Evaluation of a Preventive Program to Reduce Sensitization at a Beryllium Metal, Oxide, and Alloy Production Plant

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Objective: We evaluated a workplace preventive program's effectiveness, which emphasized skin and respiratory protection, workplace cleanliness, and beryllium migration control in lowering beryllium sensitization. **Methods:** We compared sensitization prevalence and incidence rates for workers hired before and after the program using available cross sectional and longitudinal surveillance data. **Results:** Sensitization prevalence was 8.9% for the Pre-Program Group and 2.1% for the Program Group. The sensitization incidence rate was 3.7/1000 person-months for the Pre-Program Group and 1.7/1000 person-months for the Program Group. After making adjustments for potential selection and information bias, sensitization prevalence for the Pre-Program Group was 3.8 times higher (95% CI = 1.5 to 9.3) than the Program Group. The sensitization incidence rate ratio comparing the Pre-Program Group to the Program Group was 1.6 (95% CI = 0.8 to 3.6). **Conclusions:** This preventive program reduced the prevalence of but did not eliminate beryllium sensitization.

Since the late 1980s, surveillance in the United States for beryllium sensitization as a risk marker for chronic beryllium disease (CBD) has relied on the beryllium lymphocyte proliferation test (BeLPT).[1] Use of this tool has led to the recognition that the Occupational Safety and Health Administration's permissible exposure limit for beryllium air concentration did not protect workers' health and that process-related risks for beryllium sensitization existed that had not been evident from environmental measurements. The BeLPT has also been used to evaluate the impact of preventive interventions on the rate of sensitization in new employees.[2–4] Our study similarly uses the BeLPT to assess the impact of enhanced preventive measures in the largest United States primary beryllium materials production plant.

The production plant opened in 1953 with copper-beryllium alloy production, followed by beryllium metal operations in 1957, and beryllium oxide production in 1958. Beryllium metal "pebbles" were produced from beryllium hydroxide through a series of wet and furnace (fluoride and reduction) chemical processes. The pebble processes were discontinued in October 2000 due to the need for extensive equipment upgrading; the post-2000 source of beryllium metal is stockpiled material, which is reduced to powder for further processing. The plant also recycles scrap beryllium and alloy metal.

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The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

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Workers at this facility participated in a plant-wide survey in 1993–1994 to determine the prevalence of beryllium sensitization and CBD.[5] The prevalence of beryllium sensitization (confirmed abnormal BeLPT) and newly diagnosed CBD were 6.9% and 3.8%, respectively, among 627 workers. The survey found three areas associated with elevated risk of beryllium sensitization: beryllium oxide ceramics production (among workers employed in that area before its 1982 relocation to another facility), the pebbles plant, and the analytic laboratory.

In response to this survey, the company made several changes to plant production areas in 1996 and 1997 in an effort to reduce airborne beryllium levels (Table 1). Among the changes, the company enclosed the beryllium oxide production area and the fluoride and reduction furnaces in the pebbles plant, and these areas became a restricted access zone with a limited group of workers, most of whom had already worked in this area. In 1997, the company offered the BeLPT to these workers. Fifty-seven were tested, and six (10.5%) were confirmed as sensitized; among the 31 workers hired after the 1993–1994 survey, five (16.1%) were confirmed as sensitized. In 1998, the company also added new ventilation to the fluoride and reduction furnaces.

In 1999, a second cross-sectional survey showed no reduction in sensitization and CBD, despite engineering improvements.[6] Among all participants, sensitization and CBD were 10.7% and 4.2%, respectively, and for those hired after the 1993–1994 survey, 10.4% were confirmed as sensitized, and 2.2% were diagnosed with CBD.

On February 21, 2000, the company began to implement an enhanced preventive program known as the Beryllium Worker Model to reduce potential occupational exposures. The program involved a combination of increased workplace orderliness and cleanliness, dermal and respiratory protection, personal cleanliness (skin, clothes, and shoes), particle migration control involving work practices and engineering controls, and worker training and involvement. Compared to previous preventive efforts, the model emphasized increased interruption of multiple pathways of potential beryllium migration from work processes to the skin and lungs[7] (Table 2).

Although not part of the preventive program, the pebbles plant, one of the known high-risk processes, was shut down in October 2000, not long after the enhanced preventive program began. In the program, surveillance of new employees with BeLPTs at hire and at frequent intervals early in employment tenure was begun to monitor the impact of the enhanced preventive program. The timing and frequency of testing was also motivated by previous studies that had identified workers with abnormal BeLPT test results within months of hire.[2,8,9]

This report is an evaluation of the effectiveness of the enhanced preventive program using existing BeLPT surveillance data. Comparing longitudinal incidence data for the workers hired after the program began and cross-sectional prevalence data for the workers hired in a comparable period of time before the program's implementation required estimating both prevalence and incidence for the two groups, with attention to the possible influences of shutting down the pebbles plant and the stages of preventive program implementation.

TABLE 1. Examples of Preventive Efforts, 1996 Through 1999

Year	Control Type	Description of Control
1996	Engineering	Installed walls enclosing the oxide operations and the fluoride furnaces, reduction furnaces, scrap reclamation, beryllium vacuum casting, and the pebble mill area.
1997	Administrative	Implemented restricted access zone in pebbles plant and oxide furnace area.
1997	PPE	Pebbles plant workers required to wear half-face air-purifying respirators while in restricted access zone.
1997	Engineering	Constructed new alloy plant cast shop and finishing strip mill to "clean plant" design standards.
1998	Engineering	HEPA filters added to air handlers in East Administration Building. HEPA filters added to air handlers for break areas in BE products, pebbles plant operators, and alloy melting and casting operations.
1998–1999	Engineering	Rebuilt fluoride and reduction furnace processes including new ventilation systems.
1999	Engineering	All new employees required to wear loose-fitting power air-purifying respirators while in manufacturing buildings.

PPE, personal protective equipment; HEPA, high-efficiency particulate air.

TABLE 2. Examples of Enhanced Preventive Program After the 1999 Survey

Year	Control Type	Description of Control
2000	Administrative/PPE	New employee program included medical surveillance, loose-fitting powered air-purifying respirators, and skin protection.
		Booties required over shoes in plant areas that did not require respiratory protection.
2001	Engineering	Migration controls (such as boot scrubbers and air showers in transition zones) installed in melting and casting areas.
2001	Administrative	Smoking banned in production areas.
		Workers required to remove gloves and wash hands before eating, drinking, or smoking.
		Regular toolbox safety meetings led by supervisors.
		Visibly dirty uniforms required shower, clean uniforms, and incident report.
		"Visibly clean" standard required for all materials such as pallets and trailer vans.
		Purchased contractor vehicles to keep vehicles on plant site.
		Hand cleaning wipes installed in transition areas.
		Hand washing required between glove changes.
		"Visibly clean" housekeeping standards.
2001	PPE	Half-mask respirators or powered air-purifying respirators required in production facility based on beryllium airborne levels.
		Nitrile glove use required in all production areas.
		Gloves required for handling work boots.
		Respiratory protection required for roof work.
		Water-resistant garments replaced waterproof ones in production areas.
		Respirator use required when removing boots.
2002	Engineering	Tacky mats installed in transition areas between nonproduction and production areas.
2002–2004	Engineering	Some administration offices in the production buildings physically separated from production areas.
2003	PPE	Woven respirator belts replaced with non-woven belts.
		Aprons/smocks required in areas where uniforms may become visibly dirty (except where fire hazard may exist).
2005	Administrative	Tool areas in maintenance support cleaned and reorganized to minimize beryllium exposure.
2005	PPE	Laceless boots replaced laced boots.

PPE, personal protective equipment.

METHODS

Study Subjects

We compared workers hired before the program (Pre-Program Group) to workers hired after the preventive program began (Program Group). The Pre-Program Group comprised workers who had begun work on-site between January 15, 1993 and August 9, 1999, and who had participated in the 1999 cross-sectional plant survey. Some members of the Pre-Program Group also took part in the small pebbles plant survey in 1997. Those BeLPT results are included here. The Program Group comprised workers hired from February 21, 2000 to December 18, 2006 who were tested for beryllium sensitization at least one time post-hire. On the basis of the program's evolution (Table 2), this group was further subdivided into the Partial Program subgroup, hired from February 21, 2000 through December 31, 2003, and the Full Program subgroup, hired from January 1, 2004 through December 18, 2006. The Partial Program subgroup experienced ongoing refinements in education and training, improved housekeeping, reduced contamination of the skin, and increased respiratory protection. By January 1, 2004, new workers were introduced into a workplace environment in which

the program was understood by workers and management and many technical aspects of the program had been implemented, audited, and documented.

The Human Subjects Review Board of the National Institute for Occupational Safety and Health (NIOSH) reviewed and approved the study protocol for the 1999 cross-sectional survey. We obtained written informed consent from each study participant, including access to participants' prior workplace medical information. As periodic testing for sensitization for the Program Group was a component of mandatory workplace medical surveillance for new workers, written informed consent to share test results with NIOSH had not been obtained. We therefore used de-identified data for the Program Group workers under terms of a confidentiality agreement between NIOSH and the company, with an Institutional Review Board waiver; variables were limited to a unique identifier, BeLPT results (including laboratory and date), date of hire, work category, and demographic variables. This work was performed under a Memorandum of Understanding for research collaboration between NIOSH and the company first signed in 1998 and renewed in 2005.

Testing for Sensitization: Pre-Program Group

Before 2000, BeLPT testing using split samples occurred as part of systematic, facility-wide surveys conducted in 1993–1994[5] and 1999,[6] during interim testing of pebbles plant workers in 1997, and in evaluation of individual workers for medical reasons. Thus, baseline (at-hire) and interval test results were not available for most of the Pre-Program Group apart from pebbles plant workers with interim tests. To make the findings comparable to those for the Program Group (described below), whose BeLPTs were sent primarily to a single commercial laboratory, we limited our analysis to persons whose first draw was sent to Laboratory 1. We defined beryllium sensitization for the Pre-Program Group as two or more abnormal tests, with a first draw test indicating a non-normal (abnormal, borderline negative, or uninterpretable) result from Laboratory 1. Follow-up BeLPT results triggered from the non-normal result from Laboratory 1 but no other laboratories were included in the analysis. An exception to this definition occurred on 28 occasions when initial split testing results from Laboratory 1 and another laboratory were negative, but follow-up testing still occurred that was not triggered from non-normal results from any specific laboratory. In these cases, we included the follow-up BeLPT results. We did not have laboratory source data for all the 1997 pebbles survey participants and included results of split sample testing, irrespective of laboratory source of the results.

Testing for Sensitization: Program Group

Beginning in mid-February 2000, the facility began testing newly hired workers to establish beryllium sensitization status before beginning work. After the baseline BeLPT, regular testing occurred at intervals of 3, 6, 12, 24, and 48 months ("interval BeLPT"). As for the Pre-Program Group, workers were informed of their test results by the company; the company did not use test results to make decisions about continuing or terminating a worker's employment.

In most cases, Laboratory 1 conducted the baseline BeLPTs. An abnormal BeLPT had two or more stimulation indices greater than the laboratory-defined threshold.[10] A borderline negative result had a single index greater than the threshold. Tests were repeated at Laboratory 1 for borderline negative or uninterpretable results. Abnormal results were confirmed by sending split samples to Laboratory 1 and to Laboratory 2, Laboratory 3, or Laboratory 4. Sometimes during the surveillance program, first draw blood samples were split and sent to Laboratory 1 (on most occasions) and either Laboratory 2, 3, or 4.

A worker with two abnormal BeLPTs at any laboratory that was triggered from a non-normal test (abnormal, borderline negative, or uninterpretable BeLPT) at Laboratory 1 met the study definition of beryllium sensitization. We excluded workers from the Program Group if they were not initially tested at Laboratory 1 on first blood draw at hire. We also excluded test results during BeLPT intervals if they were not triggered by a non-normal test at Laboratory 1.

For our study, BeLPTs not performed directly on schedule were assigned to a testing interval (0, 3, 6, 12, 24, or 48 months). Follow-up BeLPTs were assigned to the interval of the triggering test (uninterpretable, borderline, or abnormal BeLPT). If a borderline negative test was not repeated, we considered the result to be normal.

Testing for sensitization was cross-sectional for the Pre-Program Group and longitudinal for the Program Group. To address this issue, we compared the groups using two approaches: sensitization prevalence and sensitization incidence rate.

Sensitization Prevalence Ratios

We calculated the prevalence of sensitization for the Pre-Program Group as the number of sensitized workers divided by the total number of Pre-Program Workers from the 1999 survey. We also calculated the prevalence of sensitization excluding those who had ever worked as pebbles plant operators because this high risk job title did not exist in the Program Group.

The Pre-Program and Program Groups had different quality of information in beryllium sensitization status because workers in the latter group could be tested more times than their colleagues in the former group. In the Program Group, we approximated a cross-sectional survey to equalize information quality between the two groups by using only the results available from each worker's final interval BeLPT. To determine the sensitization prevalence for this group, we used the number of workers that would have been identified as sensitized based on their final interval BeLPT divided by the total number of workers in the Program Group. Similar procedures were followed for the Partial and Full Program subgroups.

The prevalence comparison of the Pre-Program and Program Groups was performed by calculating a prevalence ratio. The 95% confidence intervals were derived using a cohort study method that accounts for the variance of both the numerator and denominator.[11]

Sensitization Incidence Rate Ratios

For the Pre-Program Group, we were unable to calculate an accurate incidence rate, as their baseline BeLPT status was unknown and no interval testing was available to estimate time to sensitization during employment. To approximate the incidence rate, we calculated the number of sensitized workers per person-time, defining sensitization-free time from the start of on-site work to the first abnormal BeLPT for sensitized workers (in either 1997 or 1999), or to the last BeLPT test for non-sensitized workers during the 1999 survey. We also calculated the incidence rate excluding those who had ever worked as pebbles plant operators.

For the Program Group, we calculated different incidence rates by either excluding (for an unadjusted incidence rate) or including (for an adjusted incidence rate) those who tested abnormal at baseline. Sensitized workers were considered sensitization-free until the time of their first abnormal BeLPT. For workers who remained sensitization-free during the surveillance period, we censored their data at the time of their final BeLPT interval. For workers who left employment sensitization-free and were rehired, the off-work period was included in the calculation of sensitization-free employment.

For both rates, we used the sum of months of sensitization-free time as the denominator. The adjusted incidence rate was calculated to create a rate comparable to that calculated for the Pre-Program Group; we included workers with an abnormal base-

line BeLPT to account for the unknown baseline status of the Pre-Program Workers. Similar procedures were followed for the Partial and Full Program subgroups.

To compare sensitization rates, we calculated incidence rate ratios by dividing the incidence rate for the Pre-Program Group by the unadjusted and adjusted rates for the Program Group. We determined the corresponding 95% confidence intervals using a binomial probability model.[12]

Statistical Analysis

To assess the similarity of the Pre-Program and Program Groups, we compared race, sex, age at hire, and work categories. We used SAS version 9.2 (SAS Institute, Cary, NC) for all analyses. We used χ^2 tests for categorical variables and Fisher's exact tests when appropriate. For continuous variables, we performed nonparametric one-way analyses of variance using median scores to account for unequal variances and non-normally distributed data and used Kolmogorov–Smirnov two-sample tests for pair-wise comparisons among subgroups. For all analyses, *P*-values less than or equal to 0.05 were considered statistically significant.

Work categories for both cohorts included 1) administration workers, who spent little or no time in the production areas; 2) production support workers, who spent at least part of a workday in the production areas but were not production workers; and 3) production workers, who spent all or most of the typical workday in production areas. For all three groups, transition between work categories due to job changes was infrequent. If a worker had changed work categories, he or she was assigned to the category likely to have the higher beryllium exposure. Production workers were assumed to have had the highest exposure and administration workers the lowest.

RESULTS

Study Subjects

Of the 291 workers who began working at this facility after January 1, 1993 and who were still employed there at the time of the 1999 survey, 264 (91%) participated in the 1999 survey. We excluded six of these workers because their initial 1999 survey BeLPTs were not done at Laboratory 1; none of the excluded had abnormal BeLPTs. The Pre-Program Group thus consisted of 258 workers. Of these, we classified two sensitized workers as nonsensitized because during baseline split testing each worker had a normal BeLPT at Laboratory 1 and an abnormal BeLPT at Laboratory 2 (with a confirmed follow-up abnormal BeLPT triggered from the Laboratory 2 abnormal test).

Between February 21, 2000 and December 18, 2006, the facility hired 369 workers. One worker with no abnormal BeLPTs was excluded because the baseline BeLPT was not at Laboratory 1. In addition, 78 workers were excluded because they completed only the baseline BeLPT; five had two or more abnormal BeLPTs during their baseline testing, and one had one abnormal test. Thus the Program Group consisted of 290 workers. For two nonsensitized Program Group workers, we excluded an abnormal baseline BeLPT. Both workers had one normal baseline BeLPT at Laboratory 1 and one abnormal baseline BeLPT at Laboratory 2, and thus the Laboratory 2 result was excluded based on our protocol. We classified two sensitized workers as nonsensitized because each had a normal baseline BeLPT at Laboratory 1 and an abnormal baseline BeLPT (which triggered a follow-up test which was also abnormal) at Laboratory 2. Again based on our protocol, the baseline Laboratory 2 BeLPT and follow-up tests triggered from it were excluded. The Partial Program subgroup consisted of 206 workers, and the Full Program subgroup had 84 workers.

No significant differences existed among the Pre-Program Group and Program Group or its subgroups with regard to sex or race (Table 3). Significant differences did exist with regard to age at hire and work category. The median age at hire was 30 years for the Pre-Program Group and 34 years for the Program Group. For the Pre-Program Group, 80% were in production, 20% in production support, and none in administration. Among the Program Workers, 69% were in production, 27% in production support, and 4% in administration.

Sensitization Prevalence Ratios

Among the Pre-Program Group, the prevalence of sensitization was 8.9% (23 of 258). For the Program Group, utilizing each worker's final interval BeLPT results, six workers (D, E, G, H, J, and K) were sensitized (Table 4), yielding a prevalence estimate of 2.1% (6 of 290). Workers E and K were considered sensitized because they had already been confirmed as sensitized during a prior BeLPT testing interval, so the subsequent abnormal test did not trigger further follow-up testing. The prevalence ratio comparing the Pre-Program Group to Program Group was 4.3 (95% CI = 1.8 to 10.4). Prevalence ratios for the Partial and Full Program subgroups are in Table 5.

Sensitization Incidence Rate Ratios

In the Pre-Program Group, 23 workers were sensitized during 6242 person-months, for an estimated incidence rate of 3.7/1000 person-months (Table 6). In the Program Group, two workers were not included in the calculation of the unadjusted incidence rate as they had abnormal test results at hire. Nine workers were sensitized during 5221 person-months, yielding an unadjusted incidence rate of 1.7/1000 person-months. The unadjusted incidence rate ratio of the Pre-Program Group to the Program Group was 2.1 (95% CI = 1.0 to 4.9) (Table 5). When the two workers (both sensitized) with abnormal BeLPTs at hire were included in the analysis for the purpose of comparison to the Pre-Program Group,

TABLE 3. Demographic Characteristics Among Workers Hired Before and After the Implementation of the Enhanced Preventive Program

Demographics	Pre-Program (n = 258)	Program (n = 290)	Partial Program (n = 206)	Full Program (n = 84)
Male *n*, (%)	200 (78%)	227 (78%)	159 (77%)	68 (81%)
White *n*, (%)	245 (95%)	265 (91%)	191 (93%)	74 (88%)
Job category *n*, (%)				
Production	206 (80%)	200 (69%)*	147 (71%)*	53 (63%)*
Production	52 (20%)	77 (27%)	51 (25%)	26 (31%)
Support administration	0	13 (4%)	8 (4%)	5 (6%)
Median age at hire (yr)	30	34†	33†	35†

*$P \leq 0.05$ for job category distribution compared with Pre-Program Group.
†$P \leq 0.05$ compared with Pre-Program Group.

TABLE 4. Program Workers With Confirmed Abnormal BeLPT During Surveillance*

Worker	Hire	3 Months	6 Months	12 Months	24 Months	48 Months
Partial Program						
A	**Abnormal† (2/3)**	No test	Normal (1/1)	Normal (1/1)	No test	No test
B	Normal (1/1)	**Abnormal (5/5)**	No test	Normal (1/1)	No test	No test
C	Normal (1/1)	**Abnormal (4/5)**	Normal (1/1)	No test	No test	No test
D	Normal (1/1)	**Abnormal (3/3)**	No test	No test	No test	No test
E	Normal (1/1)	Normal (1/1)	**Abnormal (3/6)**	Abnormal (1/1)	No test	No test
F	Normal (1/1)	Normal (1/1)	**Abnormal (3/3)**	Normal (1/1)	No test	No test
G	Normal (1/1)	Normal (1/1)	**Abnormal (2/3)**	No test	No test	No test
H	Normal (1/1)	Normal (1/1)	Normal (1/1)	**Abnormal (2/5)**	No test	No test
Full Program						
I	Normal (1/1)	Abnormal (1/2)	**Abnormal (1/4)**	Normal (1/1)	No test	No test
J	Normal (1/1)	No test	**Abnormal (5/8)**	No test	No test	No test
K	Abnormal (1/5)	Normal (1/1)	Normal (1/1)	Normal (1/1)	**Abnormal (1/1)**	No test

*If initial results were uninterpretable, interpretable repeat results are shown.
†Numbers in parentheses indicate number of abnormal results/total number of interpretable results (including confirmatory results) associated with the interval; bold lettering indicates sensitization was confirmed in that interval.

TABLE 5. Prevalence and Incidence Rate Ratios for Beryllium Sensitization by Pre-Program to Program Groups and Subgroups

Study Cohort: Referent Cohort	Prevalence Rate Ratio (95% CI)	Adjusted Incidence Rate Ratio* (95% CI)	Unadjusted Incidence Rate Ratio† (95% CI)
Include pebbles operators in Pre-Program Group			
Pre-Program: Program	4.3 (1.8–10.4)	1.8 (0.9–3.7)	2.1 (1.0–4.9)
Pre-Program: Partial Program	4.6 (1.6–13.1)	1.9 (0.9–4.5)	2.2 (1.0–5.4)
Pre-Program: Full Program	3.7 (1.0–15.5)	1.4 (0.5–5.8)	2.1 (0.6–13.1)
Exclude pebbles operators in Pre-Program Group			
Pre-Program: Program	3.8 (1.5–9.3)	1.6 (0.8–3.6)	1.9 (0.9–4.7)
Pre-Program: Partial Program	4.0 (1.4–11.6)	1.8 (0.8–4.3)	2.0 (0.9–5.2)
Pre-Program: Full Program	3.3 (0.8–13.7)	1.3 (0.4–5.5)	1.9 (0.5–12.3)

*Program Group included sensitized workers with one or more abnormal BeLPT at hire.
†Program Group excluded sensitized workers with one or more abnormal BeLPTs at hire.

TABLE 6. Incidence Rates for Beryllium Sensitization* Before and After Implementation of the Enhanced Preventive Program

	Pre-Program (n = 258)	Pre-Program Excluding Pebbles Operators (n = 232)	Program (n = 290)	Partial Program (n = 206)	Full Program (n = 84)
Sensitized† (n)	23	18	9‡	7§	2§
Adjusted sensitized‖ (n)	—	—	11	8	3
Person-months	6242	5246	5221¶	4095¶	1125¶
Incidence rate	3.7	3.4	1.7	1.7	1.8
Adjusted incidence rate	—	—	2.1	2.0	2.7

*Beryllium sensitization defined as a worker with two or more abnormal BeLPTs.
†Excluded sensitized workers with abnormal BeLPTs at hire.
‡Two sensitized workers excluded with one or more abnormal BeLPTs at hire.
§One sensitized worker excluded with one or more abnormal BeLPTs at hire.
‖Included sensitized workers with abnormal BeLPTs at hire.
¶Person-months the same for adjusted and unadjusted methods.

the adjusted incidence rate ratio was 1.8 (95% CI = 0.9 to 3.7). Analyses of the adjusted Partial and Full Programs and Program subgroups are in Tables 5 and 6.

All the sensitized Pre-Program Group worked in production. Seven of the sensitized Program Group worked in production and four were in production support. One of the four

production support workers was in the Partial Program subgroup and three were in the Full Program subgroup.

Analysis Excluding Pebbles Plant Operators

When we excluded the 26 workers from the Pre-Program Group who had ever worked as pebbles operators, 18 sensitized workers remained, for a prevalence of 7.8% (18 of 232). The sensitization prevalence of the Pre-Program Group was 3.8 times higher (95% CI = 1.5 to 9.3) than the Program Group, 4.0 times higher (95% CI = 1.4 to 11.6) than the Partial Program subgroup, and 3.3 times higher (95% CI = 0.8 to 13.7) than the Full Program subgroup. Analyses of the incidence rates and ratios are shown in Tables 5 and 6.

DISCUSSION

Beryllium workers hired after the implementation of the enhanced preventive program appeared to have about one fourth the prevalence of beryllium sensitization compared to an analogous group of workers hired before the program's implementation. Even when the higher risk pebbles plant operators were excluded from those hired before program implementation, the Program Group workers still had about one fourth the prevalence of beryllium sensitization.

The incidence data comparison was less compelling in demonstrating such protection for workers hired during the program period. Although the unadjusted incidence of beryllium sensitization among Program Group workers was half that of workers hired before the program implementation, the adjusted incidence rate including Program Group workers with abnormal tests at hire may be the more justifiable comparison. By using the adjusted incidence rate for Program Group workers compared to the estimated incidence rate for workers hired before the preventive program yielded a non-significant reduction in sensitization rate. Exclusion of pebbles plant operators reduced the protective effect of the prevention program, with no evidence of more protection to workers hired 4 or more years after the preventive program began. Had we elected to use only the last test interval data for the Program Group for the incidence comparisons, the resulting incidence rate ratio would have achieved significance. By this method, six Program Group workers would have been sensitized for 5229 person-months yielding an incidence rate of 1.1/1000 person-months with an incidence rate ratio of the Pre-Program Group to the Program Group of 3.2 (95% CI = 1.4 to 8.6). Excluding the pebbles operators, the incidence rate ratio would have been 3.0 (95% CI = 1.2 to 8.3) compared to the Program Group. Nevertheless, similarly to the prevalence comparisons, the larger ratios would have been achieved at the cost of ignoring known abnormal test results in the Program Group.

Both the prevalence and incidence comparisons suggest some beneficial effect of the preventive program. The prevalence ratios are robust in that the estimated prevalence in those hired after the preventive program is conceptually comparable to the cross-sectional prevalence of the workers hired in the 6 years before the 1999 survey. The adjusted incidence comparison is more conservative because the workers hired before the preventive program may have been sensitized at hire or at any time before the survey. The sensitization-free employment duration for the incidence calculation is thus undoubtedly larger than would have been the case if there had been interval BeLPTs for workers hired before the preventive program. That is, the estimated incidence rate of Pre-Program Group workers is likely an underestimate because the person-time denominator may be too high. This reduces the contrast in beryllium sensitization between the Pre-Program Workers and those hired after the preventive program began, reducing the apparent program effectiveness.

The Partial and Full Program subgroups did not show striking differences in effectiveness of prevention of sensitization, both appearing to have benefited in comparison to the group of workers hired before the comprehensive approach to prevention. In a large, complex facility that produces multiple forms of beryllium, implementation of the program was time-consuming and varied in success by production unit, management buy-in, and worker acceptance. Major deviations from historical practice included putting new workers in occlusive gloves, full-time respirator protection, and housekeeping to minimize beryllium migration from production sources. Such migration could result in surface contamination of clothing and work surfaces distant from its sources, as well as air contamination. Many interventions were conducted simultaneously, so it is impossible to determine which aspects of the program were most beneficial in preventing sensitization. The increase in respiratory protection was accepted by most workers, although disciplinary action by the company was ultimately necessary to achieve full worker compliance. It is heartening that early preventive efforts, however incomplete, appeared to be almost as effective in lowering sensitization rates as the program 4 years after implementation, when the Health and Safety staff felt that it was finally running smoothly. The shift in sensitization from only production workers in the 1993–1999 hires to some workers in production support in those hired after the preventive program may suggest a need for emphasis on workers thought to be at less risk, or it may at least partially reflect the greater numbers of production support workers among the Program Group.

The results at this plant complement those found for the preventive programs implemented at this company's beryllium oxide ceramics manufacturing facility[3] and copper-beryllium alloy finishing facility.[4] At the beryllium oxide ceramics manufacturing plant, a 1998 cross-sectional survey had showed that nearly 10% (7 of 74) of workers hired between 1993 and 1998 were sensitized to beryllium.[2] As a result, the plant enhanced its existing preventive program in 2000, introducing controls such as skin protection, air showers, and full-time use of powered air-purifying respirators. Cummings et al[3] compared BeLPT results of workers hired at the plant from 2000 to 2004 (Program Workers) with those workers hired from 1993 to 1998 (Pre-Program Workers) and found that the comprehensive preventive program reduced the detection of sensitization among new workers hired since 2000. Although 8.7% (6 of 69) of the Pre-Program Workers demonstrated sensitization, only 1% (1 of 97) of the Program Workers did, giving a prevalence ratio of 8.4 (95% CI = 1.04 to 68.49). The unadjusted incidence rate ratio of the Pre-Program Workers to the Program Workers was 8.2 (95% CI = 1.2 to 188.8), and the adjusted rate ratio was 2.1 (95% CI = 0.6 to 8.4). The authors determined that the decrease in sensitization was probably not related to a change in beryllium air levels because overall air levels were found to be similar for the two time periods. Instead other components of the preventive program, including full-time respiratory protection, improved housekeeping, and reduced contamination of work clothing and skin, were likely responsible.

At the copper-beryllium alloy finishing facility, a 2000 cross-sectional survey found that 7% (10 of 144) of workers were sensitized to beryllium.[9] Risk was associated with work in and around the wire annealing and pickling process. Thomas et al[4] found that 11.6% (5 of 43) of workers hired from 1993 to 2000 (Pre-Program Workers) before the start of the comprehensive preventive program were sensitized whereas only 2.4% (2 of 82) of workers hired from 2000 to 2006 (Program Workers) after the start of the preventive program were sensitized. This gave a prevalence ratio of 4.8 (95% CI = 1.0 to 23.6). The unadjusted incidence rate ratio comparing the Pre-Program Workers to Program Workers was

2.0 (95% CI = 0.5 to 10.1). An adjusted incidence ratio was not calculated because there were no Program Workers with abnormal BeLPTs at hire. Workers hired after the enhanced preventive program had approximately a fifth of the risk of becoming sensitized than workers hired before the program; however, low statistical power in this small workforce prevented a definitive conclusion about the program's efficacy. A major part of the program at this facility involved enclosing the wire annealing and pickling process to create a restricted access zone. Full-time respirator use was only required in this area, and among maintenance mechanics for specific tasks.

Similar findings were thus observed at all three beryllium facilities. Common to all three preventive programs was the goal to interrupt exposure pathways to the skin and lungs. Nevertheless, due to differences in beryllium forms, processes, production equipment, physical layouts of the three facilities, and associated differences in beryllium air levels, the application details differed among the facilities. Improved housekeeping and dermal protection were implemented at all three facilities. Dermal protective equipment was required for all workers based on the possibility of beryllium sensitization by the dermal route. Skin exposure to soluble beryllium salts had previously been shown to induce cutaneous hypersensitivity.[13] Full-time respirator use was also implemented in areas thought to be at elevated risk.

A limitation in our study was the differences in data collection methodologies between the Pre-Program and Program Groups. We compensated for this by using both incidence and prevalence analysis approaches to make the data from the two groups as similar as possible. Another limitation was the lack of job title information for the Program Group. In the Pre-Program Group, all the sensitized workers worked in production, and we were able to determine who had ever worked as a pebbles operator. In the Program Group, the majority of the sensitized workers also worked in production and the rest in production support. Nevertheless, because the surveillance data set was de-identified and thus did not contain detailed job information, we could not conduct more specific job-related analyses. Also, most of the workers in the Pre-Program and Program Groups had been employed for less than 2 years. The duration has been too short to document reduced incidence of CBD. It will be important to evaluate whether the reduction of sensitization in early employment persists for a longer period of time, both in those who remain employed and thus exposed, as well as in those who leave employment.

Finally, these results are subject to problems observed with pre-post comparison studies, notably that differences between groups, other than the ones measured, may account for at least some of the variation. This may be true of a study with outcome measures based on the BeLPT, as the few laboratories in the United States that perform this test may have varied in their methods over time, and test factors, such as human serum lot, can influence test results. The BeLPT is subject to interlaboratory and test-to-test variation, and laboratory performance has varied over time.[9,14,15] There is evidence for this kind of variability within plant-specific data collected at this company, eg, increases in prevalence of sensitization at two facilities when comparing surveys in 1992[16]–1998[2] and 1993–1994[5]–1999[6]; in both cases, the prevalence of sensitization increased without obvious evidence for adverse changes in working conditions. An alternate explanation is that workers with less than 1 year's tenure were not tested in the 1992 and 1993–1994 surveys, and subsequent studies have demonstrated a higher prevalence of beryllium sensitization among short-term workers.[2,8,9] Furthermore, repeat testing over time influences the cumulative rate of sensitization.[17] We attempted to mitigate these possible phenomena by using a single laboratory for the recognition of an initial abnormal test, but this does not eliminate test-based variability as a potential source of error.

The majority of Program Workers had their baseline BeLPTs completed at Laboratory 1. As noted in the results, we excluded from analysis abnormal baseline BeLPTs that did not conform to the testing protocol for four workers. These four workers had first-draw split samples that were sent to both Laboratory 1 and Laboratory 2. All four workers had an initial abnormal test at Laboratory 2 and a normal test at Laboratory 1; two of these workers were confirmed positive at Laboratory 2 but not Laboratory 1. Laboratory 2 may have been experiencing quality control issues around the time these workers were tested.[4] Based on our protocol, these four workers were not included in the adjusted incidence rate. When we included these four workers' abnormal results and re-ran our analyses, we did observe decreased adjusted incidence rate ratios, reflecting the inclusion of an additional two workers with sensitization at baseline. The adjusted incidence rate ratio of the Pre-Program Group to the Program Group was 1.5 (95% CI = 0.8 to 3.0). Excluding the pebbles operators, the adjusted incidence rate ratio was 1.4 (95% CI = 0.7 to 2.9) compared to the Program Group.

CONCLUSION

This investigation is consistent with other studies in indicating that a comprehensive preventive program can have an impact on reducing sensitization in beryllium-naïve workers. These findings suggest that progress is being made in preventing beryllium-related disease, although beryllium sensitization has not been entirely eliminated. Longer-term follow-up of both current and former workers is required to determine if the observed reduction in prevalence and perhaps incidence of beryllium sensitization persists over time and whether this is followed by a reduction in CBD.

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