

Long-Term Efficacy of a Program to Prevent Beryllium Disease

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Background In 2000, a manufacturer of beryllium materials and products introduced a comprehensive program to prevent beryllium sensitization and chronic beryllium disease (CBD). We assessed the program's efficacy in preventing sensitization 9 years after implementation.

Methods Current and former workers hired since program implementation completed questionnaires and provided blood samples for the beryllium lymphocyte proliferation test (BeLPT). Using these data, as well as company medical surveillance data, we estimated beryllium sensitization prevalence.

Results Cross-sectional prevalence of sensitization was 0.7% (2/298). Combining survey results with surveillance results, a total of seven were identified as sensitized (2.3%). Early Program workers were more likely to be sensitized than Late Program workers; one of the latter was newly identified. All sensitization was identified while participants were employed. One worker was diagnosed with CBD during employment.

Conclusions The combination of increased respiratory and dermal protection, enclosure and improved ventilation of high-risk processes, dust migration control, improved housekeeping, and worker and management education showed utility in reducing sensitization in the program's first 9 years. The low rate (0.6%, 1/175) among Late Program workers suggests that continuing refinements have provided additional protection against sensitization compared to the program's early years. *Am. J. Ind. Med.* 56:733–741, 2013. © 2013 Wiley Periodicals, Inc.

KEY WORDS: beryllium; hypersensitivity; safety management; occupational exposure; program evaluation

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INTRODUCTION

In 2000, the world's largest producer of beryllium and beryllium-related products introduced a comprehensive preventive program at its facilities that was designed to prevent beryllium sensitization and, thereby, chronic beryllium disease (CBD). In general, the preventive program included targeted engineering controls designed to lower airborne exposures, as well as emphasis on dermal and increased respiratory protection, and particle migration control through improvement of workplace orderliness and cleanliness [Deubner and Kent, 2007; Materion Brush, Inc., 2009]. The preventive program was adapted to address the unique circumstances of each facility. Examples of some elements included: engineering controls such as particle migration controls (e.g., air showers), tacky mats in transition areas, and physical separation of administrative

from production areas; administrative controls such as restricting access to some areas, and requiring glove removal and hand-washing prior to eating, drinking or smoking; and personal protective equipment such as respiratory protection, dermal protection, and waterproof smocks in wet areas. At its three largest facilities, medical surveillance with beryllium lymphocyte proliferation testing (BeLPT) for sensitization was required at regular intervals for newly hired workers.

Prior to the implementation of the preventive program, prevalence of beryllium sensitization was 9.2% (34/370) in workers at three facilities with up to 6 years work tenure [Cummings et al., 2007; Thomas et al., 2009; Bailey et al., 2010]. Evaluations of the program's efficacy showed promising results during the initial years of the program for current workers. Cummings et al. [2007] showed that the comprehensive preventive program reduced beryllium sensitization in new workers more than eightfold during their first years of employment at the company's beryllia ceramics facility; sensitization prevalence among workers hired in an interval of similar duration prior to program implementation as determined in a cross-sectional survey was 8.7% compared to 1.0% among those hired afterward. Thomas et al. [2009] showed a more than fourfold reduction for the company's copper-beryllium alloy finishing facility; cross-sectional survey prevalence of sensitization was 11.6% for those hired before the program compared to 2.4% for those hired afterward. Bailey et al. [2010] also showed a reduction of similar magnitude at the company's primary beryllium materials production plant, where sensitization was 8.9% before the program and 2.1% afterward.

This study addresses the following questions in the company's beryllia ceramics, copper-beryllium alloy finishing, and primary beryllium production facilities for workers hired after the comprehensive preventive program was implemented:

1. What was the longer-term efficacy of the program in preventing both sensitization and CBD?
2. Have former workers who were not identified as sensitized during employment developed sensitization after leaving employment?
3. Has the program's evolution over time showed continued reductions in rate of sensitization?

MATERIALS AND METHODS

Survey Eligibility and Participation

All workers hired at the company's three largest facilities after implementation of the preventive program were eligible to participate in the National Institute for

Occupational Safety and Health (NIOSH) cross-sectional survey, including those who had left company employment. Eligible were those hired between: January 1, 2000 and December 23, 2008 at the beryllia ceramics facility; February 21, 2000 and February 11, 2009 at the primary production facility; and June 1, 2000 and April 27, 2009 at the copper-beryllium alloy finishing facility. Start dates are based on each facility's implementation of the program and are consistent with earlier evaluations [Cummings et al., 2007; Thomas et al., 2009; Bailey et al., 2010]. End dates reflect cross-sectional fieldwork dates. The cross-sectional survey protocol was reviewed and approved by the NIOSH Institutional Review Board; written informed consent for blood draws, questionnaires, and access to company medical records was obtained from each participant.

The company provided contact information for eligible workers. For current workers, we made presentations and posted information about the cross-sectional survey at the plants. For former workers, we sent informational letters and contact forms indicating interest in participation (with self-addressed prepaid return envelopes) to addresses updated via commercially available databases. Three mailing attempts were made, including a certified FedEx letter. All workers were also provided the NIOSH toll-free telephone number to ask questions or schedule or refuse participation. The following constituted refusal: returned contact sheet indicating "not interested"; verbal refusal by telephone; lack of response after certified letter was received and signed for by household member with same surname; no-show for scheduled appointment; or lack of return telephone call after contact was made with worker's household.

Current workers completed questionnaire interviews and had blood drawn during paid work hours. Former workers completed interviews and blood draws at data-collection sites located near each plant, and were compensated with \$70 in gift cards for travel to/from the site and time away from current jobs. Former workers no longer living in the general areas around the plants were interviewed by telephone and had blood drawn at nearby health departments or other clinics.

Evaluation for Beryllium Sensitization and CBD

Cross-sectional survey BeLPT testing

Initial and follow-up blood samples for the cross-sectional survey BeLPTs were collected by NIOSH representatives between May 2008 and January 2010. All initial blood samples were collected in duplicate and sent overnight to two laboratories that performed testing using published criteria [Frome et al., 2003]. A BeLPT

was interpreted as *abnormal* if two or more stimulation indices (ratio of proliferation rate in beryllium-exposed cells to rate in unexposed control cells) of the six combinations of concentration (1, 10, or 100 μM) and duration (5 or 7 days) were greater than the laboratory-determined threshold, *borderline negative* if a single ratio was greater than the threshold, and *normal* if no ratios were greater than the threshold. Additional blood was drawn and the test repeated to confirm an abnormal result (e.g., if an individual's initial split blood sample returned one abnormal and one normal result), for clarification of a borderline negative result, or when the laboratory deemed the results uninterpretable. Redraws were sent to both laboratories for single abnormal or borderline results, and to the same laboratory for retest of an uninterpretable result. A person was considered to be *sensitized to beryllium* if two or more BeLPTs were abnormal, either from separate laboratories or from repeated testing at the same lab. Participants who did not meet this definition were classified as *not sensitized*.

Medical records review (company medical surveillance)

Survey participants provided permission to obtain copies of their medical records, including previous BeLPT results from company medical surveillance, clinical evaluations for CBD, and other records related to beryllium exposure. Company medical surveillance included single-sample BeLPTs at hire (baseline) and at 6-, 24-, and 48-month intervals, followed by 5-year intervals; in the first years of the program, testing also took place at 3- and 12-month intervals. Abnormal results led to split-sample confirmatory testing, while borderline or uninterpretable tests resulted in redraws submitted to the same lab for follow-up testing.

For both cross-sectional and serial medical surveillance testing, we considered a participant to be *sensitized* to beryllium if any two BeLPTs were found to be abnormal (i.e., confirmed). We classified participants who did not meet this criterion to be *non-sensitized*.

Prior to 2001, those with confirmed abnormal results were offered clinical evaluation for CBD. After 2001, they were referred to the Energy Employees Occupational Illness Compensation Program, which paid for clinical evaluations. A full clinical evaluation included bronchoscopy with transbronchial biopsy and bronchoalveolar lavage (BAL). A lymphocyte proliferation test was performed on the lavage fluid (BALLPT) to detect lung sensitization to beryllium; biopsies were evaluated for granulomas and mononuclear cell interstitial infiltrate. We considered a sensitized worker to have *CBD* if the evaluation identified granulomas or other pathological abnormalities consistent with CBD.

Survey Questionnaires

Trained NIOSH representatives conducted questionnaire interviews on the same day as blood was drawn (except for former workers who had moved). The questionnaire included a work history and questions on work-related dermatologic conditions. The work history comprised beryllium job history, plant-specific occupational exposures, and frequency of respirator use. Survey participants described each job/process worked, with start/end dates, respirator use, and amount of time spent on that job/process on a typical workday. Participants were also asked about incidents which they believe led to high beryllium exposure and whether they were wearing respiratory protection or had skin contact with beryllium during the incident.

Data Analysis

Based on their work histories, workers were assigned to one of the following categories: production, production support, and administration. Production workers operated production equipment and spent all or most of a typical day in production areas. Production support workers spent at least part of a typical day in production areas (e.g., supervisors, janitors). Administration workers spent little or no time in production areas (e.g., office staff).

There was little transition among work categories. However, workers who did change category were assigned to the category likely to have higher beryllium exposure, with production workers considered to have the highest and administration workers the lowest expected exposure [Schuler et al., 2005]. We also identified those who had ever worked in a job that had been identified as higher risk in previous studies: lapping and machining of fired parts at the beryllia ceramics facility [Kreiss et al., 1996; Henneberger et al., 2001]; wire pickling and annealing, drawing, and point and chamfer at the copper-beryllium alloy finishing facility [Schuler et al., 2005]; and alloy melting and casting, metal and oxide production, and maintenance mechanic work at the primary production facility [Schuler et al., 2012].

We calculated time in two ways, based either on time worked or on time elapsed from first exposure. *Work tenure* was the interval between a participant's date of hire and date of employment termination (former workers), or date of first cross-sectional survey blood draw (current workers). *Time from first exposure to survey* was the interval between date of hire and date of first cross-sectional survey blood draw, regardless of employment status (current or former) or medical surveillance test results that had occurred prior to the survey; *combined time since first exposure* was the interval between date of hire and date of first abnormal blood draw (if sensitized, from either

company medical surveillance or cross-sectional survey) or cross-sectional survey blood draw (if not sensitized), regardless of employment status (current or former).

Cross-sectional sensitization prevalence was defined as the number of sensitized participants identified in the cross-sectional survey divided by the total number of survey participants. *Combined sensitization rate* was defined as the number of sensitized participants identified through either company medical surveillance or cross-sectional survey testing divided by the total number of participants.

Since the comprehensive preventive program evolved over time, we used date of hire to distinguish between Early and Late Program workers. *Early Program workers* experienced refinements and improvements over time in education and training, housekeeping, skin contamination and respiratory protection, while *Late Program workers* were introduced into a workplace in which the program was understood by workers and management and many technical aspects of the program had been implemented, audited, and documented [Bailey et al., 2010]. The hire dates distinguishing Early versus Late Program were before and after: January 1, 2002 for the copper–beryllium alloy finishing facility; January 1, 2003 for the beryllia ceramics facility; and January 1, 2004 for the primary production facility.

We categorized skin rash related to work conditions, or presence of ulcers or small craters in the skin, as ever/never. We reduced smoking history to ever- versus never-smoker.

Exclusion criteria

As our intent was to evaluate the efficacy of the preventive program at these facilities, two groups of participants were excluded from analyses subsequent to evaluation of questionnaire responses. Some participants initially identified as eligible based on date of hire reported having worked onsite before that date, typically as temporary or contract workers; we excluded those whose reported onsite date predated facility inclusion criteria dates. “*Date of hire*” in these analyses thus refers to the earlier of worker- or company-provided onsite date. We also excluded those who reported any type of beryllium production work or who spent more than incidental time in production areas at other beryllium-using facilities. If the participant was unsure if a previous employer had used beryllium, we contacted the company regarding beryllium use during the period reported by the participant.

In addition, some participants had abnormal BeLPT results during at-hire (baseline) company medical surveillance program testing. As we were interested in incident cases of beryllium sensitization, these participants, as well

as workers without documented company medical surveillance results, were also excluded.

Statistical analyses

We used SAS version 9.2 (SAS Institute, Cary, NC) to analyze data. We examined group differences with χ^2 tests for categorical variables, using Fisher’s exact tests when appropriate. The Wilcoxon–Mann–Whitney *U*-test was used when categorical responses were non-normally distributed. For continuous variables, we performed non-parametric one-way analyses of variance using median scores to account for unequal variances and non-normally distributed data. $P < 0.05$ was considered to be significant, and $0.05 \leq P < 0.10$ was marginally significant.

RESULTS

Survey Population

We located 584 of 777 (75%) prospective participants, including all current workers and 62% of former workers (Fig. 1). Among those located, 63% (367/584) participated, with a higher rate among current (72%) than former workers (55%, $P < 0.01$). By facility, overall participation ranged from 57% to 66%, and was highest for current workers at the beryllia ceramics facility (85%), and for former workers at the primary production facility (63%). Participants did not differ significantly from non-participants with regard to gender (78% vs. 82% males, respectively, $P = 0.21$) or age at hire (median 37 vs. 39 years, $P = 0.53$).

Based on information provided in questionnaires and company medical records, we then excluded 69 participants: 28 had worked onsite prior to program start dates; 29 reported beryllium exposure at other workplaces; 6 had no medical surveillance data; 5 had abnormal BeLPTs during at-hire medical surveillance testing (2 were confirmed abnormal at hire, 2 had one abnormal test at hire and were confirmed during subsequent interval testing, and 1 had one abnormal test at hire that was never confirmed); and 1 had only worked for the company in a non-beryllium facility. All subsequent analyses refer to the remaining 298 participants.

Demographics

Participants reported mostly Caucasian race (95%; Table I). Median age at hire was 37 years. There were no significant differences between current and former worker participants with regard to race, age at hire or smoking status, nor between Early and Late Program participants for race, age at hire, or work tenure.

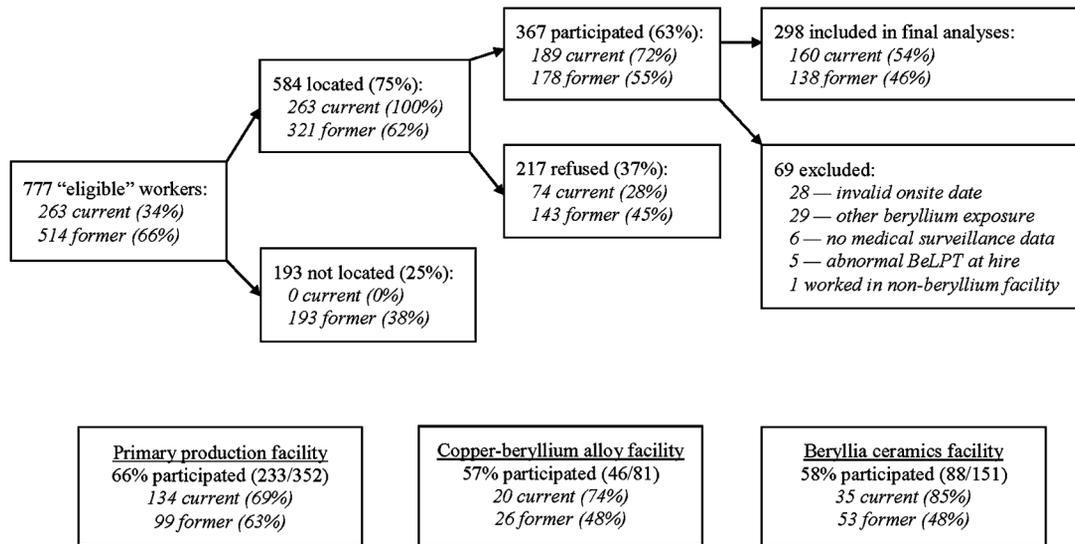


FIGURE 1. Study participation for current and former workers, and by plant.

Beryllium Sensitization and CBD

Cross-sectional survey BeLPT testing

Among 160 current workers, 1 received confirmed abnormal BeLPT results through the cross-sectional survey testing. This participant was hired during the Late Program period and worked in production-area jobs. Of 138 former workers, 1 received confirmed abnormal BeLPT results through the cross-sectional testing. This participant

was also a production worker and was hired during the Early Program period. Thus, the cross-sectional sensitization prevalence was 0.7% (2/298; Table II).

Medical records review (company medical surveillance)

In the company’s medical surveillance during workers’ active employment, six workers, all hired in the Early Program period, were identified as sensitized (including

TABLE I. Demographic Characteristics and Skin Symptoms

	All	Former workers ^a	Current workers	Early Program workers ^b	Late Program workers	Non-sensitized ^c	Sensitized
Gender: % male (n)	78 (231/298)	73 (101/138)	81* (130/160)	70 (86/123)	83*** (145/175)	78 (226/291)	71 (5/7)
Race: % Caucasian (n) ^d	95 (253/266)	97 (116/119)	93 (137/147)	97 (107/110)	94 (146/156)	95 (246/259)	100 (7/7)
Age at hire: median years (mean) ^e	37 (38)	38 (39)	36 (37)	36 (38)	38 (38)	37 (38)	39 (42)
Work tenure: median mos. (mean) ^e	20 (31)	12 (20)	25** (40)	21 (41)	20*** (24)	20 (31)	29 (42)
Time from first exposure to survey: median mos. (mean) ^e	55 (58)	97 (78)	26** (40)	101 (97)	23** (30)	54 (57)	99* (91)
Combined time since first exposure: median mos. (mean) ^e	53 (56)	96 (75)	25** (39)	101 (93)	23** (30)	54 (57)	6** (15)
Ever smoked cigarettes: % yes (n)	53 (158/298)	55 (76/138)	51 (82/160)	47 (58/123)	57* (100/175)	53 (155/291)	43 (3/7)
Early Program % (n)	41 (123/298)	65 (89/138)	21** (34/160)	—	—	40 (117/291)	86** (6/7)
Rash or skin problem: % (n) ^d	13 (38/293)	11 (15/134)	14 (23/159)	20 (24/120)	8** (14/173)	5 (2/38)	2 (5/255)
Ulcers or small craters in skin: % (n) ^d	1 (2/296)	1 (1/136)	1 (1/160)	2 (2/121)	0 (0/175)	0 (0/2)	2 (7/294)

^aComparisons were between Former and Current workers.

^bComparisons were between Early and Late Program workers.

^cComparisons were between Non-sensitized and Sensitized workers.

^dSome participants elected not to provide responses.

^eComparisons were between medians.

* 0.05 ≤ P < 0.10, ** P < 0.05, *** P < 0.01 for mean, P = 0.91 for median ANOVA.

TABLE II. Beryllium Sensitization by Source of BeLPT Results

	% Sensitized (n)		
	All	Early Program workers ^a	Late Program workers
Combined data	2.3 (7/298)	4.9 (6/123)	0.6** (1/175)
Cross-sectional survey	0.7 (2/298)	0.8 (1/123)	0.6 (1/175)
Company medical surveillance	2.0 (6/298)	4.9 (6/123)	0.0** (0/175)

^aComparisons were between Early and Late Program workers.

** $P < 0.05$.

the former worker described above), for a surveillance sensitization prevalence of 2.0% (6/298) (Table II). Five had confirmed abnormal BeLPTs during their first year of employment and one during the 24-month interval testing.

Combined cross-sectional survey/ company medical surveillance testing

Combining the cross-sectional and medical surveillance data, seven total participants were identified as sensitized. One had been identified by the company and reconfirmed through cross-sectional testing with multiple abnormal BeLPTs; one identified by the company had a single abnormal (unconfirmed) BeLPT in cross-sectional testing; one had no abnormal results during company medical surveillance but was confirmed sensitized in cross-sectional testing (the current worker described above); and four were identified during medical surveillance but had normal results during cross-sectional testing, for a combined sensitization rate of 2.3% (7/298; Table II). All sensitized were current workers at the time they were first identified as such. Five of the seven sensitized were clinically evaluated for CBD (71%). One, who was identified as sensitized less than 1 year after hire, was diagnosed with CBD shortly thereafter. Combined sensitization rate was used in all subsequent analyses.

Since four of the six identified as sensitized through medical surveillance while working had normal results during cross-sectional testing, we also evaluated the cross-sectional test results for the five with abnormal at-hire tests. Four of the five had normal results during cross-sectional testing; one of the two who were confirmed abnormal at hire had an unconfirmed abnormal cross-sectional result.

Demographic characteristics and skin symptoms

There were no meaningful differences between sensitized and non-sensitized participants with regard to gender, race, age at hire, median work tenure, or smoking

status (Table I). Sensitized workers had a marginally longer median time from first exposure to survey (i.e., date of hire to date of first cross-sectional survey blood draw, regardless of employment status or medical surveillance test results) than non-sensitized workers ($P = 0.06$), as well as longer median combined time since first exposure (i.e., date of hire to date of first abnormal blood draw [from either source] if sensitized, or to date of cross-sectional survey blood draw if not sensitized, regardless of employment status; $P < 0.01$). Early Program workers were significantly more likely to be sensitized than Late Program workers (4.9% vs. 0.6%, $P = 0.03$) (Table II).

No significant differences in prevalence of sensitization were noted for presence or absence of self-reported skin symptoms (Table I). Early Program workers were more likely to have reported rash or skin problems than Late Program workers ($P < 0.01$).

Work history

Among all participants, 67% worked primarily in production jobs, 31% in production support (but not production jobs), and 2% in administrative jobs only (Table III). More former (74%) than current workers (61%) were in production ($P = 0.02$) and in production support ($P = 0.03$). Both former ($P < 0.01$) and Early Program ($P = 0.01$) workers were more likely to have reported involvement in a possible high-exposure incident. About half of all participants (49%) who reported the latter stated that they had had skin exposure to beryllium during these incidents (data not shown), with more Early Program (61% vs. 31% of Late Program, $P = 0.07$) workers reporting such exposure.

Five percent of those who had ever worked a previously identified high-risk job were sensitized versus 1% of those who had not ($P = 0.04$; Table III). However, the differences in sensitization prevalence observed among work categories of production (6/199), production support (1/92), and administration (0/6), or in self-reported high-exposure incidents were not significant.

TABLE III. Work Categories, High-Risk Processes, and High-Exposure Incidents, and Sensitization by Work Category and Exposure

	All ^a	Former workers ^b	Current workers	Early Program workers ^c	Late Program workers	% Sensitized when response was:	
						"Yes" ^d	"No" ^d
Production: ^e % (n)	67 (199/297)	74 (101/137)	61** (98/160)	67 (82/123)	67 (117/174)	3 (6/199)	—
Production support: ^e % (n)	31 (92/297)	25 (34/137)	36** (58/160)	32 (39/123)	31 (53/174)	1 (1/92)	—
Administration: ^e % (n)	2 (6/297)	1 (2/137)	3 (4/160)	2 (2/123)	2 (4/174)	0 (0/6)	—
Worked known high-risk job/process: % (n)	33 (97/297)	36 (49/137)	30 (48/160)	37 (45/123)	30 (52/174)	5 (5/97)	1** (2/200)
Reported high-exposure incident: % (n)	13 (39/290)	20 (26/131)	8** (13/159)	19 (23/118)	9** (16/172)	3 (1/39)	2 (6/251)

^aSome participants elected not to provide responses.

^bComparisons were between former and current workers.

^cComparisons were between Early and Late Program workers.

^dPercent (number) of participants who were identified as sensitized among those in a work category, or by response to the high-risk or high-exposure questions.

^eParticipants who had worked in multiple categories were assigned to the category assumed to have the highest exposure.

** $P < 0.05$.

DISCUSSION

Nine years after the initiation of a program designed to prevent beryllium sensitization, and thus CBD, a cross-sectional survey of 298 current and former workers hired during the program identified two as beryllium-sensitized (0.7%). Including pre-existing company medical surveillance data with the cross-sectional results, the combined sensitization rate was 2.3% (7/298). In prior studies of this preventive program, when medical surveillance data from the program's early years were compared to a pre-program interval of comparable duration, sharp declines in sensitization had been observed [Cummings et al., 2007; Thomas et al., 2009; Bailey et al., 2010]. Combining pre-program cross-sectional survey results from all three plants, sensitization prevalence for those hired in the 5–6 years before program implementation was 10.1% (38/377). Comparing this pre-program prevalence to the current study's cross-sectional prevalence (0.7%), sensitization was greatly reduced in the 9 years after the preventive program was begun. Because at-hire testing was not available for pre-program survey participants, a more similar comparison would include current study participants who had one or more abnormal results during at-hire testing but who had been excluded from previous analyses (3/303, 1.0%); sensitization was still reduced tenfold. It was not possible to directly compare the combined sensitization rate to the pre-program prevalence. Thus, these results, as well as those from earlier assessments of this preventive program's efficacy [Cummings et al., 2007; Thomas et al., 2009; Bailey et al., 2010], demonstrate that longer-term follow-up of this preventive program continued to show an ongoing reduction in sensitization compared to survey results from these plants collected just prior to program inception.

Of note is that only one of the six participants who had been identified as sensitized during company medical surveillance was re-identified as sensitized with confirmed abnormal results in the new cross-sectional testing, and one participant was newly identified as sensitized. An additional surveillance-identified sensitized participant had a single abnormal result in the cross-sectional testing. It is worth noting that we used split-sample testing on first blood draw, which is considered to increase the probability of identifying sensitization [Kreiss et al., 1997]. The finding that persons who are at one point in time considered to be sensitized using the criterion of two abnormal BeLPTs may subsequently have normal test results has been previously reported [Cummings et al., 2007; Thomas et al., 2009; Bailey et al., 2010; Schuler et al., 2012]. There may be a variety of reasons, including variation in immune response over time, the use of different testing laboratories in surveillance and the cross-sectional survey, and the possibility of false abnormal and/or false normal test results [Kreiss et al., 2007]. However, most studies reported in the literature are cross-sectional. In studies that reported more than one opportunity for testing individuals for sensitization, those participants already identified as sensitized were not retested so it is not known whether subsequent test results would have been different. We would point out that this discussion of variation in test results over time is an analytical discussion. In the workplace, once a worker was identified as sensitized through medical surveillance he or she retained that designation regardless of subsequent BeLPT results. In addition, the decision to remain employed or to leave employment subsequent to identification of sensitization rested with the employee.

Our assessment of Early versus Late Program workers showed that six of the seven total participants who were

sensitized were hired in the early stages of the preventive program at their respective plants; 4.9% (6/123) Early Program versus 0.6% (1/175) Late Program workers were sensitized, an eightfold difference. This suggests improvement in the preventive program over time. (However, we would also note that the Late Program workers had fewer opportunities for testing for sensitization.) Our analyses showed that despite similar work tenure durations, Late Program workers reported fewer incidents that may have resulted in high beryllium exposure, with a smaller percentage of Late Program workers reporting skin exposure from these incidents. Late Program workers were also less likely to have reported rash or skin problems.

Data on CBD status were not available during the earlier evaluations of the preventive program that utilized de-identified datasets [Cummings et al., 2007; Thomas et al., 2009; Bailey et al., 2010]. One case of CBD was identified among this study's participants. The individual was diagnosed approximately 1 year after being hired. Prior to hire, the individual had been employed at another company whose facility had been used in the past for manufacturing beryllium materials. It is unknown if this individual had any exposure to legacy beryllium while working in that facility.

Some participants (19%, 69/367) were deemed to be ineligible for these analyses based on our inclusion/exclusion criteria. As this was an evaluation of the efficacy of this preventive program, we excluded those who reported having worked with beryllium at other facilities ($n = 29$), and those who began work at these facilities prior to program implementation ($n = 28$). However, it is possible that some participants who reported no prior beryllium work and were thus included in our analyses were unaware of previous beryllium exposure, so we reanalyzed the data including the 29 participants with other beryllium work. The cross-sectional (0.6%, 2/327) and combined prevalence rates (2.1%, 7/327) were unchanged, and there were no meaningful changes to the results from the questionnaire data. Among the six participants excluded for missing medical surveillance data, all received normal BeLPT results during participation in the cross-sectional survey.

This project has several strengths, including being the first evaluation of the effectiveness of a program to prevent beryllium sensitization that included former workers. We found that former workers, who were tested 3 months to 9 years after leaving employment and were more likely to have been hired in the early, developmental years of the preventive program, had not developed newly identified sensitization after leaving employment. This does not, however, suggest that those who leave employment without having been identified as sensitized are clear of any ongoing or future risk. Other studies have identified

sensitization among beryllium workers after leaving employment [Schuler et al., 2008].

Other strengths include the use of split sample blood draws for the cross-sectional BeLPTs and inclusion of company medical surveillance data. Split samples on first blood draws increase the identification of sensitization [Kreiss et al., 2007]. The inclusion of additional periodic BeLPT results (company medical surveillance data) provided a more complete assessment of all cases of sensitization, as the surveillance data identified five workers who would not have been detected as sensitized if we had relied solely on the cross-sectional survey data.

This project has several limitations. The small number of sensitized individuals limited our ability to detect and report differences between sensitized and non-sensitized workers, or between subgroups (current vs. former, Early vs. Late Program). The small numbers precluded analyses by plant or details on jobs and processes worked. We were able to observe that all sensitization occurred among production workers.

Since the elements of the comprehensive program were not introduced one at a time, it was not possible to determine the relative efficacy of any individual element. For example, workers began to wear nitrile gloves to keep beryllium off of their hands at the same time as many administrative control elements were implemented.

Another possible limitation involves the use of different laboratories for BeLPT testing. The two labs used for the cross-sectional survey BeLPTs were different from the labs the company usually used for medical surveillance or for pre-program cross-sectional surveys. Previous studies have shown that there can be significant differences in BeLPT results between labs [Kreiss et al., 1997; Deubner et al., 2001], and these differences may be an indication of laboratory testing quality problems [Thomas et al., 2009]. Quality issues arose during the data-collection phase of the cross-sectional survey. Between June 2008 and June 2009, there were no significant differences in either the number of abnormal or non-normal (borderline, uninterpretable) tests reported by the two labs used for the cross-sectional survey. However, beginning in July 2009, one lab reported a significantly higher number of uninterpretable results than the other lab ($P = 0.01$), though the number of abnormal results was not different between the two labs ($P = 1.0$). The problem was eventually identified by the laboratory (a contaminated reagent) and remedied. While this highlights a benefit of using split samples for BeLPT, it is unlikely that this specific issue affected the results of this project. When we recognized the possible problem, we split all redraws for uninterpretable BeLPTs and sent blood samples to both labs, and there were no subsequent abnormal results among these participants. Our inability to reconfirm sensitization in four of the six workers identified as such during company medical

surveillance, and three of the four identified as sensitized after an abnormal BeLPT at hire, is consistent with other reports in which individuals with abnormal BeLPTs at one point in time tested normal at another point in time, as stated above. Another point worth noting is that the laboratories used in this study and by the company utilized varying criteria both for determining stimulation index thresholds and for classifying tests as “uninterpretable.” For the former, we used the laboratory-determined threshold when interpreting test results, and we do not believe the latter had much impact as uninterpretable tests were repeated at the same laboratory.

The final limitation to this project was the somewhat low participation rate (63%), especially among former workers (55%), as we would have missed any sensitization present in those who did not participate. However, we would note this is unlikely to have biased the results since sensitization status is unknown in the absence of testing.

CONCLUSIONS

This cross-sectional survey of current and former beryllium workers identified one new person as sensitized, while four persons previously identified as such during medical surveillance were not re-identified as sensitized. These longer-term findings, 9 years after program inception, suggest that the combination of increased respiratory and dermal protection, enclosure and improved ventilation of high-risk processes, dust migration control measures, improved housekeeping, and worker and management education reduced the rate of beryllium sensitization in workers in previously high-risk facilities approximately tenfold. The lower rate of sensitization among Late Program workers suggests that the continuing refinements made to the preventive program have provided additional protection against beryllium sensitization compared to the early years of program implementation.

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