Solubility and Chemistry of Materials Encountered by Beryllium Mine and Ore Extraction Workers

Relation to Risk

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Objective: Beryllium mine and ore extraction mill workers have low rates of beryllium sensitization and chronic beryllium disease relative to the level of beryllium exposure. The objective was to relate these rates to the solubility and composition of the mine and mill materials. **Method:** Medical surveillance and exposure data were summarized. Dissolution of BeO, ore materials and beryllium hydroxide, $Be(OH)_2$ was measured in synthetic lung fluid. **Result:** The ore materials were more soluble than BeO at pH 7.2 and similar at pH 4.5. $Be(OH)_2$ was more soluble than BeO at both pH. Aluminum dissolved along with beryllium from ore materials. **Conclusion:** Higher solubility of beryllium ore materials and $Be(OH)_2$ at pH 7.2 might shorten particle longevity in the lung. The aluminum content of the ore materials might inhibit the cellular immune response to beryllium.

A large fraction of beryllium in global commerce originates at a Utah mine and ore-extraction mill which started production in 1969. As for many years no worker exposed to beryllium solely at these facilities had been detected with chronic beryllium disease (CBD), there was doubt whether the materials present at these facilities could induce CBD.[1] This changed in 2009 when a worker without beryllium exposure outside the mill was diagnosed with CBD using standard criteria, two positive beryllium blood lymphocyte proliferation tests (BeLPTs) and lung biopsy demonstrating noncaseating granulomatous inflammation.

The objective of this article is to provide information on beryllium sensitization (BeS) and CBD in workers at the mine and mill and explore hypotheses that the degree of risk may be related to the solubility and/or aluminum content of the beryllium materials.

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THE MINE AND MILL

The Utah mine ore contains beryllium in the nominal form of bertrandite, a hydrated beryllium silicate. Bertrandite is found in low concentration within a 2- to 12-meter thick layer of volcanic ash lying at an angle of approximately 25° to the surface in a desert area of hills cut by faults. This ore is located by analyzing drill samples. Contractor workers open pits by removing non-beryllium rock overburden. Company workers use earth-moving equipment to remove the ore and form ore piles nearby. Eight persons run all mine operations, including engineering, financial planning, analyzing drill and mining ore samples for beryllium content, maintaining equipment, and mining. Contractor workers load the ore into covered transport trucks, drive to the mill, and drop the ore into bins.

The mill processes the Utah bertrandite ore as well as imported beryl (aluminum beryllium silicate) ore into beryllium hydroxide, $Be(OH)_2$. The bertrandite ore is crushed and wet ground into slurry. Beryl ore is melted in a carbon arc furnace and poured into water to form a glassy frit. The frit is heat treated and ground into powder. Although the processes are separate and differ in detail, beryllium is dissolved from bertrandite ore slurry and frit with sulfuric acid and heat and separated from solids by countercurrent washing.

Other metals are removed from the beryllium sulfate solutions in a multi-step process that includes solvent extraction. At the final step, $Be(OH)_2$ is precipitated and packaged in plastic drums as a damp white powder. A portion is sold internationally for processing into copper- and nickel-beryllium alloys. The remainder is processed further by the company in an Ohio facility[2] into pure beryllium metal, copper, nickel and aluminum metal alloys, and beryllium oxide (BeO) powder.

The mill workers have potential exposures to beryllium in particle form as beryl and bertrandite ore dust, frit, $Be(OH)_2$, and aerosolized wet or dried beryllium salt, primarily beryllium sulfate. The mill production workers are supported by maintenance workers, laboratory workers, and an administrative staff.

METHODS

Solubility Characteristics of Mine and Mill Beryllium-Containing Materials

The company contracted with the University of Utah to investigate the solubility characteristics of beryl and bertrandite ore, frit, and $Be(OH)_2$ relative to BeO. The solubility study methods and results have been reported in detail elsewhere.[3] Briefly, the materials studied were BeO, $Be(OH)_2$, bertrandite ore, beryl ore, frit, and a pure silica (SiO_2) control. Duplicate 250 milligram-samples of ground materials were agitated at room temperature in 400 mL of a synthetic lung fluid at both pH 4.5 and 7.2. Baseline measurements of beryllium, aluminum and silica content, as well as photomicrographs, and surface area measurements were obtained. Aliquots were removed on days 0, 2, 8, 18, 32, 64, and 128, filtered (cutoff pore size 0.45 μm) and analyzed for beryllium, aluminum and silicon content. Nanoparticle formation and equilibration was observed in some materials after 18 days.[3] Because we thought it unlikely this would occur in the lung and intracellular environments as beryllium ions would react with the organic molecule milieu or be otherwise dispersed, we chose the 18-day results for this analysis. Duplicate results were generally close so we used the mean of the two results. Results were calculated as follows: concentration beryllium, aluminum, or silicon

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Materion Brush Inc. manufactures beryllium materials. Materion Natural Resources Inc. mines beryllium ore and converts ore into beryllium hydroxide. Both are wholly owned subsidiaries of Materion Corporation.

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in the filtrate (g/m^3), proportion dissolved (concentration times fluid volume divided by initial content), concentration divided by surface area of initial sample, ($[g/m^3]/m^2$), and proportion dissolved divided by surface area of initial sample ($/m^2$). We inferred rate of dissolution from the concentration of elements in the aliquots at 18 days.

Some of the analyses detected elements that were not expected to be present in the initial samples and this was interpreted as analytic process carry over. We therefore do not report Be and Al in SiO_2, nor Si or Al in BeO or $Be(OH)_2$. Also, we did not correct for supernatant volume changes or material removed via sampling, as these corrections through 18 days are small and identical for all materials.

Beryllium Blood Lymphocyte Proliferation Test Surveys

To investigate the potential for BeS in 1996 the company surveyed company mine and mill workers using the BeLPT and follow-up bronchoscopy for workers with positive BeLPTs or clinical symptoms or signs suspicious for CBD.[1] Participation was voluntary and written informed consent was obtained. In 2001 it offered testing to current company workers who were hired after 1996 or who had declined testing in 1996. A third survey in 2009 offered testing to all current workers. We calculated rates in two ways. One was the rate of BeS and CBD combined divided by the total number of persons who participated at least once in one or more of the surveys. The other was to estimate the cumulative rate of BeS and CBD combined by compounding the rate in a first round of testing with the rate in those who participated in a second round of testing using the equation $p_c = 1-[1-p_1][1-p_2]$, where p_1 and p_2 are the proportion BeS and CBD combined identified in the first and second rounds.

The 1996, 2001, and 2009 worker surveys were conducted using methods previously reported.[1] Workers were offered voluntary BeLPT tests split to two laboratories and opportunity for follow-up bronchoscopy for the diagnosis of CBD. The offer was accompanied by detailed orientation on the characteristics of BeS and CBD and the BeLPT, the purpose of the medical surveillance survey, and the manner in which results would be reported in individual and group form and analyzed relative to exposure. Written informed consent was obtained. Because this was medical surveillance for the primary purpose of improving internal company efforts to more effectively protect workers, the surveys were not conducted under the auspices of an institutional review board. Employees were aware of long standing commitment by the company since the 1940s to communicate what is learned regarding beryllium health effects, often in collaboration with university, government, and privately employed scientists. Written informed consent for disclosure of potentially identifying information was obtained from the worker whose work history is discussed in this article.

Workers with two positive BeLPT tests or a positive beryllium bronchoalveolar lavage lymphocyte proliferation test were considered to be beryllium sensitized. Workers with BeS and a lung or lymph node biopsy demonstrating noncaseating granulomatous inflammation were diagnosed with CBD.

The mine and mill survey results were compared to two other company facilities surveyed by nearly identical methods: a beryllium ceramics facility surveyed in 1992[4] and 1998[5] and a copper-beryllium alloy facility surveyed in 2000.[6] These surveys were also conducted with informed consent, initial blood samples split to two BeLPT laboratories with identical protocols for repeat testing of indeterminate or borderline test results, BeS defined by two positive tests, offer of bronchoscopy, and the same diagnostic criteria for CBD. In the alloy 2000 survey the performance of one of the laboratories suggested low sensitivity and specificity for CBD, and the results were disregarded.[6] Thus, laboratory performance may have led to underestimation of the prevalence of sensitization and CBD in the alloy facility survey.

Cumulative CBD

To provide an overall measure of CBD risk at the three facilities we divided the number of CBD diagnoses known to the company among persons who had ever worked at the facility by the accumulated person-years.

Beryllium Exposure

The objective of beryllium exposure assessment was to estimate the level of exposure at the mine and mill worker population relative to the beryllium ceramics facility and the alloy facility worker populations. We utilized previously published exposure data[1,4–6] supplemented by more recent sampling data from the mine and mill. To indicate the variation of recent exposure in several production areas, we summarized personal lapel sample data collected from 2004 to 2009.

RESULTS

Mine and Mill Worker Surveillance Surveys for Beryllium Sensitization and CBD

In 1996, 77 of the 88 eligible workers were tested with the BeLPT. Two were identified as BeS and one as CBD, for a combined rate of 3.9%. In 2001, 36 persons who were not already BeS were eligible and 32 participated. Two were identified as BeS, and one of these was subsequently diagnosed with CBD, for a combined rate of 6.5%. In 2009, of 70 eligible persons, 56 participated. Of 55 who were not already BeS, one was identified as BeS, a rate of 1.8%. Combining the results, a total of 120 persons underwent testing for a total of four BeS and two CBD, for a combined rate of 5.0%. By rounds of testing, 5 of the 120 persons (4.2%) were detected as CBD or BeS in first participation in a survey and 1 of the 47 (2.3%) in the second participation for a cumulative rate of 6.3% [100(1−(1−0.042) (1−0.023))] (Table 1).

These results were compared to two other plants, one a copper-beryllium alloy strip and wire finishing facility with lower air levels, and the other a BeO ceramics manufacturing facility with higher

TABLE 1. Comparison of Mine and Mill, Alloy Plant and Ceramics Plant on the Number and Percent Sensitized to Beryllium or Chronic Beryllium Disease Detected by Beryllium Blood Lymphocyte Proliferation Test Surveys, and Number of Detected Cases of Chronic Beryllium Disease Among Persons Who Ever Worked in the Facility and the Rate per 10,000 Person Years at Risk

	Beryllium Extraction Mine and Mill	Copper-Beryllium Alloy Finishing	Beryllium Ceramics Manufacturing
BeS + CBD			
Round 1	5/120 (4.2%)	10/144 (6.9%)	8/136 (5.9%)
Round 2	1/47 (2.3%)		8/77 (10.4%)
Cumulative	6.3%		15.7%
CBD			
Year opened	1969	1951	1980
Year summed	2009	2001	1999
CBD diagnoses	2	7	25
Person-years	11,513	13,129	10,698
CBD/10,000 person years	1.7	5.3	23.4
Relative rate	1	3.1	13.5

BeS, beryllium seusitization; CBD, chronic beryllium disease.

air levels. In terms of surveys, in a single BeLPT survey[6] the alloy facility had a BeS + CBD rate of 10 of 144 (6.9%). Workers at the ceramics facility had combined BeS + CBD rates of 8 of 136 (5.9%) in a first survey,[4] 8 of 77 (10.4%) in a second survey[5] for a cumulative rate of 15.7% [100(1–(1–0.059)(1–0.104))], which has been previously assessed.[7]

Cumulative CBD

The number of cases of CBD and rate of CBD per 10,000 person-years at risk were for the mine and mill through 2009, 2 and 1.7; alloy through 2001, 7 and 5.3; and ceramics through 1999, 25 and 23.4. The mine and mill rate of cumulative CBD was one-third that of the lower exposure alloy facility and one-thirteenth that of the higher exposure ceramics facility.

Work History of the Mill Worker Diagnosed With CBD in 2009

The person identified as BeS in 2001 and diagnosed in 2009 with CBD spent 23 of 31 years in the area where purified $Be(OH)_2$ was precipitated and drummed. This person additionally worked 1.5 years in the beryl furnace area, where there was potential beryl dust and frit exposure, and 6.3 years in the area where the ground bertrandite slurry is mixed with sulfuric acid. This worker had no industrial exposure to beryllium in any other workplace. This worker also operated a farm and raised horses.

Beryllium Exposure

Mine and mill

Beryllium air levels at the mill could exceed 0.2 $\mu g/m^3$ 8h time weighted average (TWA) in many production areas and 2.0 $\mu g/m^3$ in some.[1] Work patterns tended to circulate workers in different areas and job changes were frequent. The mill administrative area was physically separate from the production area but there was intermingling, workers entering the administrative areas for meetings and sharing a common lunchroom. The population median average exposure was approximately 0.2 $\mu g/m^3$ 8 h TWA, based on exposures measured in 2000. Beryllium exposure was to beryllium in beryl and bertrandite ore, frit, beryllium salts, and $Be(OH)_2$. Frequency of exceeding 2.0 $\mu g/m^3$ 8h TWA was highest in the $Be(OH)_2$ production area (hydrolysis). BeO has been detected in samples from ventilation ductwork in the beryl furnace area.[8] Table 2 summarizes exposure levels in several worker categories areas in the period 2004 to 2009. Beryllium air exposures were highest for production workers processing beryl and frit, crushing and grinding bertrandite ore, and precipitating and drumming $Be(OH)_2$. They were lower for maintenance, mining, and laboratory workers.

Alloy Facility

Risk of BeS and CBD in the alloy facility was confined to persons who had worked in the wire area,[6] where exposures at times exceeded 0.2 $\mu g/m^3$ 8 h TWA. These exposures occurred because a high exposure potential wire anneal and pickle process was co-located with wire drawing and other wire manufacturing processes with much lower exposure potential. In the rest of the facility, strip rolling, anneal and pickle and age hardening, and administration, and in maintenance work, beryllium exposure very rarely exceeded 0.2 $\mu g/m^3$ 8 h TWA. The median population average exposure was 0.02 $\mu g/m^3$ 8 h TWA. Controlling exposure originating in the wire anneal-pickle area effectively reduced BeS in new hires.[9] Beryllium exposure was in the form of copper beryllium alloy, BeO mixed with CuO, and beryllium salts associated with pickling operations.

Ceramics Facility

In the beryllium ceramics facility exposures exceeding 0.2 and even 2.0 $\mu g/m^3$ 8h TWA were likely in many areas of the manufacturing area. Median population average exposure was 0.35 $\mu g/m^3$.[4] Administrative personnel were physically separated from production areas but there was intermingling of personnel. Complete separation of administrative areas from manufacturing areas combined with strict migration control and protection of all persons entering the manufacturing area effectively reduced the rate of sensitization of newly hired workers.[10] Exposure was to BeO only.

Beryllium Dissolution

The primary data in the dissolution study was the concentration of the elements in the supernatant fluid removed at 18 days (Table 3, Figure 1). The three ores were tightly grouped in terms of beryllium concentration at both pH 7.2 and 4.5. Concentrations of aluminum from the ores were higher at both pH. Beryllium concentrations from BeO and $Be(OH)_2$ were lower than from the ores at pH

TABLE 2. Areas of Exposure and Air Concentrations of Beryllium, 2004 Through 2009, Collected by Personal Breathing Zone Samplers*

Primary Material	Operation	*N* Samples	Mean $\mu g/m^3$	95th Percentile
Beryl	Beryl furnace	36	0.64	2.25
Beryl and frit	Furnace pour, heat treat, grinding	28	0.99	2.29
	Mining on equipment	47	0.07	0.19
Bertrandite	Mining on foot	32	0.07	0.15
	Loading, crushing, and grinding ore	26	0.55	1.30
	Beryl sulfanation and countercurrent	22	0.33	1.03
$BeSO_4$	Bertrandite sulfuric acid leaching	44	0.05	0.11
	Bertrandite countercurrent	50	0.16	0.69
	Solvent extraction	35	0.23	0.66
$Be(OH)_2$	Precipitation and drumming	34	0.76	2.23
Mixed	Maintenance	50	0.11	0.27
	Laboratory	48	0.04	0.09

*Day-to-day sample variation is high due to variation in production scheduling. Some jobs may have different components. For instance the person running the bertrandite counter current operation also makes periodic surveillance rounds throughout the rest of the plant. Operators running one operation may fill in on other operations as needed. Beryl ore and bertrandite ore extraction are not run at the same time; so individual workers may switch back and forth between beryl and bertrandite extraction operations. Work downstream from the merging of the beryl and bertrandite beryllium sulfate streams is more stable. This includes solvent extraction and $Be(OH)_2$ precipitation and drumming.

TABLE 3. Concentrations of Beryllium, Aluminum and Silicon in Supernatant at 18 Days, Proportion in Solution, Concentration Per Sample Surface Area, and Proportion Dissolved Per Sample Surface Area*

	Element pH	BeO	$Be(OH)_2$	Bertrandite	Beryl	Frit	SiO_2
Concentration at 18 days, g/L (× 1000)	Be 7.2	0.03	0.2	0.4	0.3	0.2	
	4.5	1.0	4.5	0.2	0.2	0.3	
	Al 7.2			2.7	0.7	0.5	
	4.5			2.2	0.8	0.7	
	Si 7.2			15.7	3.1	2.4	24.5
	4.5			12.2	1.5	0.6	0.8
Proportion dissolved at 18 days (× 100)	Be 7.2	0.01	0.2	18.1	1.0	0.6	
	4.5	0.55	3.5				
				10.4	0.8	1.1	
	Al 7.2			6.1	0.7	0.5	
	4.5			4.9	0.7	0.6	
	Si 7.2			13.2	1.7	1.3	8.3
	4.5			10.3	0.8	0.3	0.3
Concentration per surface area at 18 days $(g/L)/m^2$ (× 1000)	Be 7.2	0.05	0.9	0.03	0.5	0.2	
	4.5	1.8	21.4	0.02	0.5	0.4	
	Al 7.2			0.2	1.6	0.8	
	4.5			0.2	1.7	1.0	
	Si 7.2			1.1	6.8	3.5	1.6
	4.5			0.9	3.2	0.8	0.05
Proportion dissolved per surface area at 18 days/m^2 (× 100)	Be 7.2	0.02	0.7	1.3	2.1	0.9	
	4.5	0.8	16.6	0.8	1.8	1.6	
	Al 7.2			0.4	1.4	0.7	
	4.5			0.4	1.5	0.9	
	Si 7.2			0.9	3.7	1.9	0.5
	4.5			0.7	1.7	0.5	0.2

*To simplify comparison results are multiplied by 100 or 1000.

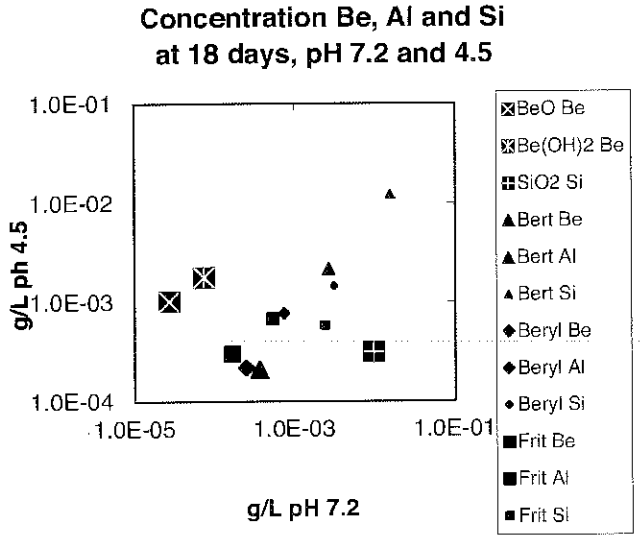

FIGURE 1. Concentration of Be, Al, or Si at 18 days, all materials pH 7.2 and 4.5.

7.2 and higher at pH 4.5. The concentrations of both aluminum and silicon from bertrandite were high compared with beryl and frit.

When adjusted for the element content of the starting materials (Table 4), the proportion of the three elements dissolved at both pH were notably higher for bertrandite (Table 3, Figure 2) compared with beryl and frit, which were tightly grouped, suggesting some factor differentiated bertrandite. Be from BeO was the element dissolved in lowest proportion than any element at pH 7.2. At pH 4.5 all the elements and materials, except bertrandite, had similar proportions dissolved.

The concentration of the elements in solution adjusted for the surface area of the samples (Table 3, Figure 3) lowered the relative position of Be, Al, and Si from bertrandite and Si from SiO_2, as these were the two highest surface area materials (Table 4).

With adjustment for both initial content of elements and surface area there was relatively tight grouping of all three elements in the ores and frit, with the proportion/m^2 dissolved being similar at both pH (Table 3, Figure 4). BeO, $Be(OH)_2$, and SiO_2 were each separated from the ores and frit. SiO_2 and $Be(OH)_2$ dissolved at about the same rates as the ores and frit at pH 7.2, but at pH 4.5 $Be(OH)_2$ dissolved much faster and SiO_2 much slower. In contrast, BeO dissolved much slower than any of the other materials at pH 7.2, and at about the same rate as the ores at pH 4.5.

DISCUSSION

The rates of combined BeS and CBD and of cumulative CBD in the mine and mill workers were marginally lower than those of the alloy workers who had lower beryllium exposures and lower than those of the ceramics workers. These comparisons suggest that risk at the mine and mill was low relative to the degree of airborne beryllium exposure. The study of beryllium solubility was initiated to suggest explanatory hypotheses.

TABLE 4. Characteristics of Samples Used in the Solubility Study

Initial	BeO	$Be(OH)_2$	Bertrandite Ore	Beryl Ore	Frit	SiO_2
Sample weight (g)	0.250	0.250	0.251	0.251	0.250	0.251
Volume (L)	0.4	0.4	0.4	0.4	0.4	0.4
Be (%)	36.0	20.5	0.32	4.2	4.2	
Al (%)			7.0	17.8	17.9	
Si (%)			18.8	29.6	29.6	46.7
Surface area (m^2/g)	2.30	0.84	55.0	1.84	2.77	60.7
Surface area/sample (m^2)	0.57	0.21	13.8	0.46	0.69	15.2

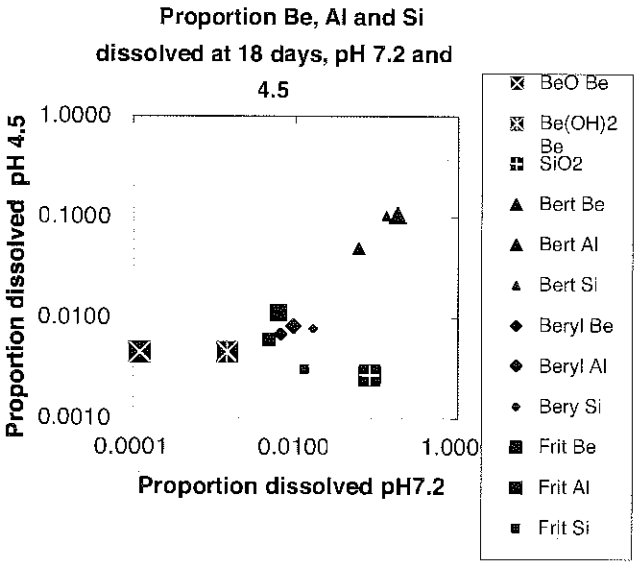

FIGURE 2. Proportion of Be, Al, or Si in sample in solution, at pH 7.2 and 4.5 days.

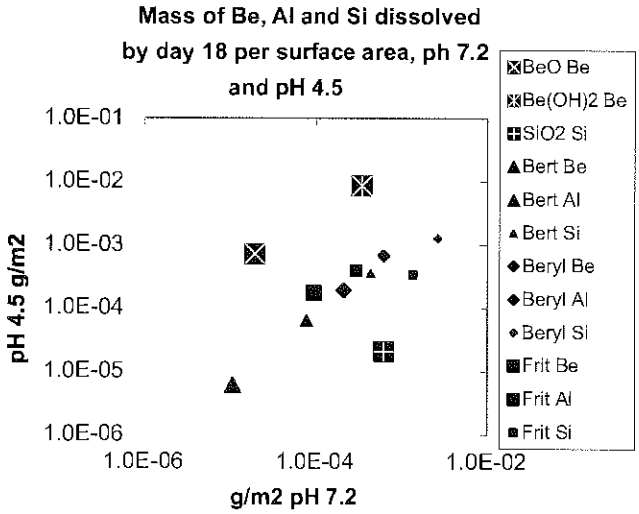

FIGURE 3. Concentration per sample surface area of Be, Al or Si at 18 days, at pH 7.2 and pH 4.5.

The motivating hypothesis was that materials at the mine or mill might be either so soluble or so insoluble that despite beryllium particles reaching the lung the exposure to the lung would be very different from that produced by BeO, the positive control. In the experiment more beryllium dissolved from $Be(OH)_2$ and BeO at pH 4.5 than from the ores, while the opposite occurred at pH 7.2 (Figure 1). However, the beryllium content and surface areas of the samples varied widely. When beryllium content was adjusted the proportion of beryllium dissolved was highest for bertrandite at both pH (Figure 2). Adjusting for surface area only, beryllium was given off most slowly by bertrandite at both pH. The apparent higher proportion of beryllium dissolving from bertrandite is therefore not a characteristic of the nominal chemical form, beryllium silicate, but of the larger surface area of the bertrandite sample.

With adjustment for both beryllium content and surface area, the pure substances, BeO, $Be(OH)_2$, and SiO_2 are clearly separated from the ore materials, bertrandite, beryl and frit (Figure 4). The tight grouping of the content and surface area adjusted values for beryllium, aluminum and silicon from bertrandite, beryl and frit indicates all three elements dissolved together from the surface in proportion to their abundance, suggesting uniform matrix dissolution.

The rate of dissolution per area of surface implies loss of volume which, when divided by the surface gives the thickness of what is dissolved or, with spherical particles, the decrease in radius. Time to spherical particle disappearance is a linear function of particle

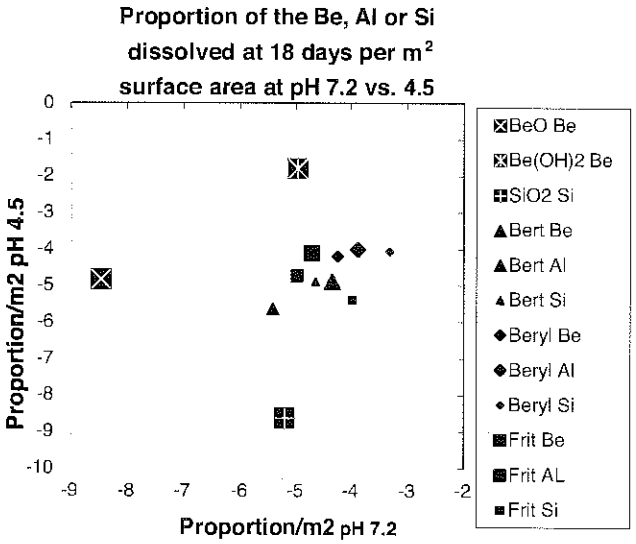

FIGURE 4. Proportion of Be, Al, or Si in solution at 18 days per sample surface area, at pH 7.2 and 4.5.

radius. Smaller particles disappear first, and release their total mass sooner than larger particles. In this study all the materials would be calculated to lose radius at about the same rate at pH 7.2 except for BeO, which would lose radius much more slowly. In contrast, at pH 4.5 all the materials would lose radius at about the same rate, except for $Be(OH)_2$ which would lose radius much faster, and SiO_2, much more slowly.

The lung sorts particles by aerodynamic diameter and the deposition fraction (fraction of particles reaching the lung which are retained) also varies with particle size. As the density of all these materials (data not shown) is similar, similar concentrations of beryllium in the air breathed in the form of same sized particles will result in a similar mass of beryllium deposited in the lung. For the same amount of beryllium the required masses of bertrandite and beryl are 108 and 12 times the required mass of BeO. One hundred eight bertrandite particles and 12 beryl particles of the same size would contain the same mass of beryllium as one BeO particle. The total surface areas of the bertrandite and beryl particles would be higher by the same ratios. Since the greater masses and surface area exactly offset the lower concentration, the amount of beryllium released will be, at the beginning, proportional to the rate of radius reduction, and would decrease with the surface area as particles get smaller. Overall, compared with BeO, the same amount of beryllium inhaled as same size particles of bertrandite in extracellular fluid at pH 7.2 would release more of its beryllium mass in a shorter period of time.

When ingested by phagocytic cells and contained in phagolysosomes at pH 4.5 the surviving and presumably smaller bertrandite particles, now containing in aggregate less total mass of beryllium than BeO, would continue to lose radius, now at about the same rate as BeO. It could be surmised that bertrandite would deliver less beryllium to the intracellular compartment, while BeO would release more. Therefore BeO, due to its lower solubility in extracellular fluid at pH 7.2, might be more efficient in delivering beryllium where it counts, to the antigen-presenting cell.

Bertrandite particles contain masses of aluminum and silicon 22 and 59 times the mass of beryllium and atom ratios of 7 and 19, respectively. The comparative mass ratios for beryl and frit are 4 and 7, and atom ratios 1.4 and 2.3, compared with none in BeO or $Be(OH)_2$.

As bertrandite, beryl or frit dissolve in the phagolysosome of an antigen-presenting cell aluminum and silicon are released with the beryllium.

Could the aluminum or silicon released by the ores interfere with the development of a cellular immune (Th1) response? The observation of relatively lower rates of BeS and CBD in the mine and mill relative to beryllium exposure levels is supported by a much lower rate of BeS (0.3%–0.5%) observed relative to beryllium exposure in aluminum smelter pot room workers.[11,12] The authors of the aluminum pot room studies suggested that the lower immunogenicity of beryllium in pot rooms might be due to its soluble form. However, the concept that beryllium solubility per se interferes with sensitization to beryllium is contradicted by the finding that soluble beryllium salts, especially beryllium fluoride, readily induce BeS via the skin.[13] In the beryllium industry beryllium fluoride salt furnace operations have been associated with high risk of sensitization and CBD.[2]

In Germany, effects of beryllium exposure have been sought in beryl gem (emerald, aquamarine) cutters.[14] Beryllium blood lymphocyte proliferation testing of 54 beryl cutters with significant airborne beryllium exposure resulted in one positive test (2%) and the person, a long tenured beryl cutter, had no clinical disease. Beryllium blood lymphocyte proliferation testing of 84 persons diagnosed with sarcoidosis in Germany or Israel identified 34 persons as BeLPT positive, and one of these, a German, gave an occupational history of gem cutting.[15] These studies do not contradict the hypothesis that simultaneous aluminum exposure might lower the risk from beryllium. It is suggestive in this regard that the one worker to be diagnosed to date with CBD unambiguously related to work at the mill worked predominantly in a job with one of the highest beryllium exposures and no aluminum exposure.

Two hypotheses may be advanced regarding the possible effect of simultaneous beryllium-aluminum exposure. One is that aluminum, dissolving in the phagolysosome along with beryllium, exerts a direct toxic or inhibitory effect,[16] which interferes with the immune response to beryllium. The effect need not kill the antigen-presenting cell, but it would be sufficient if it would interfere with the antigen-presenting process.

A second hypothesis is that aluminum inhibits cellular (Th1) immunity by favoring the development of humoral (Th2) immunity. Aluminum compounds used as immune adjuvants typically stimulate Th2 but not Th1 responses unless other Th1 stimulatory factors are present.[17] There are also mechanisms for cross inhibition between the Th1 and Th2 responses. Beryllium-specific antibodies have been identified[18] and associated with beryllium exposure.[19] It would not be unexpected to detect both Th1 and Th2 responses associated with beryllium exposure, both present in some individuals, and also competing. Were continual release of aluminum along with beryllium in the lung to favor Th2 response this would help explain the low rates of BeLPT detected BeS or CBD relative to exposure in workers exposed to beryl and bertrandite ores or frit, to beryl in gem cutting and polishing, or to mixed beryllium-aluminum compounds in aluminum smelting.

Limitations

Although we have confidence in our characterization of the relative degree of beryllium exposure in the three beryllium facilities, we did not create exposure estimates for the individual workers who participated in the surveys. This would have allowed an analysis that could more convincingly demonstrate the lower risk of BeS and CBD in mine and mill workers relative to exposure. Our solubility study was a range-finding exercise intended to be hypothesis generating, not hypothesis testing. We had considered that differences in solubility between BeO and the materials present at the mine and mill might lead to lower risk either through higher or lower solubility relative to BeO. This study contradicts the idea that lower solubility is a likely explanation of the lower risk of BeS and CBD found in this setting.

The weakness of the data presented here to support the solubility hypothesis is that removal of beryllium particles from the lung, how particles are sequestered in extra- and intracellular compartments, and their times of residence are not taken into account. The other weakness is that it does not take into account the mixture of particles of different sizes that reach and are retained in the lung. Although it has been hypothesized that very large particles (>10 mm) may cause BeS in the upper respiratory tract or gastrointestinal tract[20] and that small particle fraction may be the relevant exposure metric for CBD,[21,22] it remains to be demonstrated that any particle size fraction outperforms the total mass of beryllium less than 10 mm in aerodynamic diameter in predicting risk of BeS or CBD. Therefore the solubility of different beryllium materials would have to be applied across the entire size range of particles deposited in the lung to predict likely lung extracellular and intracellular dose to the lung over time.

CONCLUSIONS

Rates of BeS detected by BeLPT surveillance in a beryllium mine and mill population appear lower than the rates in other beryllium workers with higher and lower exposure profiles. Also this population has had a relatively low cumulative rate of chronic beryllium disease.

The mine and mill population has little opportunity for exposure to BeO, a common factor in beryllium metal and ceramic production facilities. The bertrandite and beryl ores, and beryl frit contain both beryllium and aluminum.

Solubility studies demonstrate that $Be(OH)_2$, beryl, bertrandite and frit are more soluble than BeO at pH 7.2, and as soluble at pH 4.5. We hypothesize that the relatively low rates of BeS and CBD in the mine and mill population may be due to faster dissolution of $Be(OH)_2$, bertrandite, beryl and frit particles in the lung at neutral pH, reducing the particle load available to undergo phagocytosis by antigen-presenting cells. We offer an alternate hypothesis that aluminum exposure accompanying beryllium exposure might interfere with the beryllium cellular immune response.

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