change in rates for any of the diagnostic categories evaluated.

The upturn in the rate of endocrine and metabolic diagnosis rates among both men and women at other sites may in part reflect changing rates of diabetes mellitus, the rate of this disease having risen sporadically among women at other sites from 1995 through 2001 and among men at other sites from 1995 to 2000. Neither gender at INL showed evidence of an increase in diabetes mellitus.

We found no evidence of an increased occurrence of MS or of diagnoses involving the blood forming organs among any of the groups evaluated.

We also compared the experience of INL and other workers from the perspective of job categories. Overall, men had lower rates than did women, regardless of job category. We observed no job category with rates or a trend that should raise particular concern, but rates varied considerably over time in most job categories. Management and In-House Professionals were exceptions, exhibiting little change over the eight years at INL or other sites. INL men and women had variable rates but no evidence that workers in any job category were at special risk. Among workers at other sites, recent increases were noted among women in Administrative Support, Technical Support, and Security. Men at other sites experienced a recently increased rate among Technical Support workers and a more slowly increasing rate among Service personnel. We found it interesting that the rates of men and women paralleled each other closely over the eight years among Line Operators and Technical Support workers, although the rates among men were consistently lower than those of women. Other groups did not display this consistency.

Conclusions

Most of our analyses focused on categories of related autoimmune diseases or diseases believed to be related. Some specific diagnoses, e.g., FM and MS, were singled out because they were identified as diseases of special concern. Some diagnoses included in our analyses are not commonly agreed upon as being autoimmune in origin. They were included to ensure that potentially important diagnoses would not be overlooked. Analyses of all autoimmune diseases collectively are of limited use in identifying whether particular groups of workers are at increased risk. It is likely that any occupational exposure linked to autoimmune disease at INL or elsewhere will not affect the risk of all diagnoses strongly enough that we could detect the increased risk. While an exposure linked to a general increase in the risk of all autoimmune diseases cannot be ruled out, to date no such exposure has been identified in the scientific literature. Existing research suggests that the interplay of genetic and environmental factors ultimately producing clinical disease is complex. In other words, not all autoimmune diseases have a common origin or arise from a common exposure, so analyzing them all together could obscure an important, more specific exposure relationship. While we lacked industrial hygiene exposure data for individuals, we were able to analyze the occurrence of autoimmune disease among workers in various job categories. The job categories are a rough surrogate for exposure, useful in broadly categorizing workers with similar functions and work environments.

Keeping the above caveats in mind, the results presented in this report do not point to a cause for concern regarding the occurrence of autoimmune disease at INL compared with a number of other sites in the DOE complex. In general, rates at INL were lower for various autoimmune diseases than were the rates we observed among the comparison sites. While it is possible that health care delivery in the geographic area around INL differs from delivery elsewhere, the differences are unlikely to be so great as to produce the consistent disparity we found between INL and other sites. It is possible that the rules under which workers are required to report for occupational medicine clearance before returning to work may be applied differently at various sites, thus affecting the likelihood of identifying a worker absent for a new diagnosis of autoimmune disease, but we were not able to verify that all sites apply the Order 440.1 requirements consistently. Other, similar assessments conducted by the Office of Epidemiology and Health Surveillance have not found the application of clearance rules to be a significant factor in variation observed across sites.

The rates based on first reports fluctuated widely from year to year at INL and at the other sites in many cases. The most plausible explanation for most of this variation is that the rates were calculated based on very small numbers. We found no consistent changes among men at INL, and among women only endocrine and metabolic conditions showed a recent increase, the importance of which can be assessed by future surveillance.

Many patterns of disease occurrence among workers were similar to those in other populations. Rates were generally higher among women and tended to increase with age. However, no particular occupational group appeared to be at higher risk of disease. We noted a long term increase in the rate of musculoskeletal conditions collectively and FM among women at sites

other than INL. It is possible that the increase in FM reflects, at least in part, the increasing acceptance of this condition as a specific diagnosis among medical professionals.

Our analysis of IISP data indicated that INL workers are at lower risk for autoimmune disease than are workers at other sites. We found no job category at high risk. NIOSH staff who reviewed the illnesses among RESL workers and the SOMD both found insufficient indication of a disease cluster to warrant further investigation. We concur with that conclusion, but do have a number of recommendations.

RECOMMENDATIONS

Although we identified no clear indication of a cause for concern at INL, there are additional steps which can be considered to respond more fully to the worker's health concern:

- More systematic, repeated industrial hygiene monitoring of the facility can be conducted, including the maintenance of organized records of measurements and findings. An effort should be made to link exposure data to individuals, or at least to specific work areas.
- Compilation of a comprehensive work history for each RESL employee, including the employee's recall concerning the estimated frequency of all potential past and present exposures, is encouraged. Site industrial hygiene and occupational medicine staff should review the histories to identify any potential exposures of concern.
- Ensure that regular industrial hygiene monitoring of the RESL facility is conducted and that the results of monitoring are made readily available to all workers employed at the facility.
- Continued on-site occupational medical monitoring of RESL workers should be conducted. We recommend that clinical information on affected RESL employees be provided to the SOMD or his designee. Participation would be voluntary, but full cooperation by all RESL employees would increase the likelihood of success for this type of surveillance

REFERENCES

- Bierl, C; Nisenbaum, R; Hoaglin, DC; Randall, B; Jones, A-B, Unger, ER; Reeves, WC (2004) Regional distribution of fatiguing illnesses in the United States: a pilot study. *Population Health Metrics*: 2
- Bigazzi, PE. (1997) Autoimmunity caused by xenobiotics. *Toxicology*: 119; 1-21
- Centers for Disease Control and Prevention –CDC. (2003) Chronic Fatigue Syndrome- CFS Information. Available online: <http://www.cdc.gov/ncidod/diseases/cfs/info.htm>
- Cooper, GS; Miller, FW; Pander, JP. (1999) The Role of Genetic Factors in Autoimmune Disease: Implications for Environmental Research. *Environmental Health Perspectives Supplements*: 107; S5
- Davidson, A and Diamond B. (2001) Advances in Immunology: Autoimmune Disease. *The New England Journal of Medicine*: 345(5); 340-350
- D’Cruz, D. (2000) Autoimmune diseases associated with drugs, chemicals, and environmental factors. *Toxicology Letters*: 112-113; 421-432
- Dooley, MA and Hogan, SL. (2003) Environmental epidemiology and risk factors for Autoimmune disease. *Current Opinion in Rheumatology*: 15; 99-103.
- Dunkin, MA, et al. (2002) *Questions and Answers about Autoimmunity*. Washington, DC: National Institute of Arthritis and Musculoskeletal and Skin Diseases, NIH Publication No. 02-4858.
- Hathout EH, et al. (2001). Diabetic Autoimmune Markers in Children and Adolescents With Type 2 Diabetes. *Pediatrics*: 107 (6);102-106.
- Introduction: Possibly Autoimmune Diseases*. (n.d.). Retrieved July 21, 2005, from http://www.wrongdiagnosis.com/p/possibly_autoimmune_diseases/intro.htm
- Jacobson, DL; Gange, SJ; Rose, NR; Graham, NMH. (1997) Epidemiology and Estimated Population Burden of Selected Autoimmune Diseases in the United States. *Clinical Immunology and Immunopathology*: 84(3); 223-243
- Loveren, HV; Vos, JG; Germolec, D; Simeonova, PP; Eijkemanns G; McMicheal, AJ. (2001) Epidemiologic associations between occupational and environmental exposures and autoimmune disease: Report of a meeting to explore current evidence and identify research needs. *International Journal of Hygiene and Environmental Health*: 203; 483-495

Olson JC, O'Connell BA. (2001). Autoimmune diseases. In: Hofmann M, Hooper MA, eds. *Connecticut Women's Health*. Hartford, CT: Connecticut Department of Public Health, 2001:128-42

Powell, JJ; Van de Water, J; Gershwin, ME. (1999) Evidence for the Role of Environmental Agents in the Initiation or Progression of Autoimmune Conditions. *Environmental Health Perspectives Supplements*: 107; S5

Seattle Post-Intelligencer. February 10, 2005. Idaho to study MS link, nuclear testing

Shomon, MJ. (2002). *Living Well With Autoimmune Disease: What Your Doctor Doesn't Tell You That You Need to Know* (First Edition). New York: HarperCollins, HarperResource.

Sutton PRN (1987). Does Fluoride Ingestion Affect Developing Immune System Cells? *Medical Hypotheses* 23; 335-336

White, KP; Harth, M. (2001) Classification, Epidemiology, and Natural History of Fibromyalgia. *Current Pain and Headache Reports*: 5; 320-329

APPENDIX A

DEPARTMENT OF HEALTH AND HUMAN SERVICES



Memorandum

Date January 28, 2005
From Elena Page, HETAB, DSHEFS (R-10)
Subject Close-out of HETA 2005-0034

To HETA File 2005-0034
Through: Chief, HETAB ___ ___ (R9)
Chief, Medical ___ ___ (R-9)

This Health Hazard Evaluation (HHE) request was from the President of the International Federation of Professional and Technical Employees (IFPTE) Local 9, at the Idaho National Environmental and Engineering Laboratory, a Department of Energy (DOE) Facility. The request was to investigate a possible cluster of autoimmune disease among employees in the Radiological and Environmental Sciences Laboratory (RESL). Steve Ahrenholz of the Health-Related Energy Research Branch and I called representatives of the DOE Occupational Safety and Health office to discuss the HHE. They notified us that they were aware of the concerns and were looking into it themselves, and did not feel an HHE was needed. We agreed that I would contact the requester to discuss the issues further, and to decide if an HHE was warranted. I spoke to the requester, who referred me to another union official who could provide me with the details of the concerns. This individual reported that of approximately 40 employees in the RESL, one had (MS), one had an inflammatory arthritis with an elevated erythrocyte sedimentation rate, but no other autoimmune markers, and one had fibromyalgia. These individuals worked in different areas of the lab with different exposures. In addition, one employee had symptoms consistent with MS, but had not been diagnosed with MS. I explained to both union officials that this did not appear to be a cluster of autoimmune disease, but actually 3 unrelated diseases in employees who did not share job exposures, and that I did not feel an investigation was warranted. They declined receiving written information explaining what we had discussed on the phone. I advised both union officials and the DOE Safety and Health officials that I would be closing the HHE with this memo to the file.

Elena Page, M.D., M.P.H.

Keywords: autoimmune, multiple sclerosis, fibromyalgia, arthritis
SIC: 8734 (testing laboratories)

Determination: negative

[Note: The referenced bargaining unit was Local 94, not Local 9, per information provided by a site bargaining unit representative. – CHS]

APPENDIX B

CONDITIONS AND DISEASES INVOLVING AUTOIMMUNITY*

INFECTIOUS AND PARASITIC DISEASES (001-139)
Lyme disease (Erythema chronicum migrans)
Reiter's syndrome
Sarcoidosis
Behcet's disease
NEOPLASMS (140-239)
Autoimmune lymphoproliferative syndrome
ENDOCRINE, NUTRITIONAL, AND METABOLIC DISEASES, AND IMMUNITY DISORDERS (240-279)
Grave's disease without thyrotoxic crisis/storm
Grave's disease with thyrotoxic crisis/storm
Hashimoto's thyroiditis
Insulin dependent diabetes mellitus
Hypoparathyroidism
Cushing's syndrome
Addison's disease
Polyglandular syndrome
Essential mixed cryoglobulinemia
Primary agammaglobulinemia
Autoimmune disease NEC
DISEASES OF THE BLOOD AND BLOOD-FORMING ORGANS (280-289)
Pernicious anemia
Autoimmune hemolytic anemia
Idiopathic thrombocytopenia purpura
DISEASES OF THE NERVOUS SYSTEM AND SENSE ORGANS (320-389)
Stiff Man syndrome
Multiple sclerosis
Guillain-Barre
Chronic inflammatory demyelinating polyneuropathy
Myasthenia gravis
Uveitis
Meniere's disease (inner ear disease)
DISEASES OF THE CIRCULATORY SYSTEM (390-459)
Rheumatic fever
Acute rheumatic heart disease
Rheumatic heart disease
Cardiomyopathy
Raynaud's syndrome

Polyarteritis nodosa
Goodpasture syndrome
Other specified hypersensitivity angiitis
Wegener's granulomatosis
Temporal/giant cell arteritis
Thrombotic microangiopathy
Takayasu arteritis
Vasculitis
Degos' disease
DISEASES OF THE RESPIRATORY SYSTEM (460-519)
Idiopathic pulmonary fibrosis
DISEASES OF THE DIGESTIVE SYSTEM (520-579)
Regional enteritis (Crohn's disease)
Regional enteritis, unspecified site
Ulcerative colitis
Ulcerative colitis, unspecified site
Autoimmune hepatitis
Primary biliary cirrhosis
Celiac sprue
DISEASES OF THE GENITOURINARY SYSTEM (580-629)
Nephritis and nephrosis in diseases classified elsewhere
IgA nephropathy
Interstitial cystitis
DISEASES OF THE SKIN AND SUBCUTANEOUS TISSUE (680-709)
Dermatitis herpetiformis
Pemphigus vulgaris
Bullous pemphigoid
Cicatricial pemphigoid without ocular involvement
Cicatricial pemphigoid with ocular involvement
Discoid lupus
Psoriasis
Lichen planus
Scleroderma
Alopecia areata
Vitiligo
DISEASES OF THE MUSCULOSKELETAL SYSTEM AND CONNECTIVE TISSUE (710-739)
Systemic lupus erythematosus
CREST syndrome
Sicca syndrome
Dermatomyositis
Polymyositis
Mixed connective tissue disease
Arthropathy associated with GI

Rheumatoid arthritis
Ankylosing spondylitis
Polymyalgia rheumatica
Fibromyalgia
Polychondritis
SYMPTOMS, SIGNS, AND ILL-DEFINED CONDITIONS (780-799)
Chronic fatigue
Antiphospholipid syndrome

**List compiled based on information from the American Autoimmune Related Diseases Association (<http://www.aarda.org/>), conditions recognized by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (Dunkin 2002), and supplemented with diagnoses published in Shomon (2002). Additional potentially autoimmune diseases were identified in Introduction: Possibly Autoimmune Diseases (2005).*

APPENDIX C

STANDARDIZED OCCUPATIONAL CATEGORIES

Management (M) – Predominately office work at a desk; first level supervisor and above; anticipated risks primarily ergonomic

Administrative Support (A) – Predominately office work at a desk; heavy computer usage; anticipated risks primarily ergonomic. This category includes but is not limited to information technology, clerical, and secretarial staff.

In-House Professionals (I)– Predominately office work at a desk typically without supervisory responsibilities. The risks are primarily ergonomic.

Field Professionals (F)– Frequently works outside of their office in areas such as but not limited to laboratories, testing areas, and construction areas. Potential for exposure to chemical or radiation hazards.

Technical Support (T)– Workers who typically support the field professionals and have hands-on work situations. Potential for exposure to chemical or radiation hazards; the potential for exposure may be higher than for the field professionals.

Bio hazard (B)– Workers who have the potential for exposure to biological hazards. This includes medical technicians, nurses, laboratory staff, animal caretakers, physicians, and veterinarians.

Service (S)– Typically includes but is not limited to custodians, drivers, laborers, laundry workers, linemen, mail clerks, pilots, railroad engineers, records center workers, stationary engineers, utility workers, and water plant operators. These workers support and maintain the facility's infrastructure and have the potential for a broad range of exposures. Most work is not performed sitting at a desk.

Security and Fire (E) – Typically includes protective forces and firefighters.

Crafts (C)– Typically includes bargaining unit employees and laborers. They have the potential for a broad range of exposures.

Line Operators (O)–Typically workers who are involved in process, operation, or line activities at the facility. Potential for chemical and/or radiation exposure on a regular basis.

Guests (G) – Employees on short-term assignments or internships. Typically includes guest scientists, postdoctoral fellows, co-op students, and interns. Potential for exposure dependent on job assignment.

Unknown (U) – Job title is missing.