Recent Chronic Beryllium Disease in Residents Surrounding a Beryllium Facility

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Rationale: **Between 1948 and 1969, cases of community-acquired chronic beryllium disease (CA-CBD) were reported in neighborhoods surrounding beryllium facilities. Further surveillance was not performed in these communities, and additional cases have not been reported.**

Objectives: **To increase awareness of recently diagnosed cases of CA-CBD in residents surrounding a beryllium facility.**

Methods: **Medical records were reviewed from individuals in a community surrounding a beryllium manufacturing facility in Reading, Pennsylvania. Definite cases of CBD required (*1*) an abnormal beryllium lymphocyte proliferation test in blood or bronchoalveolar lavage and (*2*) biopsy evidence of granulomatous inflammation. Probable cases of CBD either displayed an abnormal blood test to beryllium and radiographic evidence consistent with disease, or met epidemiologic criteria for CBD based on the Beryllium Case Registry criteria. Cases with occupational or potential paraoccupational exposure were excluded.**

Measurements and Main Results: **Sixteen cases of potential community-acquired CBD were evaluated. From these, eight cases of community-acquired CBD were identified (five definite and three probable). The cases' initial year of residence began between 1943 and 1953 and continued until 1956–2001. Six of the eight cases required medical treatment and three of the cases died since diagnosis.**

Conclusions: **Cases of CBD meeting current immunologic diagnostic criteria and attributable to industry-associated environmental exposure were detected among residents of a community surrounding a beryllium manufacturing facility. Most were diagnosed years after exposure cessation. The frequency and extent of beryllium disease in this community are unknown. We anticipate that not only have cases been misdiagnosed in this community but that more cases of CBD will be diagnosed in the future.**

Keywords: chronic beryllium disease; berylliosis; beryllium; community

AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

No cases of community-acquired chronic beryllium disease (CA-CBD) have been reported in the medical literature since 1969. As a result, the risk of CA-CBD is unrecognized, and it is possible that cases are being misdiagnosed as other lung disease.

What This Study Adds to the Field

Cases of CBD meeting current immunologic diagnostic criteria and attributable to industry-associated environmental exposure were detected among residents of a community surrounding a beryllium manufacturing facility. Health care providers should continue to consider CBD in the differential diagnosis of patients with respiratory disease who reside near beryllium facilities with known or potential previous cases of CA-CBD.

In the 1940s, chronic beryllium disease (CBD) (1, 2), a granulomatous disease that predominately involves the lungs, was first described. Within a few years, cases of CBD were also detected among residents of communities surrounding beryllium manufacturing facilities from air pollution and among spouses of workers in the facilities from contaminated clothing that was brought home (3–5). The first cases of community-acquired CBD (CA-CBD) were reported from Lorraine, Ohio (6). The rate of CBD in this community was similar to that found within the workplace, even though measured beryllium exposures were significantly lower in the community (3). This led to speculation that the CA-CBD cases were due to suspended respirable particulate in the community ambient air and a radiologic survey was performed in Lorraine, Ohio, and reported in 1949 (3). All but one of the CA-CBD cases lived within 0.75 (1.2 km) mile from the facility and ambient beryllium concentrations ranged from 0.004 $\mu g/m^3$ to 0.02 $\mu g/m^3$, with an average of 0.01 $\mu g/m^3$. Eisenbud and colleagues (3) suggested that, based on production rates, exposures in the past may have been as much as 10 times higher (0.1 $\mu g/m^3$). The 0.01-$\mu g/m^3$ level, averaged over a 30-day period, became the U.S. Environmental Protection Agency community standard for beryllium exposure.

As CA-CBD cases were being reported in Lorraine, Ohio, cases were also reported from a facility near Reading, Pennsylvania. This facility was involved in the manufacture of beryllium oxide, alloys and metal, and the production of beryllium tools and metal products (7, 8). Twenty-one CA-CBD cases were diagnosed at distances ranging from 0.6 to 5.3 miles (1–8.5 km) from the beryllium facility (5). After the report of the original outbreak of CA-CBD, three additional cases of CA-CBD were diagnosed (9, 10). However, since 1969, no further cases of CA-CBD have been reported in the medical literature. In the 1980s, bronchoalveolar lavage (BAL) studies in subjects with CBD proved that CBD was a hypersensitivity disorder (11, 12) and testing the lymphocyte proliferative response to beryllium (BeLPT) became part of the diagnostic criteria for CBD (13). Subsequently, the BeLPT was used in cross-sectional studies to screen current and former workers for evidence of beryllium sensitivity (BeS) and CBD (14–17). These studies demonstrated that occupational CBD was often misdiagnosed and underrecognized.

Using current diagnostic testing, we were involved in the evaluation of the diagnosis of a case of nonoccupational CBD from the community surrounding this beryllium facility in Read-

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ing, Pennsylvania. This led to the diagnosis of additional cases of nonoccupational CBD from this community who were referred by family members or an attorney that became involved in the case. Here, we report these cases of CA-CBD diagnosed with state-of-the art immunologic tests. These cases have been previously reported in abstract form (18, 19).

CASE REPORT

A 72-year-old woman with chest radiographic abnormalities noted for 6 years before evaluation in 1999 was referred by her pulmonary physician for evaluation of significant respiratory symptoms, including shortness of breath and chest tightness with minimal exertion. Previously, her abnormal chest radiograph had been attributed to heart failure because she had undergone heart bypass surgery in 1991. In 1950, she moved into a new home 0.3 miles (0.5 km) from a beryllium manufacturing and fabricating facility. Neither she nor any of her family members worked at the plant and no one who worked at the plant lived in her home. At the time of evaluation, she was noted to have clubbing. A chest radiograph revealed upper lobe predominant nodularity and a computed tomography (CT) scan of the chest indicated hilar adenopathy together with the nodular changes (Figures 1A and 1B). Her pulmonary function tests indicated a severe gas exchange abnormality with a diffusion capacity for carbon monoxide ($D_{L_{CO}}$) of 4.5 ml/minute/mm Hg (22% of predicted) with normal spirometry and lung volumes and a decline in pulse oximetry from 90% at rest to 79% with exertion at sea level. A blood BeLPT was abnormal with a peak stimulation index of 18.6, as was a BAL BeLPT with a peak stimulation index of 340, indicating sensitization to beryllium. A transbronchial biopsy demonstrated multinucleated giant cells and histiocytic aggregates and the BAL lymphocyte count was elevated, consistent with CBD. As a result of this testing, the patient was diagnosed with CBD and started on treatment with oxygen, prednisone, and eventually methotrexate with some initial improvement. She died of CBD within 3 years of diagnosis despite therapy.

METHODS

Study Definitions

We defined CBD as definite if subjects met current diagnostic criteria for CBD. Specifically, these subjects demonstrated evidence of beryllium sensitization with an abnormal blood or BAL LPT and pathologic findings, in lung tissue, consistent with granulomatous inflammation, such as granulomas, multinucleated giant cells, and/or mononuclear cell infiltrate. Subjects were classified as probable CBD, if they had evidence of clinical disease with beryllium sensitization demonstrated by an abnormal blood or BAL LPT and had chest radiographic or CT evidence consistent with CBD, such as nodular interstitial abnormalities, with upper lobe predominance (20–22). In addition, subjects who did not have the opportunity to have a BeLPT before their demise and who met the definition provided by the Beryllium Case Registry criteria were also considered to have probable CBD; these individuals had evidence of clinical, pathologic and physiologic, or radiographic course consistent with CBD (4, 14). These criteria are used currently by the U.S. Department of Labor for cases diagnosed before 1993, before the BeLPT was available. These subjects with definite or probable CBD were considered to have definite or probable CA-CBD, respectively, if they had lived in the vicinity of a beryllium facility and had no evidence of occupational or paraoccupational (living with a worker exposed to beryllium) exposure to beryllium.

Study Design

A case series was established of subjects who had lived in the vicinity of the Reading, Pennsylvania, beryllium facility noted above and who underwent clinical evaluation or whose medical records were available for review by two of the authors (L.A.M. and M.D.R.). Sixteen potential

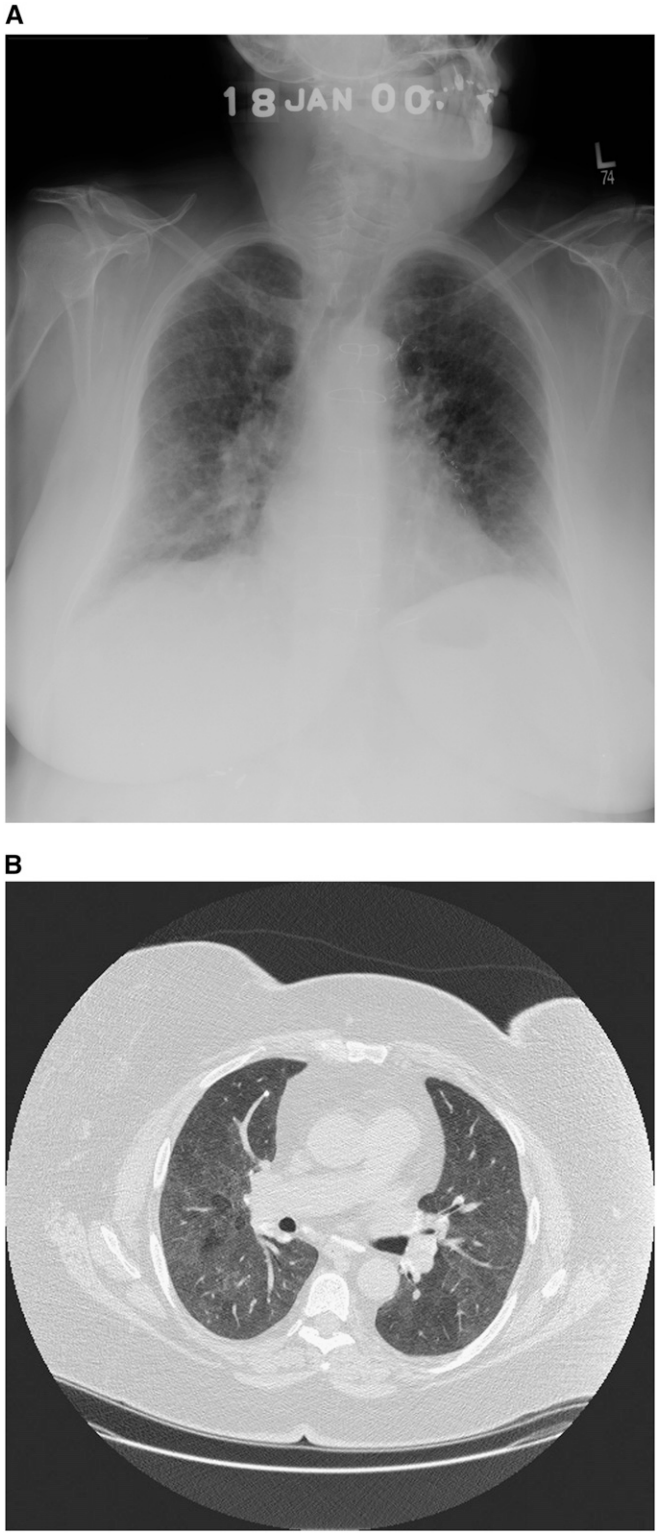

Figure 1. Chest imaging from two of the cases of community-acquired chronic beryllium disease (CBD). (*A*) A representative posteroanterior chest radiograph from case 1 demonstrating upper lobe predominant reticulonodular opacities, consistent with CBD. This patient had a prior median sternotomy for atherosclerotic heart disease, which is evident on the radiograph. (*B*) A representative high-resolution computed tomography scan lung window from case 1 demonstrating ground-glass opacifications and calcified hilar and mediastinal adenopathy.

subjects were identified. Those subjects with a history of occupational or potential paraoccupational beryllium exposure from a family member who worked in the beryllium facility were excluded from the study. Medical records were reviewed from each potential case of CA-CBD to determine if they met criteria for definite or probable CA-CBD as noted above. If a case met the definition of CA-CBD, information regarding the years of residence and proximity to the beryllium facility, demographic information (age, sex, smoking status), pulmonary function, chest radiography, and blood, BAL LPT, and biopsy results, if available, were recorded, together with the need for therapy. This study protocol was approved by the institutional review boards of National Jewish Medical and Research Center and Hospital of University of Pennsylvania.

RESULTS

Cases of CA-CBD

Clinical evaluations were performed or the medical records were reviewed on 16 cases for consideration of CA-CBD. Four of the 16 cases did not meet the case definition for probable or definite CBD. Four cases met the case definitions of CBD, but they were excluded because they appeared to have had a potential for beryllium exposure from working in the plant (three subjects) or from a family member who worked in the plant (one subject). Thus, a total of eight cases of CA-CBD (five with definite CBD and three with probable CBD) were identified who met our case and exclusion criteria. Four of the five cases of definite CA-CBD and one case with probable CA-CBD were personally interviewed by Dr. Rossman and no source of potential beryllium exposure was identified except through the ambient air. The detailed medical records of one case of definite CA-CBD and of two cases of probable CA-CBD, including occupational and social history, were reviewed by Dr. Maier to exclude the possibility of any beryllium exposure except from the industry-associated environmental exposure. The demographics of these eight cases are presented in Table 1. Of note, all of them were women and the majority were never-smokers.

Of the eight cases of CA-CBD, five cases (including the case reported above) met our definition of definite CA-CBD (cases 1–5 in Table 2). Of the three cases with probable CA-CBD, one case (case 6) met our clinical definition of probable CBD (i.e., clinical course and radiology consistent with CBD, positive BeLPT, but no pathology-proven granulomatous disease), and two cases (cases 7 and 8) met the epidemiologic criteria of the former Beryllium Case Registry criteria for CBD (i.e., clinical course, pathology, and radiology consistent with CBD, but no BeLPT available). Neither case 7 nor case 8 was provided with the opportunity to have a recent version of the BeLPT and died before this test could be obtained.

Clinical Features of CA-CBD

A number of the definite and probable cases of CA-CBD were initially diagnosed with other diseases. Cases 3 and 8 were diagnosed with sarcoidosis, even though a diagnosis of CBD had been considered for both at the time of lung biopsy. An early form of the blood BeLPT was initially obtained on case 3 after her biopsy in 1972, but it was normal. On request from the patient, she underwent reevaluation for CBD in 2000 and was found to have an abnormal BAL BeLPT. Case 8 initially presented with symptoms, which worsened during her two pregnancies, similar to cases reported by Hardy (4). Attempts were made to evaluate her lung tissue for the presence of beryllium soon after her biopsy, because of her concern regarding CA-CBD, but there was an insufficient amount of tissue to perform this analysis. She requested additional evaluation for CBD until her demise, but a blood BeLPT was never obtained.

Case 2 was initially misdiagnosed with silicosis based on a lung biopsy obtained in 2000 when she presented with chest pain, even though she had no history of silica exposure. Re-review of her lung biopsy revealed granulomas consistent with CBD, not silicotic nodules. CA-CBD was considered as a diagnosis in case 5 when she was a young adult, 10 years before she was provided with a definitive diagnosis. In addition to CBD, case 5 was also diagnosed with lung cancer. Beryllium has been implicated as a potential carcinogenic agent. Because she was a nonsmoker and had the potential for substantial exposure because she had lived, played, and worked within a few miles of the plant off and on since childhood, her lung cancer may have been related to her beryllium exposure. Of note, the lung cancer risk associated with beryllium exposure appears to be related to very high exposures to beryllium (23). She was unable to undergo pneumonectomy required for surgical resection of her tumor because of her poor lung function secondary to her CBD. A number of these cases (cases 1–3, 5, 7, and 8) had chest radiographic abnormalities noted for years before a diagnosis of CBD was made (range, 6–28 yr). These changes were similar to those seen in cases of occupational CBD (Figures 1A and 1B). Cases 4 and 6 underwent clinical evaluation at early stages of disease, without a prolonged history, after their mother was diagnosed with probable CA-CBD (case 7). The diagnosis of two of these cases was made *post mortem* (cases 7 and 8).

The pulmonary function data from all of the cases are presented in aggregate in Table 3. The subjects demonstrated significant abnormalities. Some subjects demonstrated a predominant gas exchange defect to a greater degree than restrictive or obstructive defects. Case 1 demonstrated an individual with an isolated diffusion defect, whereas the others tended to display a combination of restrictive and/or obstructive disease with a reduced D_{LCO}. Only two cases had normal pulmonary physiology. Reflective of the severity of their disease, six of eight of the cases (75%) were treated for their CBD with prednisone, one of whom was also treated with methotrexate. Despite therapy, three cases have subsequently died as a result of their CA-CBD, and of these, two died before the time a diagnosis was made.

TABLE 1. DEMOGRAPHIC INFORMATION AND OTHER INFORMATION FOR CASES OF COMMUNITY-ACQUIRED CHRONIC BERYLLIUM DISEASE

	No. Cases	Percentage or Range
Female sex	8	100%
Age, yr	67	50–83
Smoking		
Never	5	62.5%
Former	3	37.5%
Distance from plant, mi (km)	0.37 (0.60)	0.1–1.05 (1.6–1.7)
Treatment (yes)	6	75%

Total cases = 8.

Location of CA-CBD Cases

The residence of the cases is shown in Figure 2, by case number. The predominant wind direction in this area is southeast. However, the majority of cases resided northeast of the beryllium facility in a housing development that was built in the 1950s. As shown in Table 1, the cases' average distance from the beryllium facility was 0.37 miles (0.6 km), ranging from 0.1 to 1.05 miles (0.2–1.7 km) away.

DISCUSSION

We report on eight cases diagnosed with CBD between 1999 and 2002 who had lived in the vicinity of a beryllium facility in Reading, Pennsylvania. In the absence of evidence of past

TABLE 2. SUMMARY OF CASES OF COMMUNITY-ACQUIRED CHRONIC BERYLLIUM DISEASE

Subject No.	Years of Residence	Year of Biopsy	Latency*	Blood BeLPT	BAL BeLPT	CA-CBD Category†	Year Deceased
1‡	1950–1999	1999	49	18.6	340.0	Definite	2002
2§	1951–1956	2000	49	19.1	10.5	Definite	—
3‖	1953–1984	1972	19	2.1	11.0	Definite	—
4	1950–1969	2002	52	480.4	103.6	Definite	—
5	1953–2001	1999	46	39.7	NA	Definite	—
6	1951–1973	2001	50	110.9	3.8	Probable	—
7	1950–2000	2000	50	NA	NA	Probable	2000
8‖	1943–1961	1978	35	NA	NA	Probable	2000

Definition of abbreviations: BAL = bronchoalveolar lavage; BeLPT = lymphocyte proliferative response to beryllium; CA-CBD = community-acquired chronic beryllium disease; NA = not applicable.

* Latency = the time from first potential exposure to beryllium until diagnosis.

† CBD category: *see* definitions in text.

‡ Initial case.

§ Diagnosed with silicosis.

‖ Diagnosed with sarcoidosis.

occupational or paraoccupational exposure to beryllium in these subjects, we consider these cases to be CA-CBD as a result of environmental pollution by the beryllium facility. The diagnoses of the majority of these cases were based on current diagnostic criteria, with demonstration of a beryllium-specific immune response on blood or BAL LPT testing and evidence of granulomatous inflammation on lung biopsy (5 of 8 cases). Two were diagnosed on the basis of the Beryllium Case Registry criteria (cases 7 and 8), because they died before a blood LPT could be obtained, whereas one case was diagnosed with probable CA-CBD with radiographic abnormalities and the demonstration of an abnormal immune response to beryllium (case 6). These cases demonstrate that, as with occupational CBD, CA-CBD from environmental beryllium exposures can occur long after the exposure has ceased. Our experience indicates that such cases are prone to be misdiagnosed. Three of the cases were initially diagnosed with other lung diseases, primarily sarcoidosis, but also silicosis.

Three of the cases were family members, consisting of a mother and two sisters, suggesting the influence of genetic susceptibility factors that we know are important in risk of sensitization and disease today (24, 25). These cases demonstrated a range of disease severity. Most had significant physiologic abnormalities, with a striking gas exchange defect noted on D_{LCO} and requirement for systemic therapy. The latency from first exposure to disease onset also varied, but was noted to be as long as 52 years after first exposure. These are the first cases of CA-CBD reported since 1968, using current immunologic criteria, and the first cases of CA-CBD whose exposures began in the 1950s. This report raises a number of questions regarding the prevalence of CA-CBD and where else it may be found.

TABLE 3. CLINICAL FEATURES OF THE CASES OF COMMUNITY-ACQUIRED CHRONIC BERYLLIUM DISEASE, FOCUSING ON MEASURES OF PULMONARY IMPAIRMENT

Case	$FEV_{1.0}$ (%)*	FVC (%)*	$FEV_{1.0}$/FVC	TLC (%)*	D_{LCO} (%)*
1	103	101	79	88	22
2	89	86	82	85	110
3	62	80	59	98	ND
4	73	76	79	89	64
5	71	81	70	81	46
6	106	116	75	118	98
7	55	73	60	68	25
8	28	26	88	40	23
Mean	73.4	79.9	74	83.4	55.4

Definition of abbreviations: D_{LCO} = diffusion capacity of carbon monoxide; ND = not done.

Total cases = 8.

* % predicted.

As noted above, cases of CA-CBD were first reported from this community surrounding a beryllium manufacturing and fabrication facility in 1959 (5), and a total of 33 cases were reported through the 1960s (9, 10). Initially, a medical survey was undertaken with review of medical records from local hospitals and physicians, using a definition of disease to detect CA-CBD based on that used by the Beryllium Case Registry (5), as was a 12-month air pollution survey to determine beryllium exposures in the community (26). From the initial medical survey, 21 cases of CA-CBD were found who had not worked in the plant or had no opportunity for contact with beryllium workers, with potential for community exposures starting in 1937, when the plant opened, until the 1950s when the study was conducted (5). The cases of CA-CBD lived up to 5 miles (8 km) from the facility, with more than half of the cases residing 4 or more miles (6.4 km) downwind from the facility. In contrast, all of our cases of CA-CBD resided less than 1.5 miles (2.4 km) from the facility in a heavily residential area, with most exposures beginning in the 1950s. The potential exposures to these individuals, based on the 1958 ambient air sampling, may have ranged, on average, from 0.0155 to 0.028 $\mu g/m^3$, with some exposures potentially over 0.35 $\mu g/m^3$. In comparison, ambient beryllium levels were measured in other parts of Pennsylvania averaging 0.0002 $\mu g/m^3$ (26). Reports from Sanderson and coworkers indicate that exposures within this facility were likely to be constant between 1935, when it opened, and 1960, when control measures were put into place (7). It is likely that exposures in the community were also similar for these time periods and during the time that our cases were living within the community. Company records indicate that community ambient beryllium concentrations were reduced during the 1960s and again during the 1970s, although periods of elevated levels were observed at some sampling points.

Additional undiagnosed cases of CBD may have occurred due to exposures in this community during the 1950s and later. As noted above, in the original investigations of CA-CBD, Beryllium Case Registry criteria were used to provide a diagnosis of CA-CBD (3–5). The use of the BeLPT has changed the diagnostic criteria for CBD. Before the use of the BeLPT, a case of CBD was only accepted if there was definite evidence of beryllium exposure (4). Because a positive BeLPT demonstrates that a person has been exposed to beryllium, the onus is now on trying to determine how the exposure occurred, rather than on having to prove exposure. This has resulted in the U.S. Department of Energy lowering the action level for beryllium in the workplace to 0.2 $\mu g/m^3$ from the OSHA (Occupational Safety and Health Administration) levels of 2 $\mu g/m^3$ (27). Although it is always possible that some unknown paraoccupational exposure could have accounted for the development of CBD in the patients on whom we are

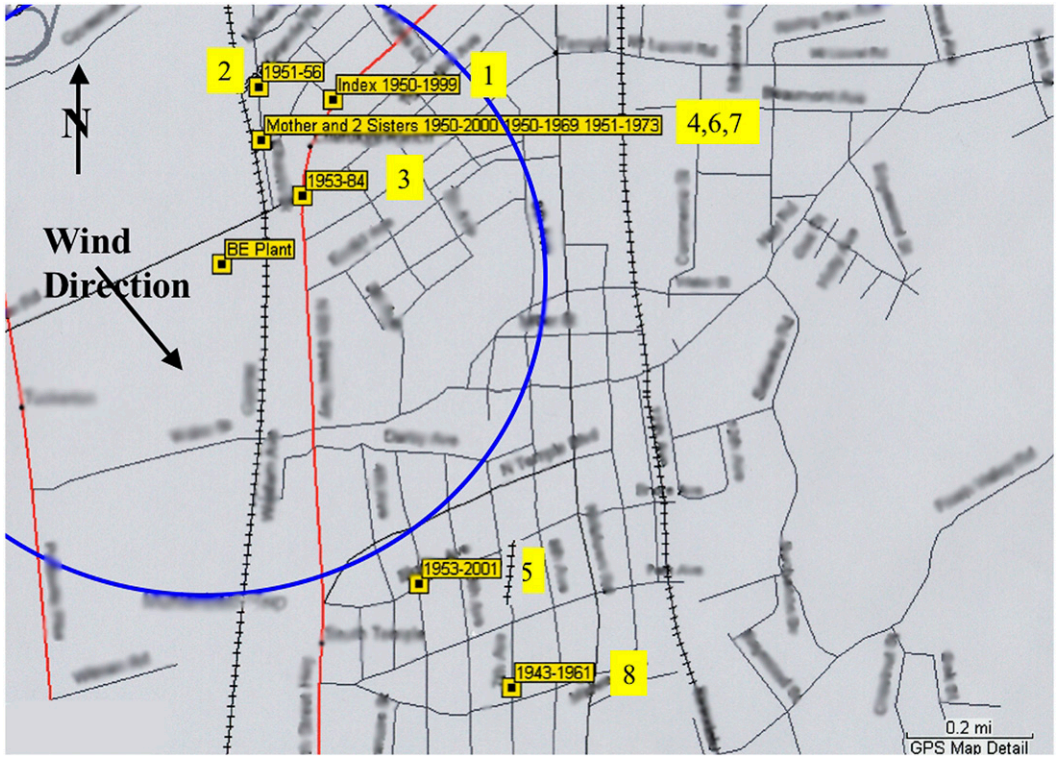

Figure 2. This map demonstrates where the cases of community-acquired chronic beryllium disease resided in relationship to the plant. The *longest arrow* indicates the primary wind direction. The cases' residences are indicated by their case number with the sentinel case indicated by "1." The scale of the map is provided at the *bottom,* representing 0.2 miles (0.32 km).

reporting, no known paraoccupational exposure was discovered and good history was obtained to help avoid this bias. Thus, we believe that the industry-associated environmental exposure to beryllium at some point during the cases' residence in the community immediately surrounding this plant must have been sufficient to cause sensitization to beryllium and disease.

Over the past 20 years, we have learned that the BeLPT is critical in establishing a diagnosis of CBD (11–13). Surveillance efforts in the workplace have indicated that when an initial CBD case with symptomatic disease, and radiographic and physiologic abnormalities is detected, a number of other cases of CBD will be detected using the BeLPT for screening (15–17). Beryllium sensitization, a precursor to CBD in which individuals have an immune response to beryllium based on the BeLPT but have not yet developed CBD (28), has been found in most of the workplace studies conducted to date using the BeLPT and in studies of former workers who had initial exposure years before medical surveillance (15, 29). Thus, if a medical surveillance with the BeLPT were performed in this community, we would anticipate that additional cases of beryllium sensitization and CBD should be detected.

To estimate the population at risk from the industry-associated environmental beryllium exposure from this plant, we made several assumptions. Because the cases that we described lived within 1.05 miles (1.6 km) of the plant on average, we assumed that anyone living within 1.5 miles (2.4 km) of the plant might be at risk. Because significant changes in the emissions of the plant did not occur until the late 1960s, we assumed that individuals living within 1.5 miles (2.4 km) of the plant before 1969 would be at greatest risk. On the basis of the 2000 Census, four census tracts contain the population that lived within 2 miles (3.2 km) of the beryllium plant (census tracts 124, 125, 127, and 128) and housed 17,958 individuals. According to the census data, of the 7,424 households in these census tracts, 23.4% were owner- or renter-occupied in 1969 or earlier. Thus, 23.4% of the population or 4,202 persons may have lived in the immediate neighborhood during the time that there were significant emissions of beryllium from the plant. If we assume that 50% of these individuals lived within 1.5 miles (2.4 km) of the plant, then at least 2,101 persons had potential industry-associated environmental exposure to beryllium. This estimate does not include individuals who lived in this neighborhood and had moved out before 2000. Thus, the estimate of 2,101 individuals is probably low. It is important to note that five of our eight cases on whom we have reported no longer lived near the plant. On the basis of cross-sectional surveys of workers exposed to occupational beryllium, 3 to 10% of workers may develop CBD or beryllium sensitization (30). Thus, we would estimate that between 63 and 210 individuals in this community could have developed beryllium sensitization or CBD or would develop these conditions.

Three of eight (38%) of the cases of CA-CBD presented in this study were initially misdiagnosed as having another lung disease or were not provided with a specific diagnosis, despite significant radiographic and physiologic abnormalities. CBD has been commonly misdiagnosed as sarcoidosis and one of the original outbreaks of CBD associated with the fluorescent lamp industry was called "Salem sarcoidosis" before the association between beryllium exposure and CBD was made (4). We have previously reported on a case of CBD misdiagnosed as silicosis (31), although this has not been commonly reported. The use of the BeLPT helped clarify the diagnosis of CA-CBD in the majority of these cases and, with the lack of workplace exposures noted, provides attribution of exposures to a community that was known to have cases of CA-CBD years prior. This report suggests that physicians evaluating cases of sarcoidosis or other respiratory complaints in residents of communities surrounding beryllium facilities with known previous cases of CA-CBD should consider the diagnosis of CBD and have BeLPT testing performed as part of the diagnostic workup.

These cases of CA-CBD demonstrated significant pulmonary impairment, including evidence of obstructive, restrictive, and gas exchange defect in the majority of cases. Also reflecting severe disease was the need for treatment in 75% of the cases. Despite treatment, at least three cases of CA-CBD have succumbed to their

disease, due to respiratory insufficiency, indicating that low levels of exposures with significant disease latency can result in significant morbidity and mortality. The cases' years of residence in this community surrounding the beryllium facility varied from 5 to 50 years. The latency between first potential exposure and development of CA-CBD disease varied between 19 and 52 years, and is similar to that reported in the workplace (32). Our report of community cases at potentially low levels of exposure suggests that even low-level exposures may cause significant disease given sufficient latency. This may have important implications for long-term effect of low-level exposures for current beryllium workplaces and workers. Most important, these cases have public health implications for communities surrounding beryllium facilities. First, it suggests that low concentrations of industry-associated environmental beryllium exposures continue to result in CA-CBD, and that, similar to beryllium workers, once exposed, community members have a lifelong risk of developing CA-CBD. Second, with sufficient latency, even low levels of exposures such as those sustained in a community, can produce disease with significant morbidity and mortality. Finally, the extent of disease in the community is unknown at this time, as the number of community members alive and at risk is not clear, and the number of cases of CBD and BeS has not been determined. This suggests that a community with evidence of CA-CBD such as described above would likely benefit from a cross-sectional study with the BeLPT to identify individuals with BeS and CBD and to define the population at risk in terms of year of residence and distance from the plant.

Conflict of Interest Statements: L.A.M. has evaluated and testified on behalf of community members surrounding this facility; while she has received no direct monetary compensation for this work, National Jewish has been remunerated for her time and effort. J.W.M. has no financial relationship with a commercial entity that has an interest in the subject of this manuscript; he has provided expert testimony in a lawsuit involving potential community exposures and their potential health effects to individuals surrounding this facility and one other facility in Florida; he has received no direct monetary compensation for this work since, as an employee of National Jewish, he is paid only a salary for this work; although National Jewish Medical and Research Center does offer a BeLPT test, he is not associated with the laboratory that conducts that testing and is not funded by that laboratory. J.L. has no financial relationship with a commercial entity that has an interest in the subject of this manuscript. M.D.R. has been compensated for consultation with lawyers representing industry in 2007; this has included lawyers representing Brush Wellman for $1,500, lawyers representing Alcoa for $3,200, and lawyers representing plaintiffs for $150; in addition, he has consulted for Lockheed Martin and been paid $3,200; he has been an expert witness and consult for both plaintiffs and industry with regard to chronic beryllium disease.

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