Efficacy of Serial Medical Surveillance for Chronic Beryllium Disease in a Beryllium Machining Plant

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There is limited information on the use of the blood beryllium lymphocyte proliferation test (BeLPT) at regular intervals in medical surveillance. Employees of a beryllium machining plant were screened with the BeLPT biennially, and new employees were screened within 3 months of hire. Of 235 employees screened from 1995 to 1997, a total of 15 (6.4%) had confirmed abnormal BeLPT results indicating beryllium sensitization; nine of these employees were diagnosed with chronic beryllium disease. Four of the 15 cases were diagnosed within 3 months of first exposure. When 187 of the 235 employees participated in biennial screening in 1997 to 1999, seven more had developed beryllium sensitization or chronic beryllium disease, increasing the overall rate to 9.4% (22 of 235). The blood BeLPT should be used serially in beryllium disease surveillance to capture new or missed cases of sensitization and disease. Beryllium sensitization and chronic beryllium disease can occur within 50 days of first exposure in modern industry. (J Occup Environ Med. *2001;43:231–237*)

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Chronic beryllium disease (CBD) is a systemic and pulmonary disease characterized by noncaseating granulomas, mononuclear cell interstitial infiltrates, and fibrosis resulting from a beryllium-specific, cellular immune response.[1] The beryllium lymphocyte proliferation test (BeLPT), which measures beryllium-specific cell proliferation in blood,[2,3] is used widely in industry as a screening test for beryllium sensitization (BeS) and CBD. The point-prevalence of abnormal BeLPT results in the beryllium-using industry ranges from 1.8% to 11.8%,[4–8] and for CBD from 1.8% to 7.8%.[4–8] The test has proved to be more sensitive and specific than historic screening methods such as chest radiography, physical examination, and spirometry.[4–6,9] Studies have shown that the blood BeLPT identifies approximately 70% to 94% of CBD cases.[6,8,10] However, other studies of blood samples split between laboratories have shown that the BeLPT can miss cases of BeS.[7,9] Because most of the population-based prevalence studies of BeS using the blood BeLPT have been cross-sectional, they provide only point-prevalence estimates of BeS and CBD.[4–8] It is likely that cases were missed in these cross-sectional studies for methodological or biological reasons, thus resulting in an underestimation of the true rates of sensitization and disease. However, it is also possible that additional cases of BeS and CBD may develop later in time, even after a normal BeLPT result. Serial screen-

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ing with the BeLPT may identify additional cases of BeS and CBD.

We do not know the precise timing of BeS and CBD onset after first exposure occurs. The latency period for CBD has been cited in the literature to range from a period of months to 40 years[11–13] and may vary widely among workers. An individual may have normal BeLPT results at one time but later develop BeS because of changes in plant and exposure conditions. Serial surveillance with the BeLPT may identify these additional cases of CBD and BeS, once prevalent cases are identified, and may help to identify new high-risk processes in beryllium areas.

Prompted by an index case of CBD in 1995, a beryllium metal machining facility initiated an ongoing medical surveillance program for beryllium disease using the BeLPT. The facility, in operation since 1969, uses a number of different processes to machine several different beryllium materials.[14] All employees are tested at 2-year intervals, with new and rehired employees initially tested within 3 months of first employment. This presented the opportunity to test the hypothesis that ongoing surveillance using the BeLPT finds new and/or missed cases of BeS and CBD. We were also able to examine the risk for BeS among newly exposed workers in modern industry.

Methods

Overview of Plant Conditions

The 100,000 square foot beryllium metal machining plant opened in 1969 and at the time of this study employed approximately 186 individuals. Processes at the plant include receipt and inspection of materials, mechanical machining and polishing, electrical discharge machining, acid etching, final inspection, and quality assurance. An office area is connected to the plant and handles management and administrative functions. Machining processes include milling, deburring, lapping, lathe operations, and grinding. The facility also uses a number of different beryllium materials, including beryllium metal, beryllium-aluminum alloy, and a beryllium metal/beryllium oxide composite called E-metal. Respiratory protection was not routinely used at the plant. During the period of medical surveillance, we performed environmental sampling for beryllium and assessed both total beryllium and particle-size–related exposure for plant machining processes.[14] This industrial hygiene sampling study at the plant found median machining exposures of 0.3 $\mu g/m^3$ and identified improvements that could be made at the plant. Since 1996 some processes were enclosed, ventilation systems were improved, a stricter uniform policy was initiated, and dry sweeping and air hoses were eliminated. Additional total beryllium and particle-size sampling was performed in 1999 to characterize the exposures in all jobs and employees at the plant. These data are the subject of a companion article that reports BeS and CBD in relation to beryllium exposures at this precision metal machining plant.[15]

Beryllium Surveillance

The company initiated plantwide testing with the blood BeLPT in May 1995. All current employees and daily contract workers were included in the screening. They provided written informed consent in compliance with a National Jewish Medical and Research Center Institutional Review Board protocol before initial venipuncture. New or rehired employees were tested with the blood BeLPT within their 3-month probation period to establish a baseline blood test result. At the time of the first round of screening, we conducted workforce presentations for all shifts on the health hazards of beryllium and on the purpose of medical surveillance for CBD. Before blood testing, each employee completed a short, self-administered questionnaire, which collected demographic and smoking data.

All employees participated in 2-year follow-up screenings, with the BeLPT conducted in May and June of each year, excluding those already detected as having BeS or CBD or those who left the company. Risk communication presentations were repeated and aggregate screening results were presented to the workforce before each new round of screening. Employees originally screened in 1995 underwent repeat blood screening in 1997 and 1999; those originally screened in 1996 had repeat blood testing performed in May 1998; and employees originally screened in 1997 had repeat screening performed in 1999.

Blood Beryllium Lymphocyte Proliferation Test

All blood specimens were shipped by overnight carrier from the plant to the Clinical Immunology Laboratory at the National Jewish Medical and Research Center. The BeLPT was performed within 24 hours of venipuncture using methods previously published.[2] Briefly, mononuclear cells were isolated from heparinized venous blood. They were placed in culture in the presence and absence of beryllium sulfate, across a three-log range of salt concentrations. We verified cell viability and reactivity using the mitogen phytohemagglutinin and antigen tetanus toxoid at optimal concentrations. Cell proliferation was measured by the incorporation of tritiated thymidine into dividing cells after 4 and 6 days in culture. The cells were harvested and the amount of radiolabel that had entered the cells was measured in a gas ionization counter. Results are expressed as a stimulation index (SI), which is the ratio of the counts per minute of radioactivity in cells stimulated with beryllium salts divided by the counts per minute for unstimulated cells. The normal range for our laboratory was based on a series of 20 blood tests performed in

persons with no known beryllium exposure, taking the mean peak SI + 2 SD. A test was considered abnormal if two or more of the six stimulation indices exceeded the normal range. A test was considered "borderline" when only one of the values exceeded the normal range. Abnormal and borderline blood tests were repeated in the same laboratory for confirmation. If the repeat test was abnormal, the employee was referred for a clinical evaluation that included BAL and transbronchial lung biopsy to determine whether CBD was present.

Clinical Assessment

All employees with two or more abnormal blood tests were referred for clinical evaluation. Forced vital capacity and forced expiratory volume in 1 second were measured with a pneumotachograph. Total lung capacity was measured in a constant-pressure body plethysmograph. The single-breath method of Ogilvie and coworkers was used to evaluate the ratio of diffusion capacity of carbon monoxide to alveolar volume. Gas exchange, maximum exercise capacity, and maximum oxygen consumption were determined with a 380 B cycle ergometer with continuous cardiac rhythm and arterial oxygen content monitoring. We used an indwelling arterial line to measure arterial blood gas at rest and after each minute of exercise. The results are reported as the partial pressure of oxygen (PO_2) and alveolar-arterial oxygen difference ($[A - a]PO_2$) at baseline and at maximum exercise. We performed bronchoalveolar lavage (BAL) using methods described previously,[16] and we reported the percent of lymphocytes in the recovered BAL fluid. We also tested for BeS by performing the BeLPT on BAL cells using methods similar to those of the blood test. Transbronchial lung biopsy was performed to confirm the existence of granulomas and/or mononuclear cell infiltrates in lung tissue.

Definitions of BeS and CBD

We defined BeS as evidence of beryllium-specific immune response, demonstrated by repeatedly abnormal blood BeLPT with no evidence of granulomas and/or mononuclear cell infiltrates on transbronchial lung biopsy. CBD was defined as evidence of BeS with granulomas and/or mononuclear cell infiltrates in lung tissue.[1] We defined "probable" CBD based on BAL lymphocytosis plus abnormal BAL BeLPT results.

Statistical Analysis

Data are presented with means and ranges as applicable. A chi-squared analysis and Fisher's exact test were used to compare differences between categorical variables. The Students *t* test and Wilcoxon's rank sum test were used to compare differences between continuous variables. All analyses were conducted using JMP® statistical software.[17]

Results

Initial Beryllium Surveillance 1995 Through 1997

All individuals currently employed or newly hired at the plant were tested with the BeLPT from May 1995 through December 1997. One hundred percent of employees participated. We tested 235 workers; 90% were male and 99% were non-Hispanic white. The average age of the participants was 39 years (range, 18 to 77). The group had been employed at the machining plant for an average of 11.7 years (range, 1 month to 29 years). Of the 235 workers, 151 were initially tested in 1995, 50 in 1996, and 34 in 1997 (Table 1). Fifteen of 235 (6.4%) had confirmed abnormal blood BeLPT results on initial screening (including the index case, in which the worker was still employed at the time of initial screening). Twelve of 15 completed clinical evaluation. Eight were found to have CBD with granulomas and/or mononuclear cell infiltrates on transbronchial lung biopsy. One individual had an abnormal BAL BeLPT (SI, 4.9) and lymphocytosis in BAL fluid (60%) but no evidence of granulomas or infiltrates on biopsy. He was classified as having probable CBD. Three had BeS without evidence of CBD on either lavage or biopsy.

Follow-Up Beryllium Surveillance in 1997, 1998, and 1999

Of the 235 individuals tested with the BeLPT in 1995 through 1997, 187 completed 2-year interval testing (Table 1). Excluded from testing were the 15 CBD and BeS cases previously diagnosed, six contract employees who the company chose not to retest, and 27 individuals no longer with the company. The participation rate among the remaining eligible employees was 100%. Five

TABLE 1
Initial and Follow-Up BeLPT Results of Biennial Surveillance for Chronic Beryllium Disease in a Metal Machining Plant, 1995–1999*

Original test year, round 1	*1995*	*1996*	*1997*	*Total*
No. tested	151	50	34	235
Abnormal, *n*/%	8 /5.3	5 /10	2 /5.9	15 /6.4
Biennial testing, round 2	*1997*	*1998*	*1999*	
No. rescreened	129	36	22	187
Abnormal, *n*/%	5 /3.9	0 /0	0 /0	5 /2.7
Biennial testing, round 3	*1999*			
No. rescreened	109			109
Abnormal, *n*/%	2 /1.9			2 /1.8
Total abnormal, n/%	15 /9.9	5 /10	2 /5.9	22 /9.4

* BeLPT, beryllium lymphocyte proliferation test.

TABLE 2
Test Results* of Employees With Abnormal Blood BeLPT Results on Biennial Rescreening in a Precision Machining Plant, 1995–1999

	Initial Screening (1995)		Follow-up Screening (1997)		Follow-Up Screening (1999)		
Patient	Test 1	Test 2/3	Test 1	Test 2/3	Test 1	Test 2/3	Final Diagnosis
1	2.3, normal	No repeat done	2.9, abnormal	4.5, abnormal	–	–	BeS
2	4.5, borderline	1.3, normal	16.6, abnormal	6.7, abnormal	–	–	CBD
3	1.1, normal	No repeat done	5.3, abnormal	4.0, abnormal	–	–	CBD
4	5.8, abnormal	1.3 /1.3, normal/normal	89.0, abnormal	14.5, abnormal	–	–	CBD
5	1.2, normal	No repeat done	9.3, abnormal	1.6/2.6, abnormal	–	–	CBD
6	1.3, normal	–	2.6, borderline	0.7, normal	1.9, borderline	4.1, abnormal	CBD
7	Uninterpretable	1.3, normal	Uninterpretable	1.6, normal	4.5, abnormal	10.4, abnormal	CBD

* Results are reported as peak stimulation index for beryllium stimulation and interpretation of test results; BeLPT, beryllium lymphocyte proliferation test; BeS, beryllium sensitization; CBD, chronic beryllium disease.

of the 187 (2.7%) subsequently had repeatedly abnormal BeLPT test results. All five had been classified as normal in the original screening, although one of the five had a borderline BeLPT result in 1995 and another had an unconfirmed single abnormal BeLPT result in 1995. All five underwent clinical evaluation. Three of the five were found to have CBD. One individual with an abnormal BAL BeLPT (SI, 54.1) and lymphocytosis in BAL fluid (22%) was classified as having "probable CBD." The other individual was diagnosed as having BeS with no evidence of CBD on lavage or biopsy. Thus, the overall rate of BeS/CBD in this workforce increased to 8.5% (20 of 235) after the second round of screening.

The employees originally tested in 1995 were again eligible for 2-year follow-up screening in 1999 (Table 1). Of the original 151 workers tested in 1995, a total of 109 were retested (100% participation among current eligible employees), and two had confirmed abnormal blood BeLPT results. On clinical evaluation, both individuals were diagnosed as having CBD with granulomas and/or mononuclear cell infiltrates on biopsy. Both had shown normal results in the 1995 and 1997 screenings. Thus, the overall rate of BeS in the workforce increased to 9.4% (22 of 235) after the third round of screening. Initial and follow-up blood test results on the employees found to have abnormal BeLPT results on the first round of biennial screening are presented in Table 2.

Clinical Evaluation Results

In summary, of the 22 employees identified as beryllium-sensitized in all three rounds of screening, 19 completed clinical evaluation. Thirteen of the 19 were diagnosed with CBD characterized by granulomas and/or mononuclear cell infiltrates on lung biopsy. Two additional individuals had abnormal BAL BeLPT results (SIs, 54.1 and 5.9, respectively) and lymphocytosis in BAL fluid (22% and 60%) and were diagnosed with probable CBD. Four of the 19 individuals were diagnosed with BeS. They had repeatedly abnormal blood BeLPT test results but no evidence of granulomas, mononuclear cell infiltrates, lymphocytosis, or abnormal lavage BeLPTs. The three individuals who were not clinically evaluated were classified as beryllium-sensitized.

Of the 19 workers evaluated clinically, there was no difference in tenure at the plant between those with BeS and those with CBD (14.0 years and 13.7 years, respectively). Those with CBD tended to be older than those with BeS (41 years vs 33.5 years, $P = 0.08$). The beryllium-sensitized individuals tended to be current smokers as compared with CBD cases (75% vs 20%, $P = 0.08$). Clinical results are presented in Table 3. Except for the index case, in which the worker presented with symptoms, most of the individuals were in the very early stages of CBD and had minimal abnormalities on pulmonary function or on exercise capacity testing.

BeS and Disease Among New Employees

Within the population screened, 60 of 235 (25.5%) were new employees who had worked in the plant for less than 1 year before blood testing. Four of the 60 (6.7%) were among the 22 employees with abnormal blood tests. All four had worked for less than 3 months when tested (range, 50 to 92 days) and reported no previous exposure to beryllium before working at the plant. Three of the four completed clinical evaluation. Two of the three evaluated were diagnosed with biopsy-proven CBD. The other was diagnosed with probable CBD because of an abnormal BAL BeLPT result and 60% lymphocytes in BAL fluid.

Discussion

This workplace beryllium surveillance program demonstrates the efficacy of repeat blood BeLPT testing at 2-year intervals in identifying additional cases of BeS and CBD. Our epidemiological investigation of this metal machining plant found that CBD and BeS continue to occur in a modern industry and can occur

TABLE 3
BAL, Pulmonary Function, and Exercise Physiology Results for the Index Case and the Surveillance-Identified CBD and BeS Patients*

	Index Case (n = 1) (mean)	Surveillance-Identified CBD Cases (n = 14)	Surveillance-Identified BeS Cases (n = 4)
Smoking			
Current smokers	–	21.4%	75.0%
Former/never smokers	100	78.6%	25.0%
Bronchoalveolar lavage			
Peak BeLPT stimulation index	95.2	19.8/1–65.1†	1.1/0.8–1.7†
Percent lymphocytes	69	41.4/10–73.5	11.7/6–15
Pulmonary function (% predicted)			
FVC	56	96.6/82–115	94.7/89–104
FEV_1	75	99.6/80–126	95.0/85–106
TLC	71	107.6/98–128	104.25/95–124
DLCO/VA	60	93.9/74–115	98.8/90–105
Exercise physiology			
Maximum workload (% predicted)	42.7	85.2/62.1–100.1	88.8/84.2–93.6
VO_2 at maximum exercise (% predicted)	41	76.7/64.2–91.6)	81.4/73.6–90.3
PO_2 at baseline‡	60	74.7/68–87.3	69.0/68–70
PO_2 at maximum exercise‡	44	79.2/64–87	74.0/64–82
(A−a) PO_2 at baseline	18	5.5/1.5–10	6.2/4–11
(A−a) PO_2 at maximum exercise	42	15.9/9.6–26	17.5/12–22

* BAL, bronchoalveolar lavage; CBD, chronic beryllium disease; BeS, beryllium sensitization; BeLPT, blood beryllium lymphocyte proliferation test; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 second; TLC, total lung capacity; DLCO/VA, ratio of diffusion capacity for carbon monoxide to alveolar volume; VO_2, oxygen consumption; PO_2, partial pressure of oxygen; (A−a) PO_2, alveolar-arterial difference in oxygen tension.

† Means/ranges.

‡ Arterial blood gases at Denver altitude of 5200 feet.

within as little as 2 months of first exposure.

Ongoing medical surveillance captures new cases of BeS and CBD. Seven of the 187 (3.7%) individuals who underwent follow-up screening at 2-year intervals developed repeatedly abnormal blood tests. All seven had been classified as normal in the original screening. Six of the seven were found to have CBD on clinical examination, but none had yet developed symptoms. Our results suggest that serial surveillance with the BeLPT can identify persons in the very early stages of CBD and justifies a 2-year interval. A previous report of repeat screening also showed the efficacy of surveillance. Stange et al[9] reported the results of 3-year retesting as part of a beryllium health surveillance program for employees of a nuclear weapons manufacturing plant who previously had negative BeLPT results. Follow-up testing 3 or more years later on 372 current and former employees identified one new case of CBD and nine new cases of BeS (2.7%). Eight of the 10 newly identified cases of BeS and CBD in that study were among the current employees who had potential ongoing exposure. As in our study, those individuals identified demonstrated BeS or the very early stages of CBD on retesting.

There is no way to know if the initially negative blood BeLPT results of the BeS and CBD cases found on follow-up evaluation were false-negative results or if these individuals were truly negative and only subsequently developed an abnormal response on the BeLPT. Previous studies suggest that some of the original normal results may have been false-negative. Kreiss et al conducted a screening study in which samples were split between two laboratories. Twenty-four cases of CBD and BeS were identified. However, using either laboratory alone would have resulted in identifying only 46.5% to 48.8% of the BeS and CBD cases.[7] Stange et al found only 21% to 38% agreement among three laboratories with split-specimens of abnormal blood,[9] although agreement on all tests, both normal and abnormal, ranged from 85% to 96%. We recently observed a 90% agreement when 29 abnormal samples were split blindly between our laboratory and a second commercial laboratory. The BeLPT, though sensitive for CBD, may have a lower specificity than was previously published. On the other hand, the test has again demonstrated its superiority to chest radiography in detecting individuals in the early stages of the development of BeS and CBD[5,9] and in detecting disease in a presymptomatic stage.

It is possible that some of the abnormal results in the second and third rounds of screening were due to

new-onset BeS and CBD resulting from ongoing cumulative exposure and significant latency. Studies of human lymphocyte antigen-DPB1 Glu69 marker for beryllium disease have shown that 83% to 97% of persons with CBD carry the marker.[18,19] These individuals may develop sensitization and disease soon after first exposure because of their genetic predisposition, whether related to this or other genetic markers. However, individuals without the marker may go on to develop BeS and CBD after a certain amount of cumulative exposure or after achieving sufficient latency.

We can roughly estimate the incidence of BeS and CBD in this group of employees. Our initial round of screening included 235 employees and identified 11 prevalent cases of BeS and CBD among the 175 long-term employees and the 4 incident cases of BeS and CBD among 60 new employees. If we assume each individual to be still at risk of developing CBD after an initial normal blood test, then new cases identified on subsequent screening would be considered incident cases, assuming previous BeLPT results were not falsely negative. Of the 187 employees with initial negative blood tests who participated in a second round of screening, 109 also participated in a third round of testing. This resulted in 356 individual tests. The seven additional individuals who were identified as having BeS or CBD on follow-up testing could be considered new-incident cases. The estimated incidence rate of BeS and CBD in this group is then 3.1% (11 of 356). However, the chance of developing sensitization after an initial normal test may not be equal for all individuals. Some employees may experience higher exposures than others, resulting in a higher risk of subsequent sensitization. In addition, some individuals might not develop disease because of a protective genetic predisposition, even with ongoing exposure.

One of the most striking observations in our study was the discovery that CBD and BeS can occur within 2 months of hire and at a median plant beryllium exposure level of 0.3 $\mu g/m^3$. Little is known of the timing from first exposure to the development of BeS and CBD. Hardy et al reported that CBD occurred within months of first exposure when describing beryllium disease in the 1940s[11]; however, this has not been reported in studies of modern-day industry. We previously described the case of a secretary developing BeS 5 months after potential beryllium contamination from renovation work. However, that individual had been employed at that beryllium-using facility for 39 months. It is probable that she had potential exposure before the renovation work.[6] Most screening studies that have been performed to date have been cross-sectional, testing long- tenured employees. The company we surveyed proposed baseline blood tests on new employees, but they were concerned that preemployment or preplacement blood testing could be interpreted as discriminatory. Therefore, they tested individuals within their 3-month probationary period. Although baseline blood tests were not available for these four individuals, none had previous employment with any potential for beryllium exposure and the three evaluated had negative dental histories for beryllium-containing crown and bridgework. All three were in the early stages of CBD and had not yet developed symptoms. These individuals were able to reduce or curtail their beryllium exposure and will be observed over time to determine the disease progression.

Reported latency from first exposure to CBD varies widely. Eisenbud and Lisson reported an average latency based on clinical symptoms between 6.6 and 11 years with a range of 1 to 41 years.[12] In this study, the comparable rates of BeS and CBD observed among the employees tested within 1 year of employment and among longer-term employees suggests that cumulative exposure might not play a role in the development of BeS and CBD in this population. The 60 new employees who had an average tenure of 3 months (range, 1 to 9 months) had a BeS/CBD rate of 6.7% (4/60). This rate was similar to the initial rate of 6.4% among longer-term employees, who had an average tenure of 15.8 years (range, 1.9 to 29.2 years). Follow-up screening increased the overall rate to 9.4%, and the rate among longer-term employees increased to 10.5%. However, 30% of new employees left employment before the second round of screening, and thus far only 8.3% of the new employees have had the opportunity for a third round of testing. Furthermore, we do not know the frequency of BeS and CBD among workers who left plant employment before our first screening. We may find additional cases of BeS and CBD as we continue to follow this newly hired segment of the workforce over time. Use of the blood BeLPT in medical surveillance has redefined latency for CBD because the blood BeLPT result is predictive of pulmonary pathology regardless of clinical stage. Longitudinal follow-up of cases will be required to determine the time from first diagnosis to the development of symptoms and pulmonary function decline.

Except for the index case of CBD, in which the worker sought medical attention because of pulmonary problems and symptoms, the surveillance-identified CBD cases were in relatively early stages, most having normal measures on pulmonary function testing. All workers with CBD had normal forced vital capacity, forced expiratory volume in 1 second, and total lung capacity measurements. Only two workers with CBD had a ratio of diffusion capacity for carbon monoxide to alveolar volume (DL_{CO}/VA) lower than the normal percent predicted value of 80%, and all workers with BeS had normal DL_{CO}/VA measurements,

consistent with our previous report on the physiology of surveillance-identified CBD.[20] On exercise physiology testing, 5 of the 14 workers with CBD achieved less than predicted maximal workload. In 8 of the 14 (57%), oxygen consumption at maximum exercise was less than 80% of predicted. One worker with BeS had a below-normal oxygen consumption at maximum exercise. However, all exercise physiology measures of gas exchange were normal in both surveillance-identified CBD and BeS cases. Except for the index case, none of the participants have required treatment with oral or inhaled corticosteroids. These results confirm that we are identifying BeS and CBD in very early stages. Screening employees at 2-year screening intervals allows for a balance between the cost and logistics involved in screening and ensures that cases of BeS and CBD are identified before symptoms are clinically apparent.

In conclusion, this study demonstrates that serial medical surveillance with the BeLPT should be conducted to capture new or missed cases of BeS and CBD. Until a new and better screening test is developed, serial surveillance with the BeLPT is our best tool for identifying BeS and early CBD. Monitoring for BeS and CBD should begin early in employment, even in those industries in which exposures are below the current Occupational Safety and Health Administration permissible exposure limit, because CBD can develop within 2 months of first exposure in the modern machining industry. Research is ongoing to identify the long-term outcomes for BeS and CBD patients who are detected through workplace surveillance. The beryllium industry and government regulators must act expeditiously to develop and enforce tighter exposure limits and mandate a medical surveillance "safety net" for beryllium-exposed workers.

Acknowledgment

This research was supported by the US Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Cooperative Agreement CCU 8112221, National Institutes of Health General Clinical Research Grant M01RR00051, National Institutes of Health Grant ES 06538, and the beryllium machining plant.

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