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Is Total Mass or Mass of Alveolar-Deposited Airborne Particles of Beryllium a Better Predictor of the Prevalence of Disease? A Preliminary Study of a Beryllium Processing Facility

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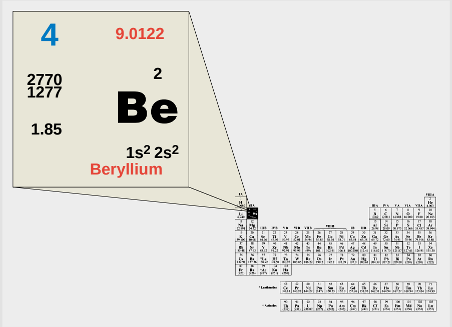


ABSTRACT

Cases of chronic beryllium disease (CBD) and beryllium sensitization continue to be identified among beryllium industry workers. The currently accepted method for measuring exposure, which involves measuring the total mass of airborne beryllium per cubic meter, shows an inconsistent dose-response relationship with the prevalence of CBD. This study was conducted to evaluate whether beryllium aerosol characteristics other than total mass may be more informative in understanding the dose-response relationship between exposure to beryllium and disease. Personal samplers (n=53) using Andersen impactors and area samplers (n=55) using microorifice uniform deposit impactors (MOUDIs) were used to collect airborne beryllium samples in five furnace areas at a beryllium manufacturing facility where prevalence rates of CBD and beryllium sensitization had been previously studied among 535 employees with significant beryllium exposure. The concentrations were expressed in terms of total mass per cubic meter and in terms of mass, number, and surface area of particles per cubic meter that are predicted to deposit in the alveolar region of the lung. Tests for linear trend of the relationships of the various exposure metrics to prevalence of CBD and sensitization showed a highly significant association between mass, number, and surface area concentration of particles predicted to deposit in the alveolar region of the lung and CBD and sensitization. The relationship between exposure and disease was observed with measurements collected with the MOUDI sampler only; exposure parameters calculated from Andersen samples did not demonstrate significant relationships with CBD or beryllium sensitization. These results suggest that the concentration of alveolar-deposited particles as measured by the MOUDI sampler, which collects finer-sized particles than the the Andersen sampler, is a more relevant exposure metric for predicting the incidence of CBD or sensitization than the total mass concentration of airborne beryllium.

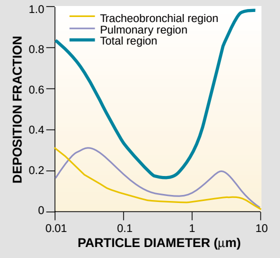
INTRODUCTION

CBD is an immunological-based disease leading to granuloma formation in the alveolar region of the lung. The current method for evaluating beryllium exposure involves measuring total mass of all airborne beryllium particles. Evaluation of other dose metrics is important for several reasons:

- A dose-response relationship is inconsistent between beryllium exposure and CBD
- Different processes generate various particle size distributions, chemical forms, and shapes of airborne beryllium
- Improved exposure assessment methods are needed.

This study was designed with four main objectives:

- Assess which characteristics of airborne beryllium particles are more predictive of the prevalence of CBD
- Help define exposure assessment strategies for future work
- Investigate worker exposure in different processing areas in a beryllium manufacturing facility
- Evaluate the relationship between different aerosol characteristics (particle size, number, and surface area as predicted to deposit in the alveolar region of the lung, International Commission of Radiological Protection curve) and prevalence of CBD and beryllium sensitization.



METHODS

Study Population

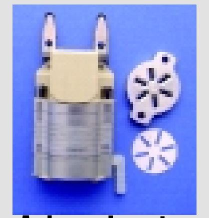
Nineteen individuals were randomly selected from a total employee population of 150 salaried and 650 hourly workers in a beryllium manufacturing facility.

Furnace Operations Studied

Beryllium oxide	• Beryllium oxide (BeO) furnace (n = 11)
Beryllium	• Ammonium beryllium fluoride (ABF) furnace • Beryllium fluoride (BeF_2) reduction furnace (combined, n = 26)
Copper-beryllium alloys	• Copper-beryllium arc (CuBe arc) furnace (n = 6)
Copper-beryllium alloys	• Copper-beryllium induction (CuBe induction) furnace (n = 12)

Data Collection Methods

- The ABF and BeF_2 reduction furnaces, which handle soluble salt, were grouped because their sensitization and CBD prevalence rates were similar and because employees worked in both areas.
- Personal lapel measurements were collected with Andersen impactors, which are six-stage impactors that separate particles from 0.5 to >10 µm in diameter.
- Area samples were collected within a few feet of the worker with MOUDIs, which are ten-stage impactors that separate particles from 0.05 to 18.0 µm in diameter.
- Impactor stages were analyzed by flame atomic absorption spectrophotometry or by graphite furnace atomic absorption spectrophotometry (<0.1 µg).
- Exposure metrics of beryllium particles evaluated the following:
  - Total mass
  - Alveolar-deposited mass (<10 µm and <3.5 µm)
  - Alveolar-deposited number (<10 µm and <3.5 µm)
  - Alveolar-deposited surface area (<10 µm and <3.5 µm).



Andersen Impactor

MOUDI

Data Analysis

- The Kruskal-Wallis nonparametric test was used to evaluate differences between process areas.
- The chi-square test for trend was used to examine association between aerosol characteristics and prevalence of beryllium sensitization and CBD.

RESULTS

Prevalence of CBD and Beryllium Sensitization

- The beryllium oxide and beryllium furnace operations (ABF/BeF_2 reduction and BeO furnaces) had the highest prevalence rates.
- The copper-beryllium alloy furnace operations (CuBe induction and CuBe arc furnaces) had the lowest prevalence rates (Table 1).

Particle Size Distribution of Beryllium

- Copper-beryllium alloy furnaces (CuBe induction and CuBe arc furnaces), as demonstrated by MOUDI samples, mostly produce a distribution of particles greater than 5 µm (Figure 1).
- Beryllium and beryllium oxide furnaces (ABF/BeF_2 reduction and BeO furnaces) demonstrate a bimodal distribution based on MOUDI samples (Figure 1), with a large amount of particles <1 µm.

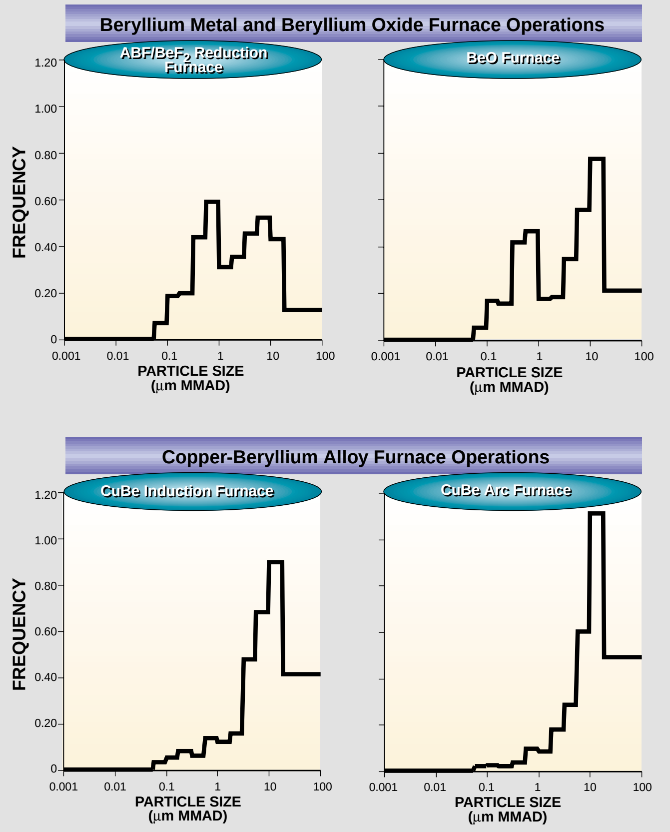


Figure 1. Particle size distribution of median total beryllium particle mass collected by MOUDI samplers

Note: MMAD - mass median aerodynamic diameter

Table 1. Number of employees, CBD and beryllium sensitization prevalence rates, and 95 percent confidence intervals by process area

Process Area	Number of Employees	Cases of CBD	Cases of Beryllium Sensitization	Prevalence Rates[a] (percent): CBD[b] (lower, upper 95% CI)	Prevalence Rates[a] (percent): Sensitization[c] (lower, upper 95% CI)
ABF/BeF_2 Reduction Furnace	195	13	25	6.7 (3.2, 10.2)	12.8 (8.1, 17.5)
BeO Furnace	61	3	6	4.9 (0, 10.3)	9.8 (2.4, 17.3)
CuBe Induction Furnace	181	5	16	2.8 (0.4, 5.2)	8.8 (4.7, 13.0)
CuBe Arc Furnace	98	2	7	2.0 (0, 4.8)	7.1 (2.0, 12.2)

Source: K. Kreiss, M.M. Mroz, and B. Zhen. 1996. Beryllium health effects surveillance at Brush Wellman's Elmore Plant. Denver, CO: National Jewish Center of Immunology and Respiratory Medicine, Department of Medicine.
Note: CI - confidence interval
[a] The cohort involved 535 persons (ever-never worked).
[b] CBD is identified by granulomas on lung biopsy in the presence of positive bronchoalveolar lavage lymphocyte proliferation test.
[c] Sensitization is identified as two positive blood lymphocyte proliferation tests.

Comparison of MOUDI and Andersen Measurements

- No correlation was found between MOUDI and Andersen measurements.
- Andersen impactor measurements were greater than MOUDI measurements (Figure 2).

Comparison of Furnace Processes

- Airborne beryllium concentrations of total mass and alveolar-deposited mass and surface area for both Andersen and MOUDI samples were significantly different among the four furnace operations.
- Alveolar-deposited number concentrations calculated from Andersen samples, but not MOUDI samples, were significantly different between furnace areas (Figure 2).

Relationship between Various Exposure Metrics and CBD

- Alveolar-deposited mass, number, and surface area concentrations of beryllium particles (<10 µm), as measured by MOUDI samplers, showed a significant trend with prevalence of CBD.
- Mass concentration of alveolar-deposited particles <3.5 µm (MOUDI) were more strongly associated with CBD and sensitization than particles <10 µm.
- Total mass concentrations showed no correlation.
- Andersen impactor measurements showed no correlation.

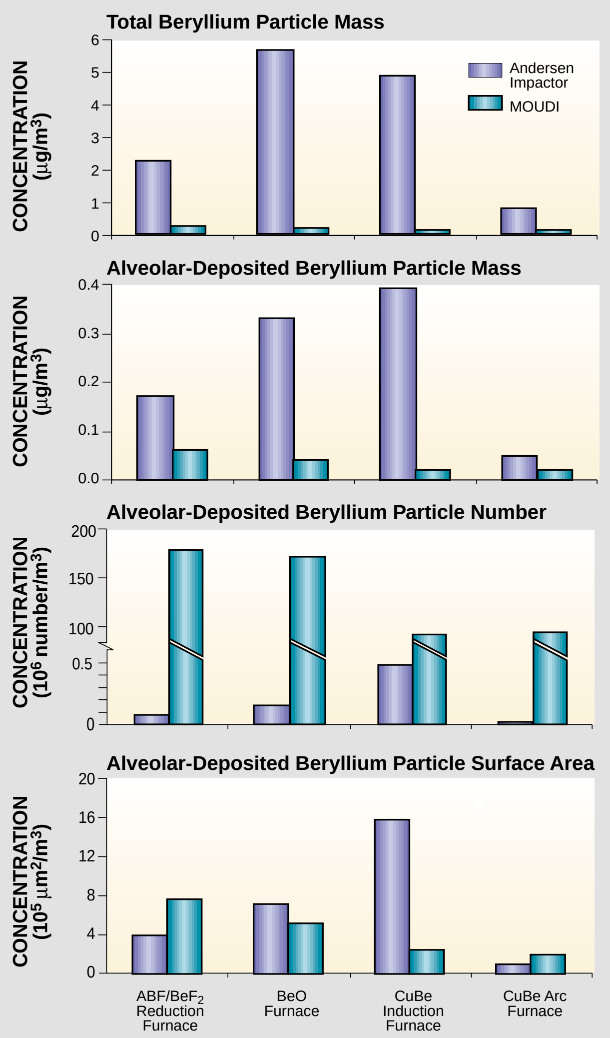


Figure 2. Concentration of the mass, number, and surface area of alveolar-deposited beryllium particles from Andersen impactor and MOUDI samples collected in different process areas

Note: Alveolar-deposited is defined as the fraction of particles smaller than 10 µm mass median aerodynamic diameter than are predicted to deposit in the alveolar region of the lung.

Scale on Y axis varies.

CONCLUSIONS

- Respirable particles might be a better dose metric and predictor of CBD than total mass measurements because the beryllium and beryllium oxide furnace operations (ABF/BeF_2 reduction and BeO furnaces), which have a greater prevalence of beryllium sensitization and CBD than the copper-beryllium alloy furnaces (CuBe induction and CuBe arc furnaces), also have a greater mass, number, and surface area concentration of alveolar-deposited beryllium particles less than 10 µm and less than 3.5 µm.
- Beryllium form might be an important risk factor for CBD because copper-beryllium alloy furnace operations report lower prevalence of beryllium sensitization and CBD in workers and produce larger-sized airborne particles (mostly nonrespirable) than the beryllium and beryllium oxide furnace operations.
- Differences in Andersen impactor and MOUDI measurements might be attributable to:
  - The smaller-sized particles collected by the MOUDIs (down to 0.05 µm) as compared with the Andersen impactors (down to 0.5 µm)
  - Proximity of the Andersen personal sampler to the emission source, thereby enabling collection of large-sized particles. (In contrast, the MOUDI sampler characterizes particles that likely remain suspended in the air because the MOUDI was not positioned directly over the source and collects fine and ultrafine particles).
  - The sampling bias of personal lapel samplers (i.e., particle resuspension from clothing).
- Further investigations are needed to evaluate the following:
  - Differences between Andersen personal lapel measurements and MOUDI area samples (i.e., side-by-side sampling with MOUDI and Andersen samplers)
  - Aerosol characteristics (morphology, chemical form, size) within all beryllium operations that report cases of workers with beryllium sensitization and CBD
  - The relationship between aerosol characteristics and prevalence of CBD associated with specific processing operations, individual worker tasks, and different forms of beryllium.