Screening for Beryllium Disease Among Construction Trade Workers at Department of Energy Nuclear Sites

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Background *To determine whether current and former construction workers are at significant risk for occupational illnesses from work at the Department of Energy's (DOE) nuclear weapons facilities, screening programs were undertaken at the Hanford Nuclear Reservation, Oak Ridge Reservation, and the Savannah River Site.*
Methods *Medical examination for beryllium disease used a medical history and a beryllium blood lymphocyte proliferation test (BeLPT). Stratified and multivariate logistic regression analyses were used to explore the risk of disease by age, race, sex, trade, duration of DOE employment, reported work in buildings where beryllium was used, and time since last DOE site employment.*
Results *Of the 3,842 workers included in this study, 34% reported exposure to beryllium. Overall, 2.2% of workers had at least one abnormal BeLPT test, and 1.4% were also abnormal on a second test. Regression analyses demonstrated increased risk of having at least one abnormal BeLPT to be associated with ever working in a site building where beryllium activities had taken place.*
Conclusions *The prevalence of beryllium sensitivity and chronic beryllium disease (CBD) in construction workers is described and the positive predictive value of the BeLPT in a population with less intense exposure to beryllium than other populations that have been screened is discussed. The BeLPT findings and finding of cases of CBD demonstrate that some of these workers had significant exposure, most likely, during maintenance, repair, renovation, or demolition in facilities where beryllium was used.* Am. J. Ind. Med. 46:207–218, 2004. *© 2004 Wiley-Liss, Inc.*

KEY WORDS: DOE; Hanford; Oak Ridge; Savannah River; beryllium; construction trades; chronic beryllium disease; blood lymphocyte proliferation test; surveillance

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BACKGROUND

In 1993, Congress added Section 3162 to the Defense Authorization Act, calling for the Department of Energy (DOE) to determine whether workers within the nuclear weapons facilities were at "significant risk" for work-related illnesses and if so, to provide them with medical surveillance. DOE initially established six pilot programs, including three programs directed at construction workers at the Hanford Nuclear Reservation in Richland, WA; the Oak Ridge Reservation in Oak Ridge, TN; and the Savannah River Site (SRS) in Aiken, SC.

It is known that workers at some DOE facilities have been exposed to beryllium Be dust or fumes [Stange et al., 2001], and that as a result some workers have developed chronic beryllium disease (CBD), a gradually debilitating lung disease [Rossman, 2001]. Inhalation of beryllium in the form of dust, fume, or aerosols can lead to a beryllium specific T-cell mediated immune response in exposed workers [Maier, 2001]. At this point, beryllium sensitization and subsequent disease are thought to be due to a multi-stage process: workers are exposed to dust or fumes on the job; a proportion of those workers become immunologically sensitized to the effects of the beryllium exposures due to genetic predisposition and exposure factors [Maier, 2002; Maier et al., 2002]. Most of those sensitized develop CBD in the future [Newman et al., 1996; Richeldi et al., 1997].

At Hanford, beryllium was a known contaminant in maintenance, overhaul, and demolition environments; this was documented as part of the needs assessment at Hanford performed prior to beginning medical surveillance. Beryllium usage was identified at five Hanford buildings between 1954 and 1989 in fuel fabrication and in research and development [Takaro et al., 2002].

When the Augusta Building Trades Medical Screening Program began, there had been no identified beryllium exposures at the Savannah River Site, but exposures were anticipated based on the Savannah River Site needs assessment. Two usage locations were known at the time of the needs assessment. In 1970, there had been an antimony-beryllium source rod failure in the 105-K reactor where workers involved in clean-up likely had some exposure, and Pu-238/beryllium sources were used in Building 777-10A (formerly Building 777-M). Some additional uses and locations, including waste disposal areas, were subsequently identified; Be-Cu shapers were used in a machining operation before 1990, and an area that had been called the ‘‘hot shop’’ might have been a location for beryllium machining operations before 1980. In addition, beryllium was handled in some glove box operations, in which beryllium was chipped from a limited number of semi-spheres of plutonium in the 1970s.

Historical documents indicated that beryllium usage at the Oak Ridge Y-12 plant site began in 1946 at one location and was extended to multiple buildings or areas in the 1950s and 1960s.

Research by the University of Cincinnati revealed the location of a number of buildings at Y-12 where beryllium or beryllium compounds/alloys were machined, ground, milled, or formed into special shapes, nuclear weapons were assembled or disassembled; a change house/locker room facility contaminated with beryllium, and a pre-wash laundry for beryllium-contaminated work clothing were also identified. In June 1997, the University of Cincinnati received personal communications from investigators at the Oak Ridge Institute for Science and Education about work locations at the Oak Ridge Y-12 plant site where beryllium sensitization occurred.

The University of Cincinnati has also identified 26 beryllium usage or disposal locations at the Oak Ridge K-25 plant site. Usage at K-25 was similar to that at Y-12 (machining, filing, sanding), but also included using beryllium components for the Aircraft Nuclear Propulsion Project in the 1940s and 1950s, as a substrate for plating in the 1970s, and for the manufacture of beryllium mirrors for the Strategic Defense Initiative in the 1980s. Beryllium contamination was found in change house and laundry facilities, in several laboratory buildings, at a sand blast and heat treatment facility, at hazardous waste storage sites, classified burial grounds, holding ponds, and retention basins, in a warehouse used for building and other materials, and at the TSCA (Toxic Substance Control Act) incinerator.

One study indicates that construction workers may be at risk for beryllium sensitization and disease [Kreiss et al., 1993]. However, no clear evidence tells us which specific construction tasks are linked with beryllium exposure, nor quantitates the risk for sensitization or CBD from construction work tasks with potential beryllium exposures. Since construction workers at Hanford, Savannah River, and Oak Ridge were mostly employed by contractors and typically not considered to be ‘permanent employees,’ work history and exposure information on them is either nonexistent or very sporadic and unreliable. In addition, most construction workers had not been included in site medical surveillance programs. Construction workers have potential for exposure to beryllium during work tasks involving repair, maintenance, renovation, or demolition in buildings where beryllium may have been used. Because of this risk a decision was made to include testing for beryllium disease in the screening programs for construction trade workers at Hanford, Oak Ridge, and Savannah River. The testing was according to the standard DOE protocol, using the BeLPT to identify potentially sensitized workers, who were then invited for a diagnostic evaluation at DOE-designated specialty clinical facilities. This study discusses findings from screening for beryllium disease among workers who completed at least one BeLPT from program inception through September 30, 2002.

MATERIALS AND METHODS

Surveillance Program Overview

The surveillance programs at the three sites were designed and implemented through a two-step process: a needs assessment characterizing site processes, work, and potential exposures, followed by development of appropriate surveillance instruments and protocols for workers participating in the screening effort. The work history collected information on the worker’s trade, and whether the worker was subjected to hazards identified during the needs assessment for that site. The medical examination includes a detailed medical history, smoking history, physical examination, and tests for health effects from specific hazards. Workers were asked about beryllium exposures in three broad areas: (1) performing or working around maintenance, repair, renovation or demolition, (2) specifically working with or around beryllium, and (3) working in buildings or areas with potential exposures to beryllium. For each component of the occupational history, exposures to the task, material, or building were ranked qualitatively on a scale of 1–5; this process, and the details of the examination protocol are described in detail in a prior publication [Dement et al., 2003].

Beryllium Disease Surveillance

The beryllium screening relies on a medical history and examination, and a beryllium blood lymphocyte proliferation test (BeLPT) according to the standard DOE protocol [DOE, 1999a]. Figure 1 shows the clinical decision logic that is applied. The first step is to collect a blood sample, which is delivered for processing at a DOE-designated laboratory. The laboratories use approved protocols for processing a blood BeLPT. If the initial BeLPT was abnormal, the worker was

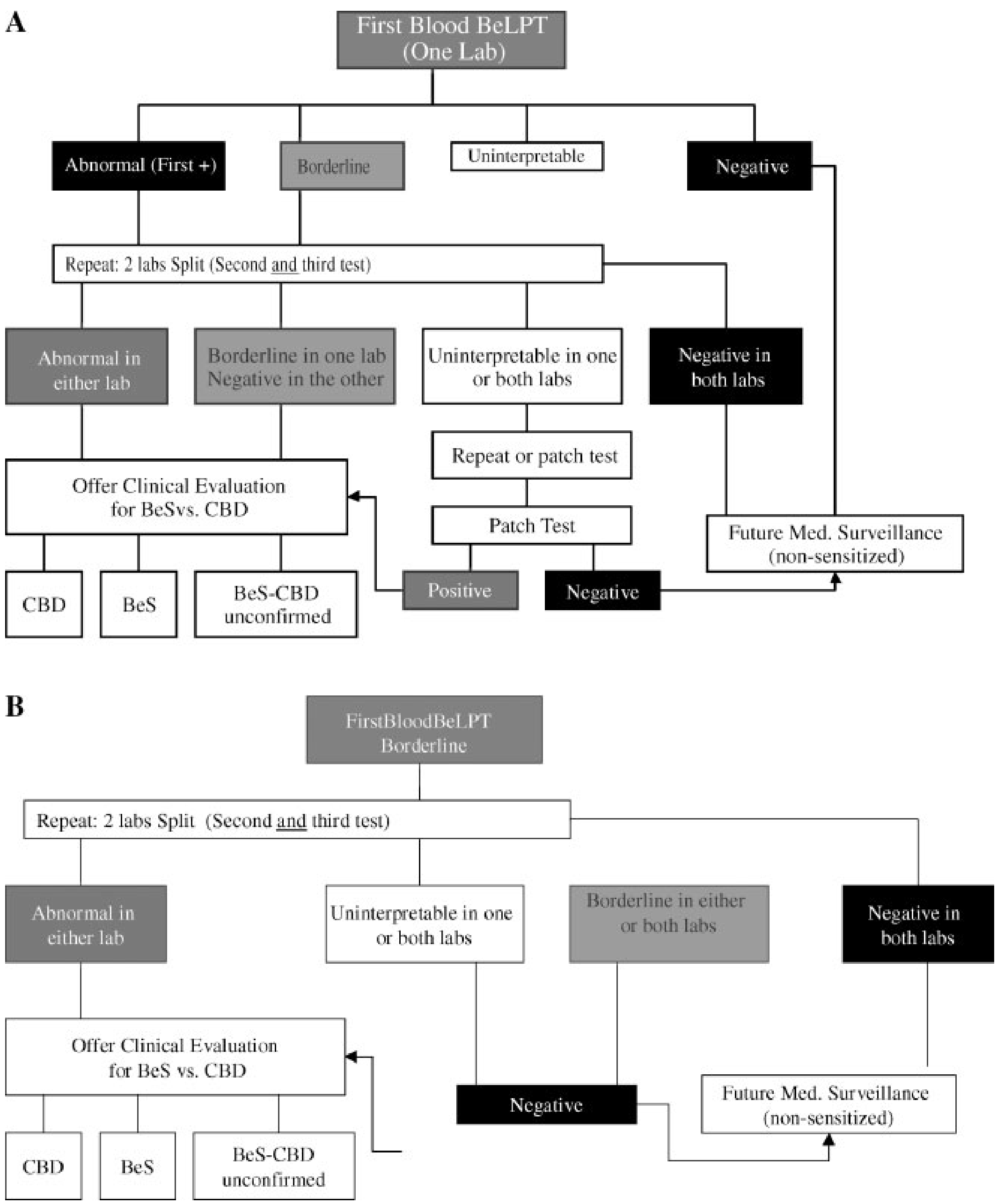

FIGURE 1. Workplace medical surveillance beryllium algorithms: One lab, then two lab split (**A**) workplace medical surveillance beryllium algorithms: One lab, then two lab split if first test borderline (**B**).

referred for a confirmatory BeLPT and for a respiratory disease module which included a respiratory history and symptom questionnaire, chest radiograph, and spirometry. The respiratory history and symptom questionnaire was adapted from the American Thoracic Society (ATS) DLD-78 questionnaire [Ferris, 1978]. Workers included in the respiratory examination receive a posterior-anterior (P-A) chest radiograph, classified by a local B-reader according to International Labor Office (ILO) Classification of Radiographs of Pneumoconiosis [International Labour Office (ILO), 1980]. For purposes of the analyses presented in this study, a parenchymal abnormality is defined as a profusion score of 1/0 or greater.

Spirometry was obtained according to the local provider's standard practices for pulmonary function tests, with [American Thoracic Society, 1987] standards serving as the acceptable benchmark test; details are provided in a prior publication [Dement et al., 2003].

A confirmed abnormal BeLPT test is defined as one abnormal plus one borderline or two abnormal tests (see Fig. 1). If a participant met the criteria described in Figure 1, he was referred for CBD medical evaluation through a program managed by the Oak Ridge Institute for Science and Education (ORISE). The CBD evaluation generally included physical examination, chest x-ray, chest CT, pulmonary function tests, pulmonary exercise study, and bronchoscopy with lavage and/or biopsy. The examining physician provided our program with a copy of the test results.

All data collected by these programs are stored in a Microsoft Access data management system (DMS). In addition to providing data storage and management capability, the DMS is used extensively for program management, quality control, and reporting. For these analyses, custom queries were developed to extract appropriate demographic, work history, exposure history, and medical information. These data were converted to SAS data sets for statistical analyses. All analyses used de-identified data. All analyses presented in this study were conducted using PC SAS Version 8 [SAS Institute, Inc, 1999].

Both descriptive and multivariate analysis methods were used. Demographic data were summarized by calculation of means and standard deviations of study parameters for continuous variables age and DOE work time and analysis of variance (ANOVA) was used to assess differences across sites. Stratified analyses were used to explore trends in disease frequency by age, race, sex, employment duration, work in buildings where beryllium was used, and cigarette smoking history. For categorical variables chi-square tests and Fisher's exact tests were used to assess association between demographic variables and the prevalence of abnormal BeLPT and trends in prevalence were tested for ordered categorical variables using the Cochran–Armitage trend test.

Unconditional logistic regression was used to further explore the risk of an abnormal blood BeLPT by duration of DOE employment, worker reported exposure to beryllium, and having worked in building with potential beryllium exposures, while controlling for potential confounders such as age, race, sex, and time period since last worked at DOE sites. For the unconditional regression analyses, a 'case' was defined as any worker with one or more abnormal BeLPT tests.

RESULTS

Table I shows the number of construction workers at risk, and the number of participants who have completed the screening program as of September 1, 2002. In all, 4,458 workers have been screened. Because participation in the program is voluntary, and workers may chose to accept only parts of the protocol, there are potential selection biases, both with regard to selection into the screening program, and in terms of the tests that participants have agreed to accept once they are in the program. Table II shows distribution by trade of the participants. A total of 3,842 workers completed beryllium testing, which is 86% of all participants.

Table III shows the distribution of workers with single and double abnormal Blood BeLPTs at each of the three facilities, and then with all facilities combined. Table III also displays demographic data by site. The proportion of workers with a single abnormal test varied among the sites and was found to be statistically significant ($P < 0.05$) while the rate of confirmed abnormal tests (double abnormals) was very similar among the three sites and not statistically different. The proportion of workers with an initial abnormal test who were confirmed abnormal with a second test was lower at Hanford than at the other two sites. Figure 2 shows that the cumulative prevalence of a single abnormal blood BeLPT declined at Hanford between 1999, when the program began, and 2002. We did not observe a similar decline at the other two sites. For most of the tests, Hanford and SRS sent initial

TABLE I. Construction Workers Exposed to Beryllium at Department of Energy Sites

Parameter	Hanford	Savannah River	Oak Ridge	All
Date site opened	1943	1949	1943	
Approximate number of workers ever employed	109,000	67,000	55,000	231,000
Number of workers potentially available for screening	30,000	37,000	8,000	75,000
Number of workers screened	1,624	1,592	1,242	4,458

TABLE II. Usual Trade of Construction Workers With BeLPT Results

Trade	Hanford	Savannah River	Oak Ridge Reservation	All sites combined (n, %)
Asbestos workers	19	32	12	63 (1.6)
Boilermaker	36	53	27	116 (3.0)
Brick masons	1	4	13	18 (0.5)
Carpenters	105	116	129	350 (9.1)
Cement masons/finishers	14	15	6	35 (0.9)
Electricians	177	281	249	707 (18.4)
Insulator	9	21	9	39 (1.0)
Ironworkers	92	53	69	214 (5.6)
Laborers	169	230	204	603 (15.7)
Machinists	8	12	7	27 (0.7)
Millwrights	58	29	20	107 (2.8)
Operating engineers	84	83	47	214 (5.6)
Painters	39	53	44	136 (3.5)
Pipefitters	280	281	129	690 (18.0)
Plumbers/steam fitters	86	7	30	123 (3.2)
Sheetmetal workers	55	62	82	199 (5.2)
Teamsters/truck driver	37	55	47	139 (3.6)
Welders	3	6	13	22 (0.6)
All Other	0	10	28	38 (1.0)

samples to the same laboratory; therefore, the trend at Hanford is unlikely to be explained by laboratory differences. However, a more detailed review of the Hanford data by time period found that workers who entered the surveillance program earlier tended to have worked at Hanford longer than those who participated in subsequent years. For example, workers who chose to participate in the surveillance program through June 1999 had worked at Hanford an average of 16.2 years compared to only 8.7 years for those participating in 2002. In addition, years of Hanford work showed a decreasing trend over the course of the surveillance program, which paralleled the downward slope in the prevalence of BeLPT abnormals. Likewise, the proportion of workers reporting to have worked in a building with potential beryllium exposures decreased with time.

Table IV shows the distribution of single abnormal tests by trade; the number of confirmed abnormals is too small to present this way. An overall chi-square test suggested significant differences ($P < 0.05$) in the prevalence of abnormal BeLPT tests among trades with five or more abnormals; the small numbers for other trades precluded finding any significant differences. With the hypothesis that exposure to construction trades occurs through maintenance and repair of beryllium contaminated mechanical systems, we analyzed the data by comparing mechanical trades (millwrights, mechanics, machinists, pipefitters, plumber/steamfitters, and sprinkler fitters) to all other trades; there was no significant difference in the test distribution between these groups. Table V shows the Blood BeLPT results by age, race, and sex; no significant differences are detected by race and sex or any significant trends with age. Table VI presents data stratified by time since first worked, time since last worked and duration of work at a DOE site. No statistically significant differences or trends were detected; however, the prevalence of an abnormal test was found to modestly increase with duration of DOE work.

Thirty-four percent of participants reported exposure to beryllium through the tasks and materials list; this ranged from a high of 50% of participants at Hanford to 20% at the Savannah River Site. Eighty-four percent of participants at the three sites reported having worked in at least one of the buildings identified as a beryllium building. Table VII shows that the risk of having a single abnormal Blood BeLPT is increased for workers who reported ever having worked in a beryllium building. Also, at Hanford, there were a number of specific buildings where a statistically significant association was observed; however, the association is much stronger considering all buildings together.

Logistic regression results are presented in Table VIII for all sites combined. For these analyses, an indicator variable was used to identify the three sites, with Oak Ridge Reservation serving as the reference cell. Workers older than 45 years were found to have increased risk of an abnormal BeLPT, although none of the odds-ratios were statistically significant. Having ever smoked, worker reported beryllium exposures, and years since last employed at DOE were not significant risk factors for an abnormal BeLPT. Having worked in a building with potential beryllium exposures was found to be a significant predictor of risk (OR = 3.4, 95% CI 1.3–8.8) as was work on the Hanford site compared to Oak

TABLE III. Demographic Characteristics of Construction and Craft Workers Completing BeLPT

Parameter	Hanford	Savannah River	Oak Ridge Reservation	All sites	Statistical significance comparing sites[e]
Number with BeLPT tests[a]	1,272	1,403	1,167	3,842	
Single abnormal BeLPT	39 (3.1%)	27 (1.9%)	19 (1.6%)	85 (2.2%)	$P < 0.05$
Double abnormal BeLPT	19 (1.4%)	22 (1.6%)	13 (1.1%)	53 (1.4%)	NS
Age[b]					
Mean (SD)	60.7 (12.7)	52.9 (12.1)	60.9 (12.8)	57.9 (13.1)	$P < 0.05$
Sex[c]					$P < 0.05$
Male (%)	1,251 (98.4%)	1,253 (89.3%)	1,144 (98.1%)	3,842 (95.0%)	
Female (%)	21 (1.6%)	150 (10.7%)	23 (2.0%)	194 (5.0%)	
Race[d]					$P < 0.05$
Caucasian (%)	1,091 (85.7%)	956 (68.1%)	1,037 (88.9%)	3,084 (80.3%)	
African-American (%)	41 (3.2%)	339 (24.2%)	42 (3.6%)	422 (11.0%)	
Hispanic (%)	30 (2.4%)	5 (0.4%)	1 (0.1%)	36 (1.0%)	
Asian/Hispanic (%)	3 (0.2%)	3 (0.1%)	0 (0.0%)	6 (0.2%)	
Alaskan/Indian (%)	13 (1.0%)	6 (0.4%)	6 (0.5%)	25 (0.7%)	
Other or missing (%)	94 (7.4%)	94 (6.7%)	81 (6.9%)	269 (7.0%)	
Years at DOE site					
Mean (SD)	12.1 (10.1)	12.4 (8.2)	15.6 (11.7)	13.2 (10.1)	$P < 0.05$

[a]Workers completing medical exams with BeLPT tests though September 1, 2002.
[b]Demographics and other data in this study are for workers completing both BeLPT Tests.
[c]Sex missing for 2 workers.
[d]Race missing for 245 workers.
[e]Chi-square tests were used for categorical variables and ANOVA tests were used for continuous variables. NS = $P > 0.05$.

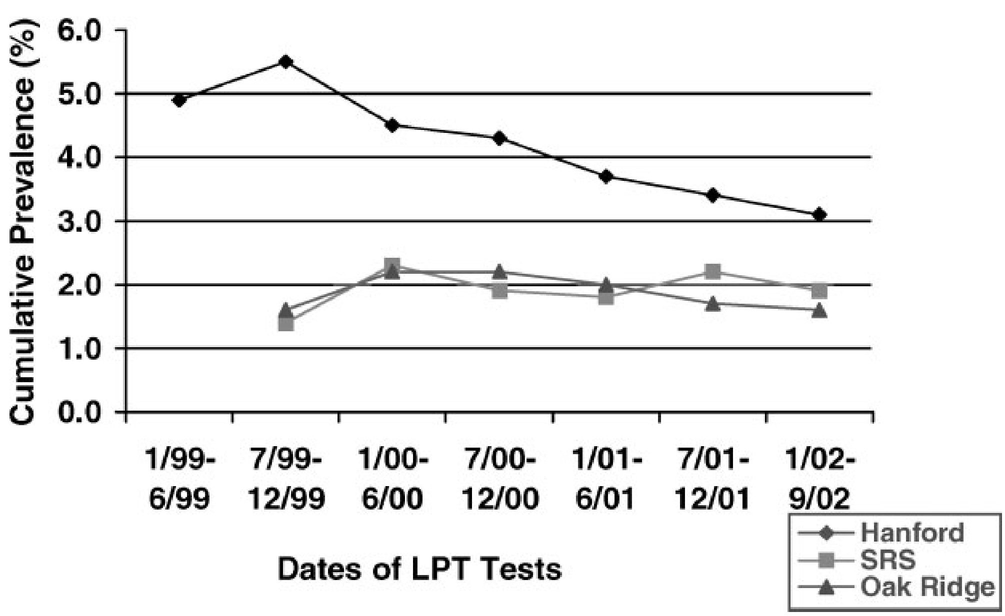

FIGURE 2. Single positive BeLPT cumulative prevalence. Results were lagged by 6 months from program start-up at each site in order to allow at least 100 BeLPT tests to have been conducted.

TABLE IV. Beryllium BeLPT Results by Usual TradeTrades With Five or More Single Abnormal BeLPT Tests for All Sites Combined

Trade	Number of workers tested	Number with 1 or more abnormal BeLPT	Overall prevalence (%)	Site with highest prevalence (no., %)
Asbestos workers	63	6	9.5	SRS (4, 12.5)
Carpenters	350	7	2.0	Hanford (3, 2.9)
Electricians	707	13	1.8	Hanford (7, 4.0)
Laborers	603	7	1.2	Hanford (5, 3.0)
Machinists	107	6	5.6	Oak Ridge (1, 14.5)
Millwrights	214	7	3.2	Oak Ridge (3, 15.0)
Pipefitters	690	14	2.0	Hanford (7, 2.5)
Plumbers/steam fitters	123	5	4.1	Oak Ridge (2, 6.7)
Sheetmetal Workers	199	5	2.5	Hanford (3, 5.5)

Chi-square tests found the prevalence to be statistically different by trade ($P < 0.05$) comparing trades with 5 or more workers with one or more abnormal BeLPT tests. The overall prevalence for all mechanical trades combined (millwrights, mechanics, machinists, pipefitters, plumber/steamfitters, and sprinkler fitters) was 2.8% versus 2.0% for all other trades, which is not statistically different (Fisher's exact test, $P = 0.16$).

Ridge Reservation (OR = 20, 95% CI = 1.2–3.6). No trends in risk with duration of DOE employment were observed.

Table IX provides descriptive information on pulmonary function, symptoms, and X-ray results for those workers with abnormal blood BeLPTs compared to those with normal tests. There are no statistically significant differences between the workers with and without an abnormal BeLPT. Five participants were diagnosed with CBD. Two had an abnormal BeLPT on cells taken during a lung washing (BAL) and an increased lymphocyte count among cells taken on lavage. A third presented with a granulomatous skin disease but had a normal BAL BeLPT on lavage; on a second evaluation the subsequent year he had an abnormal BAL BeLPT. One had a normal BAL BeLPT, but had giant cells on lung biopsy and a lymphocytosis on BAL, in the setting of abnormal lung function. Three had abnormal lung function, but also had concomitant findings of asbestos related disease. One individual with CBD had worked in a production job at a DOE facility as well as being engaged in construction work.

TABLE V. Beryllium BeLPT Results by Age, Race, and Sex

Parameter	Number of workers tested	Number one or more abnormal BeLPT and prevalence (%)	Number double abnormal BeLPT and prevalence (%)
Age (years)			
<45	637	9 (1.4)	5 (0.8)
45–54	1,018	23 (2.3)	15 (1.5)
55–64	918	20 (2.2)	17 (1.9)
65+	1,269	33 (2.6)	17 (1.3)
Race			
White	3,084	72 (2.3)	44 (1.4)
Non-White	506	7 (1.4)	5 (1.0)
Unknown	245	6 (2.5)	5 (2.0)
Sex			
Male	3,648	81 (2.2)	51 (1.4)
Female	194	4 (2.1)	3 (1.6)
Overall	3,842	85 (2.2)	54 (1.4)

Fisher's exact tests for differences in prevalence by age, race, and sex demonstrated no significant differences for single or double abnormal BeLPTs. No statistically significant trends in prevalence by age group were detected by the Cochran–Armitage trend test.

DISCUSSION

Screening workers with potential beryllium exposure using a blood BeLPT test is generally accepted as a valid indictor of both exposure and probability of developing subsequent CBD [Fontenot et al., 2000; Maier, 2001; Newman et al., 2001b]. For instance, the Department of Energy [DOE, 1999b] and the Department of Labor [DOE, 2000] accept the use of the blood BeLPT test for medical monitoring. CBD of the lung can be disabling, even fatal [Stoeckle et al., 1969; Meyer, 1994]. Treatment at an early stage for similar granulomatous diseases of the lung, such as sarcoidosis, can prevent disease progression [Rossman, 1996, 2001]. There is, therefore, a clear rationale for early detection of CBD, and a clear reason to screen for sensitization in populations at risk for CBD.

Since construction workers were mostly employed by contractors at Hanford, Savannah River, and Oak Ridge Reservation, and typically not considered to be 'permanent employees,' work history and exposure information on them is either nonexistent or very sporadic and unreliable. In order to provide meaningful medical surveillance programs for these workers, procedures have been developed for obtaining occupational and exposure histories through detailed interviews, incorporating maps, photos, and other site-specific materials intended to assist with recall. The work and exposure history process was developed to establish qualitative

TABLE VI. Beryllium BeLPT Results by Time Since First Worked, Time Since Last Worked, and Duration of Work at One of the DOE Sites

Parameter	Number of workers tested	Number one or more abnormal BeLPT and prevalence (%)	Number double abnormal BeLPT and prevalence (%)
Time since first worked at site (years)			
$\leq$20	1,083	24 (2.2)	14 (1.3)
$>$20	2,759	61 (2.2)	40 (1.4)
Time since last worked at site (years)			
$\leq$10	2,372	56 (2.4)	33 (1.4)
$>$10	1,470	29 (2.0)	21 (1.4)
Duration of DOE work (years)			
$<$5	928	18 (1.9)	13 (1.4)
5–14	1,458	31 (2.1)	15 (1.0)
15–24	881	21 (2.4)	16 (1.7)
$\geq$25	575	15 (2.6)	10 (1.7)

Fisher's exact tests for differences in prevalence by time since first worked, time since last worked, and duration of DOE work demonstrated no significant differences for single or double abnormal BeLPTs. No statistically significant trends in prevalence by duration of DOE work were detected by the Cochran–Armitage trend test.

categories of exposure frequency, where possible. We also have used trained trade and craft workers (mostly retirees), with knowledge of these sites, to conduct the work history interviews.

Data from worker interviews as well as site characterization data by building and work area are used to determine worker eligibility for the medical screening programs and to select the appropriate medical screening tests to be administered for each participant. In our population, the minority of workers had any knowledge of beryllium, let alone potential work tasks or buildings in which exposure to beryllium could have taken place. Consequently, we concluded that we could not use worker recollection of beryllium exposure as a tool to triage workers into exposed and unexposed groups. For this reason, we offered the blood BeLPT to all participants, and 86% chose to accept the test. We have no reason to believe that the 14% who did not accept the test skewed the results, since we can find no apparent differences in any significant characteristics between those who received the Blood BeLPT and those who did not.

Our data on beryllium screening shows patterns that differ from that reported in the medical literature to date. The beryllium exposed groups studied previously were primarily currently exposed workers in production facilities. Our population is quite different, in that the participants are construction workers, and had to have left construction employment at the site to be eligible. Many had left employment years before the examination took place. A lower proportion of our participants with a single abnormal Blood BeLPT were confirmed abnormal with a second test; for all sites combined, 62% were confirmed abnormal, while the same number is generally reported at 80%. At Hanford, the

TABLE VII. Summary of Odds-Ratios for Beryllium BeLPT Single Abnormals Ever/Never Employed in Buildings With Potential Beryllium Exposure

Site and parameter	Number BeLPT abnormal worker	Number BeLPT negative workers	Mantel–Haenszel odds-ratio (95% CI)
Hanford			
Ever worked in Be building	37	959	5.3 (1.3–22.1)
Single highest risk building	20	351	2.6 (1.4–5.0)
Savannah River			
Ever worked in be building	17	995	2.0 (0.5–8.8)
Single highest risk building	2	39	3.4 (0.8–15.4)
Oak Ridge Reservation			
Ever worked in Be building	26	1,245	2.7 (0.4–20.3)
Single highest risk building	12	397	2.0 (0.9–4.3)

TABLE VIII. Logistic Regression Model for All Sites Combined Case = One or More BeLPT Abnormal Results

Parameter	Odds-ratios (95% CI)
Age (years)	
<45	1.0
45–54	1.6 (0.7–3.6)
55–64	1.5 (0.7–3.5)
65+	2.2 (1.0–5.1)
Duration of DOE work (years)	
<5	1.0
5–14	0.8 (0.4–1.5)
15–24	0.8 (0.4–1.6)
25+	0.8 (0.4–1.8)
Site	
Oak Ridge (reference)	1.0
Savannah River	1.2 (0.6–2.3)
Hanford	2.0 (1.2–3.6)
Worker reported beryllium exposure	
No	1.0
Yes	1.1 (0.7–1.7)
Work in a beryllium building	
Never	1.0
Ever	3.4 (1.3–8.8)
Cigarette smoking	
Never	1.0
Ever	1.1 (0.7–1.7)
Years since last employed at DOE	
≤10	1.0
>10	0.7 (0.4–1.1)

confirmation rate was 46%, and at Oak Ridge and SRS combined it was 76%. Another way of expressing this is that at Hanford, the prevalence of a single abnormal Blood BeLPT was almost twice as high as at SRS or at Oak Ridge, which the prevalence of a double abnormal test was about the same at each site. We have no explanation for this difference except to note that a stronger association with work in a building with potential for beryllium exposures was observed for Hanford compared to the other two sites.

Of those with a confirmed abnormal Blood BeLPT who completed medical evaluation, a lower than expected proportion had evidence of CBD. With five diagnosed cases of CBD, this is a prevalence of 15% among the workers with a confirmed abnormal Blood BeLPT who completed diagnostic evaluation. Among other populations, the rate of CBD among those sensitized to beryllium is reported as over 50% [Kreiss et al., 1997].

There is significant lab-to-lab variation in the Blood BeLPT test [Deubner et al., 2001]. ORISE presented data on a comparison program among the three laboratories that do the bulk of blood BeLPT nationally for the DOE sponsored former worker programs. Lab A and Lab B agreed on 36% of abnormals (n = 178 abnormal in either lab). Lab C and Lab A agree on 30% of abnormals (n = 100 abnormal in either lab). Lab C and Lab B agree on 41% (n = 254 abnormal in either lab). (Comparisons are going on in six possible combinations of these labs; the other three have too few samples to date to report results.) These data suggest that a randomly selected test has less than a 50% chance of being abnormal in two labs testing the same sample. It also shows that no one laboratory

TABLE IX. Summary of Pulmonary Function Tests, Chest X-ray B-Reads, and Respiratory Symptoms by BeLPT Status

Parameter	Workers with one or more abnormal BeLPT	Workers with double abnormal BeLPT	Workers with normal BeLPT
Pulmonary function			
Mean (SD) percent predicted FVC	82.8 (18.1)	80.0 (18.2)	84.8 (19.0)
Mean (SD) percent predicted FEV_1	80.7 (20.3)	79.0 (21.0)	81.7 (21.7)
Chest X-ray B-readings			
Number and prevalence (%) of parenchymal changes ≥1/0	1 (1.3%)	1 (2.0%)	169 (5.3%)
Respiratory symptoms			
Cough (%)	22 (32.8%)	12 (28.7%)	1,025 (36.0%)
Phlegm (%)	27 (40.3%)	16 (37.2%)	1,872 (63.9%)
Dyspnea			
Grade 1 (%)	46 (38.7%)	30 (66.7%)	1,974 (58.9%)
Grade 2+ (%)	32 (41.6%)	22 (47.8%)	1,377 (41.3%)

Not all workers with BeLPT participated in the PFT and B-Read components of the examinations. Of the 3,842 workers with BeLPT tests, 3,271 had pulmonary function tests, and 3,256 had a chest X-ray with a B-read. For symptom data, percentages are reported for workers providing valid answers to the respiratory questionnaire. No statistically significant differences were detected comparing workers with and without an abnormal BeLPT test.

is superior to the others and agreement is similar among the labs in the QA program.

At the same time, it is premature to conclude that the low rate of CBD in our projects represents a background rate of false positives. The blood BeLPT does differentiate between exposed and unexposed groups, as a whole. In truly unexposed groups the rate of an abnormal blood BeLPT is very low. Silveira et al. [2003] presented results of beryllium surveillance at 3 sites where 516 individuals were tested prior to employment in a facility using beryllium; one was sensitized, and he had previously worked in the nuclear weapons industry. Combing these results with evaluations at other facilities with unexposed populations, she reported no sensitization among 1,184 individuals tested; sensitization was defined as a confirmed abnormal test. We can thus conclude that ''false positive'' tests, where the test is abnormal but the worker is not sensitized, may exist but are rare. There are unconfirmed single abnormals, meaning ones that are not confirmed on repeat testing. These are not necessarily false positives, nor are they truly negatives. In groups with substantial beryllium exposure some unconfirmed single abnormals go on to become double abnormal, and a substantial proportion go on to develop CBD. The data presented in this paper also show that exposure to beryllium increases the risk of an abnormal blood BeLPT; a worker with a single abnormal blood BeLPT had an odds ratio of 5 for having worked in a beryllium containing building.

In studies to date, an abnormal blood BeLPT, single or double, is an excellent predictor of CBD among current workers with known exposure in the beryllium manufacturing plants. Several published studies report that CBD is diagnosed in 50% of the screened workers with a double abnormal blood BeLPT [Newman et al., 2001a]. National Jewish Research and Medical Center has been following a group of 78 workers who had confirmed abnormal BeLPTs and did not have CBD on first evaluation; 30% of those have developed CBD over a mean follow-up time of 3.7 years, for a conversion rate of 8.2% per year [Newman et al., 2003]. So the blood BeLPT predicts CBD in workers in beryllium production facilities about 75% of the time.

We would expect that the predictive ability of the BeLPT will decline as it is used in populations with less intense exposure to beryllium. The usefulness of a screening test can be described with its sensitivity, its specificity, its positive predictive value (PPV), and its negative predictive value. Sensitivity measures how well the test detects true positives, specificity measures how well the test detects true negatives. The PPV is a measure of how many of those who test positive really have the underlying condition; it is the ratio of true positives to all positives. A test with very good sensitivity and specificity may not have a good predictive value, if the disease prevalence is low in the population being screened. For example, a test for which the sensitivity is 99.9% and the specificity is 99.9% is an excellent test. If we use this test in a population of 1,000,000, among whom 1% have the disease for which we are screening, we will detect 9990 with disease, and miss 10 with the disease. However, we will also have 990 false positives, and the PPV is 91%. As the specificity of the test declines, or the underlying prevalence of disease, so does the PPV. In one study that specifically addresses a beryllium exposed population, Deubner et al. [2001] calculated the predictive value (PPV) of the blood BeLPT in the Brush–Wellman workforce. Deubner reports that a single unconfirmed test has a PPV for CBD of 39%, a confirmed abnormal had a PPV for CBD of 45%, and a split sample reported abnormal in two laboratories had a PPV of 49%.

These results come from populations of workers with on-going exposure, and with known exposure to beryllium. However, some studies suggest that, as exposure levels decline, the rate of sensitization declines less than the rate of CBD in a population. This means that among groups of workers with low or intermittent exposure to beryllium, the predictive value of the blood BeLPT for CBD may be lower than in the populations discussed above. Stange et al. [2001] describe the prevalence of beryllium sensitization and CBD among workers at Rocky Flats tested through on-going beryllium surveillance. Sensitization was defined as a confirmed abnormal blood BeLPT. As years of exposure increased, the proportion of those examined who had CBD also increased, but the proportion of sensitization without CBD did not increase. The CBD rate increased from 0.5% among workers with fewer than 5 years of employment to 3.72% among those with 20–25 years worked at Rocky Flats. The rate of sensitization without CBD was 3% among workers with less than 5 years at the plant, and was at most 4% in groups with more years of exposure. The ratio of CBD/all sensitized (with and without CBD) is the PPV of the BeLPT. Overall, the PPV was 35% among the Rocky Flats workers described in this study; about 1/3 of those sensitized also had CBD. The PPV was 14% in those workers with less than 5 years of employment at Rocky Flats, and increased to 65% among workers with more than 20 years of work at the facility. For example, the CBD rate among the scientists/engineers who were sensitized was 23%, compared to 73% among the machinists; the confidence intervals on these rates differ, even though the number of cases is small.

Viet et al. [2000] report the results of a case-control study of CBD and beryllium sensitization among workers at Rocky Flats. They found that years of employment, an estimate of cumulative exposure, and an estimate of mean exposure all were significantly greater for the CBD cases than for their control group. For sensitization, although the results were consistently in the same direction, there was no significant difference in these exposure groupings between cases of sensitization and their control group. These results are consistent with our results where we found no trend for increased risk of an abnormal BeLPT with duration of DOE site work.

McCawley et al. [2001] report a highly significant relationship between mass concentration of particles less than 10 μ, and with particles less than 3.5 μ, and CBD ($P = 0.0004$ and 0.000003, respectively). An association was present between these metrics and sensitization, although it was not as strong ($P = 0.025$ and 0.003). The exposures were measured at five furnaces in a beryllium manufacturing facility, in locations where CBD had been previously documented. These two studies suggest that inhalation exposure to beryllium is more strongly linked to the risk for CBD than to the likelihood of sensitization, although sensitization is related to degree of exposure as well.

DOE has been conducting surveillance among current and former workers with less direct exposure, or potential exposure, to beryllium; our data among construction workers is similar to that from some of these other screened populations. Rocky Flats, Y12, and K25 are DOE facilities with significant use of beryllium, and were the first facilities targeted for medical examination programs. As researchers and DOE health and safety staff became aware of other sites where beryllium was used, even in small quantities, those additional sites were added to the medical surveillance program. As the medical community became aware that CBD cases occurred among workers with low exposure, additional workers were considered at risk and added to surveillance programs as well. The prevalence of sensitization is similar among the facilities that used beryllium; at Rocky Flats 3.7% are sensitized, 2.7% at Pantex, 3.07% at Lawrence Livermore, and 2.0% at Kansas City Plant. Of those sensitized workers who underwent bronchcoscopy, the rate of CBD varies markedly. At Rocky Flats, 45% of those completing a diagnostic evaluation have CBD, while at Pantex, Lawrence Livermore and Kansas City these rates were 25, 13, and 14%, respectively [Stange et al., 2003]. These data suggest that the positive predictive value of an abnormal blood BeLPT goes down at facilities with more limited use of beryllium than Rocky Flats.

Results presented here from screening construction workers also suggest that the dose of beryllium may affect development of CBD more than sensitization. Biologically, the dose to the lung must be an important determinant of the risk of CBD, along with host susceptibility. Exposure to beryllium leads to T-cell activation, but the amount of actual inflammation in the lung (and thus CBD) depends on the accumulation of these activated T-cells. This in turn would depend, to some degree, on the amount of beryllium resident in the lung to stimulate granuloma formation and the efficiency of antigen presentation with its known genetic determinants [Maier et al., 2002]. We do not think that we are seeing ‘‘false-positive’’ blood BeLPTs, where the abnormal test is not due to a biological response to beryllium. Rather, we believe that sensitization can occur at levels of exposure, routes of exposure, or types of exposures to beryllium that may not have as high a risk for CBD as previously reported.

Beryllium sensitization is not a disease in its own right, but is important because the presence of sensitization presents a risk of significant granulomatous lung disease. Any such biological test has a positive predictive value, which is the likelihood that if the test is abnormal the disease is present, and a negative predictive value, in which the disease is absent if the test is normal. This data on our former construction workers gives us new information about the performance of the blood BeLPT test, and its predictive value in populations with lower total lifetime exposures than that experienced in beryllium machining plants. Understanding the predictive value of the blood BeLPT in such groups is very important in deciding how aggressive to be in screening workers with exposures such as use of beryllium copper alloys and other alloys, and what to tell them about their risk of disease.

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