A Descriptive Study of Beryllium Sensitization in Former Atomic Energy Workers at the Ames Laboratory

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Abstract

The Ames Laboratory began work for the Atomic Energy Commission in 1942. Their goal pre-1960 was to mass produce uranium and thorium for use in experiments as well as weapons. During this time large amounts of beryllium were used in the process of isolating these metals. Beryllium is a light weight, spark resistant, temperature resistant metal ideal for the weapons industry. Exposure to beryllium, can cause beryllium sensitization (BeS) and Chronic Beryllium Disease (CBD). 1,146 former workers were screened for beryllium sensitivity by the Former Worker Medical Screening Program (FWP).

Of those 20 (1.7%) were confirmed BeS by the Beryllium Lymphocyte Proliferation Test (BeLPT). Due to limited information on work history and test results, 1,071 individuals were included in this study, with 19 (1.8%) confirmed BeS. On average, sensitized workers were 9 years older than non-sensitized at 71 vs. 62 respectively (p=0.000454). Those sensitized started working on site 9.5 years earlier on average than non-sensitized participants (p=0.00029) and decade of hire was statistically significantly associated with sensitization (p=0.037). All individuals sensitized began working prior to 1979. Stratifying by exposure showed no significant difference in reference to sensitization. Furthermore, no difference in sensitization was detected amongst the different production eras: uranium (1942-1949) thorium (1950-1959) and research & development (post 1960). Sensitization at the Ames Laboratory continues to be monitored in former works, even though sensitization rates are lower than other industries.

Project Background

The U.S. Department of Energy (DOE), formerly AEC, was mandated by Congress to evaluate the long-range health effects of exposures in the DOE workforce. In 2005, DOE contracted with The University of Iowa to screen former Ames Laboratory workers for health effects of exposures on site. The goal of the project is to locate and provide Ames Laboratory former workers medical evaluations.

Ames Laboratory History

In 1942, the Ames Laboratory was created to support the Manhattan Project. They developed methods to create large quantities of uranium. Through 1950 they isolated 2 million pounds of purified uranium. From 1950-1960 the Laboratory purified thorium. Post 1960, the Laboratory participated in research and development. Jobs in the Ames Laboratory ranged greatly, from secretary to physicist.

The Ames Laboratory used beryllium mainly for casting of uranium, thorium and plutonium in the early years but some beryllium was also used in research and development after 1960. Castings frequently blew out and needed machining, thus beryllium dusts were created.

Beryllium Lymphocyte Proliferation Test

The BeLPT is the protocol used by the DOE for screening individuals for beryllium sensitization. The test requires 30ml of blood drawn within 24 hours. CD4(+) T lymphocytes are isolated and cultured. Cells are then divided into seven wells. Six wells are exposed to beryllium at concentrations of 1, 10, and 100 µM BeSO4, two wells of each concentration. The lymphocytes are incubated and samples are taken and compared to control. A stimulation index (SI) is created by observing cell proliferation in experimental and control groups. If two or more wells have an SI >2.5-3 (lab specific) the test is considered abnormal, and if one well has an SI >2.5-3 the test is considered borderline. In order to be confirmed BeS, an individual must have two abnormal, or one abnormal plus one borderline test result[1].

Methods

As of July 1, 2010, 1,146 former Ames Laboratory workers have been screened. Participants' pulmonary function was analyzed by spirometry and chest x-rays were reviewed according to International Labor Organization's (ILO) system to evaluate the extent of parenchymal abnormalities (profusion). Blood was obtained from each participant for BeLPT and analyzed by an independent laboratory. All individuals had the right to refuse any part of the screening.

Of the 1,146 individuals screened, 1,071 individuals were included in this study based on the completeness of their records. All individuals included had at least one BeLPT, pulmonary function test (PFT), and chest x-ray. Furthermore, date of birth, sex, race and date of hire were required for inclusion. BeLPT results were grouped by normal, single borderline, double borderline, single abnormal and confirmed sensitized to characterize T-cell response to beryllium as a spectrum.

For those with multiple screenings, the most recent result was used for pulmonary function, and the highest ILO profusion score was used to reconcile between multiple readers. An ILO profusion score ≥ 1/0 was used to define parenchymal disease. Job titles were grouped according to no, low, or high potential for exposure to beryllium with advice from the Ames Laboratory. Participants' start dates were grouped by eras: uranium (pre-1950), thorium (1950-1960), and research (post-1960). Individuals were also grouped by decade of hire. Data was stored using Microsoft Access and analyzed with SAS.

Sensitized vs. Not-sensitized Populations

	BeS (N=19)	Not Sensitized (N=1052)	p-value	Statistical Method
Age, mean	71	61.96	0.000454	t test
Years at AMES, mean	4.11	5.33	0.527	t test
Years since started at AMES, mean	47.42	37.93	0.00029	t test
Smoking history				
Never smoker	10	681	0.27	Fisher's test
Ex-smoker	8	309		
Smoker	1	33		
Missing	0	29		
Gender				
Male	15	731	0.46	Fisher's test
Female	4	321		
PFT (mean)	N=19	N=1044		
FVC% PREDICTED	99.1	93.7	0.16	W|KW test
FEV1% PREDICTED	95.6	94.1	0.41	W|KW test
Parenchymal Disease	N=17	N=974		
Y	2	57	0.0775	Fisher's test
N	15	917		

PFT data is adjusted for smoking by never smoker, ever smoker and current smoker

Right: Beryllium Tools

Left: Uranium Puck

Beryllium Sensitization By Era

Era Hire	BeS					
	Normal	1 Borderline	2 Borderline	1 Abnormal	Confirmed	Total
Uranium Era	21 (95.5%)	0 (0%)	0 (0%)	0 (0%)	1 (4.5%)	22
Thorium Era	172 (93.5%)	3 (1.6%)	2 (1.1%)	1 (0.5%)	6 (3.3%)	184
R and D Era	813 (94.0%)	21 (2.4%)	4 (o.5%)	15 (1.7%)	12 (1.4%)	865
Total	1006 (93.9%)	24 (2.2%)	6 (0.6%)	16 (1.5%)	19 (1.8%)	1071

Fisher's exact p = 0.35

Beryllium Sensitization By Decade Hired

Decade Hire	BeS		
	Confirmed	Normal	Total
1940	1 (4.6%)	21 (95.4%)	22
1950	6 (3.3%)	178 (96.7%)	184
1960	9 (2.9%)	302 (97.1%)	311
1970	3 (1.2%)	249 (98.8%)	252
1980	0 (0.0%)	182 (100.0%)	182
1990	0 (0.0%)	112 (100.0%)	112
2000	0 (0.0%)	8 (100.0%)	8
Total	19 (1.8%)	1052 (98.2%)	1071

Fisher's exact p = 0.037

Beryllium Sensitization By Expected Exposure

Exposure Potential	BeS					
	Normal	1 Borderline	2 Borderline	1 Abnormal	Confirmed	Total
No Exposure	159 (95.2%)	2 (1.2%)	0 (0.0%)	4 (2.4%)	2 (1.2%)	167
Low Exposure	161 (97.0%)	1 (0.6%)	0 (0.0%)	2 (1.2%)	2 (1.2%)	166
High Exposure	669 (92.9%)	21 (2.9%)	6 (0.8%)	10 (1.4%)	14 (1.9%)	720
Total	989 (94.0%)	24 (2.3%)	6 (0.6%)	16 (1.5%)	18 (1.7%)	1053

Fisher's exact p = 0.50

Findings/Recommendations

- BeS rate of 1.8% is lower than in other industries that currently use beryllium such as 4.0% in mining extraction or 5.9% in beryllia ceramics[2].
- All of the BeS individuals started working at the Ames Laboratory before 1979 and, on average, were first hired at the Laboratory 9.5 years earlier than non-sensitized workers (p=0.00029). However, no significant result were found for era of hire & sensitization status.
  - Many of those sensitized were exposed to beryllium during production eras. However, the facility was not thoroughly cleaned until after OSHA was created in 1974. The facility took many years to clean.
  - Beryllium dust has been detected in the facility as recently as 2001.
  - Some individuals in the R & D era may have been exposed to beryllium dusts produced during production eras that had not been cleaned. Alternatively they may have been exposed by newly produced dusts.
  - There were no cases of BeS found in those hired post-1979, so perhaps clean up of beryllium has been effective and proper safety protocols have been instituted.
- BeS individuals were on average 9 years older than non-sensitized individuals (p=0.00045). The close association between start date and age is likely the cause to this finding.
- BeS occurred in all exposure strata which may be due to genetic susceptibility, or widespread dissemination of beryllium dusts, exposing all workers.
- BeLPT has an estimated false positive rate of 1.09% and a rate of false negative tests in those sensitized is estimated at 31.7%[3]. These estimates are based on serial testing, and not on comparisons to a gold standard.
  - Many of those with a single, not confirmed abnormal test may have BeS.
    - Eight of the 16 individuals with single abnormal tests have not been re-tested and some may ultimately be confirmed as BeS.
  - Based on these estimates it may be necessary to require multiple BeLPTs to confirm BeS and the prevalence of BeS in this study may be underestimated.
- BeS in this cohort may be an underestimated since BeS converts to CBD at 6-8% per year[4]. CBD is often lethal and those with BeS were exposed on average 30+ years ago, leaving ample time for the disease to develop.

1. Department of Energy. *DOE Specification: Beryllium Lymphocyte Proliferation Test*. 2001 Apr.
2. National Research Council. Managing Health Effects of Beryllium Exposure. Washington, DC: National Academy of Sciences; 2008. p. 55-56.
3. Strange, A et al. "The Beryllium Lymphocyte Proliferation Test: Relevant Issues in Beryllium Health Surveillance." *American Journal of Industrial Medicine*. 2004:46:453–462.
4. Newman, L.S. et al. "Beryllium sensitization progresses to chronic beryllium disease: A longitudinal study of disease risk." Am. J. Respir. Crit. Care. Med. 2005:171(1):54-60.