SARCOIDOSIS VASCULITIS AND DIFFUSE LUNG DISEASES 2014; 31; 163-169

Unsuspected Exposure to Beryllium: Potential Implications for Sarcoidosis Diagnoses

Andrew N. Laczniak[1], Nathan A. Gross[2], Laurence J. Fuortes[2], R. William Field[3]

[1]College of Medicine, University of Iowa, Iowa City, IA 52242; current address: Mallinckrodt Institute of Radiology, School of Medicine, Washington University in St Louis, St Louis, MO 63110; [2]College of Public Health, Department of Occupational and Environmental Health, University of Iowa, Iowa City, IA 52242; [3]College of Public Health, Department of Occupational and Environmental Health, Department of Epidemiology, University of Iow

Abstract. Exposure to Beryllium (Be) can cause sensitization (BeS) and chronic beryllium disease (CBD) in some individuals. Even relatively low exposures may be sufficient to generate an asymptomatic, or in some cases a symptomatic, immune response. Since the clinical presentation of CBD is similar to that of sarcoidosis, it is helpful to have information on exposure to beryllium in order to reduce misdiagnosis. The purpose of this pilot study is to explore the occurrence of Be surface deposits at worksites with little or no previous reported use of commercially available Be products. The workplaces chosen for this study represent a convenience sample of businesses in eastern Iowa. One hundred thirty-six surface dust samples were collected from 27 businesses for analysis of Be. The results were then divided into categories by the amount of detected Be according to U.S. Department of Energy guidelines as described in 10 CFR 850.30 and 10 CFR 850.31. Overall, at least one of the samples at 78% of the work sites tested contained deposited Be above the analytical limit of quantitation (0.035 μg beryllium per sample). Beryllium was detected in 46% of the samples collected. Twelve percent of the samples exceeded 0.2 μg/100 cm² and 4% of the samples exceeded a Be concentration of 3 μg/100 cm². The findings from this study suggest that there may be a wider range and greater number of work environments that have the potential for Be exposure than has been documented previously. These findings could have implications for the accurate diagnosis of sarcoidosis. *(Sarcoidosis Vasc Diffuse Lung Dis 2014; 31: 163-169)*

Key words: Chronic Beryllium Disease (CBD), Sarcoidosis, Beryllium Sensitivity, Surface Contamination, Beryllium, Occupation, Workplace, Diagnosis

Introduction

As early as the 1940s, beryllium (Be) was identified as an occupational hazard. NIOSH investigators estimated in 2004 that as many as 134,000 current workers, primarily in private industry, were potentially exposed to beryllium in the United States (1). Beryllium and beryllium compounds are listed as known human carcinogens by the International Agency for Research on Cancer (2,3). Even low inhalational exposures have been shown to cause an asymptomatic immune response called beryllium sensitization (BeS) and chronic beryllium lung disease, (CBD). Individuals with carriage of the HLA-DPB1 (GLU 69) genotype (4) are at increased risk for BeS and CBD. In addition to BeS caused by airborne exposures, BeS can occur through the tran-

Received: 26 May 2013
Correspondence: Dr. R. William Field
College of Public Health, Department of Occupational and Environmental
Health, Department of Epidemiology, University of Iowa,
S 327 CPHB, 105 River Street, Iowa City, IA 52242
E-mail: bill-field@uiowa.edu

sdermal route in humans exposed to soluble Be compounds (5). BeS can lead to chronic Be disease (CBD), characterized by granuloma formation and scarring of the lungs, in at least 30% of the population with a conversion rate of 3 to 9% a year (6).

Since 1999, the diagnosis of CBD has been defined as the detection of BeS and granulomas without the previous diagnostic requirement of overt symptomology (7).

Surface wipe sampling studies performed in areas not thought to contain contamination from Be are relatively rare in homes or work places. Following the collapse of the World Trade Center, a U.S. EPA survey of surface Be occurrence failed to find any detections, at a detection limit of 0.2 mg/100 cm^2, in a sample of 1,544 home in lower Manhattan homes (8). In a study to assess the potential for Be exposure from beryllium-containing particulate on surfaces for a cohort of Department of Defense (DOD) workers at a munitions plant in Eastern Iowa, Sanderson et al. (9) compared the Be levels in dust wipe samples to those found at reference sites with no reported prior or current Be use. The researchers sampled 95 locations in the munitions plant and compared them to 46 sampled locations in the reference sites. Beryllium was detected in 87% of the samples taken at the munitions plant, but surprisingly, it was also detected in 72% of the samples collected at the reference sites. However, at these reference sites, only seven percent of the samples contained Be concentrations above the DOE removable contamination level of 0.2 μg/100 cm^2 for release of items to the public (Table I) as compared to 27% at the munitions plant. Nonetheless, the fact that 72% of the reference samples contained Be concentrations above the limit of quantitation (LOQ) was somewhat surprising considering the owners and workers at the businesses were unaware of its presence. These results suggested that some workers were potentially exposed to work-related materials containing Be without their knowledge.

The Occupational Safety and Health Administration (OSHA) hazard communication regulation requires that workers processing products sold as Be-containing materials containing greater than 0.1% beryllium be educated in regard to the potential health risks of Be exposure. The detection of Be in non-Be using workplaces raises the question as to whether a Be-containing product is being unknowingly handled, whether the beryllium detected is a natural constituent in materials being processed nearby, or the Be source is due to "drag-in" of soils with high Be content. Identifying the presence and source of exposure can be important because the diagnosis of CBD includes, among other factors, a sound occupational exposure history. Without a history of exposure to Be, individuals with CBD have been misdiagnosed as having sarcoidosis (10,11) due to its very similar clinical presentation (12). Furthermore, the BeLPT as a screening tool has been shown to have a sensitivity rate below 70% in some studies (13). Therefore, in order to reduce misdiagnoses and judge potential health risks, it is important to first determine if the potential exists for work-related or environmental Be exposure and second to determine if the exposure is associated with Be-related adverse health effects. Such information can also be used to educate the workers' cohabitants on their potential health risks, as they may be exposed to Be via dust transferred on the workers' clothing and shoes.

The primary goal of this pilot study was to further explore the occurrence of surface deposited

Table 1. Beryllium surface contamination criteria used by U.S. Department of Energy

Limit	Reference
0.2 μg/100 cm2	10 CFR 850.31 release criteria level
	DOE surface concentration limit to determine items acceptable for release to public.
	Surface contamination must not exceed 0.2 μg/100 cm2 when released to the public for non-beryllium use.
	DOE release criteria level did not originate from an association with a specific health effect, but instead indicated the cleaning level thought to be attainable based on an opinion survey of DOE health and safety representatives.
3.0 μg/100 cm2	10 CFR 850.30 surface contamination limit
	Surfaces contaminated with beryllium dusts and waste must not exceed a removable contamination level of 3 μg/100 cm2 during non-operational periods.
	Employers must provide protective clothing and equipment where surface levels exceed 3.0 μg/100 cm2.
	Housekeeping efforts must keep surface contamination at or below this level during non-operational hours.

Be in a sample of workplaces where Be was not thought to be used or generated as a waste product in particulate form. Based on the limited sampling of the Sanderson et al. (9) study that detected trace Be concentrations at workplaces not generally considered at risk for exposure to Be, we hypothesized that there may be a wider range and greater number of work environments that have the potential for Be exposure from work-related processes than have been documented previously.

Methods

Sampling Locations

Sampling sites chosen for this study represent a convenience sample of worksites in eastern Iowa located within a 80 km radius of the University of Iowa, Iowa City, IA. It was not feasible to use a systematic sampling method that could have produced results generalizable to the rest of southeastern Iowa due to the pilot nature of this study. Therefore, the worksites were chosen to include a range of occupations as well as a smaller sample of work places that may have had the potential for Be exposure based on the literature reports (e.g., dental offices, coal plant). Attempts were made to select businesses that had been operating at their current locations for a relatively long period with the hope of collecting surface dusts originating from changing trends in work practices and materials. The southeastern portion of Iowa also had the advantage of relatively low soil Be concentrations ranging from 1 to 2 ppm (14) compared to the range of 1 ppm to 15 ppm for Be in U.S. Soils overall (15). The low soil Be concentrations reduced the possibility that the Be found in dust samples within the workplaces were the result of "tracking in" or "blowing in" of Be from shallow soil.

Surface wipe samples were collected from 29 different locations representing a range of worksites including an auto repair shop, machine shop, electronics shop, schools, bars where smoking had occurred (Be has been documented to be a constituent of some cigarettes), etc. (Table I). An average of five surface wipe samples was collected for analysis at each of the 29 study sites. The samples were collected from a variety of locations at each study site including, but not limited to, bookshelves, desktops, cabinet tops, the tops of ventilation ducts, and on the upper surface of pipes. Locations were selected based on the presence of visible dust accumulation. Sample collection focused, as applicable, on areas above obvious sources of airborne particle generation such as areas in which saws, lathes, sanders, and grinders were used. During the survey, the management of the businesses was asked if they were aware of work with any Be containing materials over the past ten years.

Sampling Methods

The method used to collect the surface wipe samples was the same as previously described in the Sanderson et al. (9) study. The quantifiable surface concentrations were divided into three concentration categories above the LOQ (Table II). The concentrations of 0.2 μg/100 cm² and 3 μg/100 cm² are guidelines cited by the DOE: Chronic Be Disease Prevention (Table I) (9) and are used as reference levels in this paper since they are frequently used by the DOE to assess varying degrees of Be surface contamination. It is important to note that the guidelines do not correlate directly with any particular health effects and are merely used to determine the appropriate protective measures to take as well as the effectiveness of cleaning efforts in work environments where Be is regularly used.

Analytical Methods

DataChem Laboratories, Inc. (Salt Lake City, UT, U.S.A., American Industrial Hygiene Association Accreditation No. 17) analyzed the wipe samples using the NIOSH 7300 Method (inductively coupled plasma-atomic emission spectroscopy) (16). Since NIOSH 7300 method is written for air samples taken on an MCE filter, DataChem has slightly modified the method by prepping wipe samples instead of the method specified for MCE filters. The analysis is otherwise exactly the same process. The analytical LOQ was 0.035 micrograms (μg) Be per sample. All values provided by DataChem were expressed in μg of Be per sample, which were then divided by the surface area in order to obtain a surface concentration of μg of Be per 100 square centimeters (μg/100 cm²).

Table 2. Summary of beryllium surface measurement results

Sampling Locations	Number of Samples	Be Concentration Categories			
		< LOQ	LOQ ≤ x ≤ 0.2 μg/100 cm2	0.2 μg/100 cm2 < x ≤ 3.0 μg/100 cm2	> 3.0 μg/100 cm2
Auto Repair Shop 1	5	1	4	0	0
Auto Repair Shop 2	5	3	2	0	0
Auto Repair Shop 3	5	2	3	0	0
Auto Repair Shop 4	5	1	3	1	0
Bar	5	5	0	0	0
Ceramics Shop	5	0	4	1	0
Coal Burning Power Plant	5	0	4	1	0
Computer Recycling Shop	5	5	0	0	0
Dental Lab 1	5	5	0	0	0
Dental Lab 2*	6	0	2	1	3
Dental Lab 3*	5	1	3	1	0
Electronics Shops	5	5	0	0	0
Feed/Fertilizer Shop	5	2	3	0	0
Fertilizer Co-op	5	0	2	2	1
Flower Shop 1	5	4	1	0	0
Flower Shop 2	5	5	0	0	0
Food Processing Co-op	5	4	1	0	0
Hog Confine 1	5	4	1	0	0
Hog Confine 2	5	4	1	0	0
Machine Shop 1	5	3	2	0	0
Machine Shop 2	5	4	1	0	0
Machine/Electronics Shop 1	5	0	5	0	0
Machine/Electronics Shop 2	5	2	2	1	0
Machine/Electronics Shop 3*	5	0	1	2	2
Restaurant	5	4	1	0	0
School 1	5	5	0	0	0
School 2	5	4	1	0	0
Overall Totals	136	73	47	10	6
Overall Percentages	100%	53.7%	34.6%	7.4%	4.4%

* *Previous reported use of commercial Be products.*

Results

Management at only four worksites, out of the 31 contacted, refused to participate in the study. At the majority of the 27 worksites sampled, the management estimated that the dust at the specific sampling locations represented years to decades worth of deposited materials. Management at only two worksites reported work with commercial Be products containing greater than 0.1% Be. In the case of these two sites, the work reportedly occurred many years ago (Table II). A total of 136 samples were collected from 27 worksites. Samples were generally collected from elevated surfaces with heights ranging from 20 cm to 284 cm (average = 169 cm) above the floor of the room. The sample areas ranged from 51 to 1,233 cm² (average = 356 cm²). Be analyses were also performed on five blank samples, all of which were found to be below the LOQ indicating that the wipes were not contaminated before the sampling, during the handling or return to the laboratory. Overall, at least one of the samples at 78% of the work sites tested contained deposited Be above the analytical limit of quantitation (0.035 μg beryllium per sample). Beryllium was detected in 46% of the samples collected with 12% of the samples exceeding the 0.2 μg/100 cm² reference concentration and 4% of the samples exceeding the 3 μg/100 cm² reference concentration (Table II).

All the samples collected at the ceramics shop, coal burning power plant, fertilizer co-op, and one of the 3 dental labs had concentrations exceeding 0.2 μg/100 cm^2. One of the samples that was collected on the side of a processing machine, used to mix and package urea and potash fertilizers, at the fertilizer co-op had a Be concentration of 6.1 μg/100 cm^2. The ceramics shops and coal burning power plants were very similar in that Be was detected in all samples from these locations, but each location only had one sample (20% for each) that exceeded the 0.2 μg/100 cm^2 reference concentration.

The samples taken from dental labs had significant variability. In total, three separate dental labs were tested, two of which reported having used Be in the past, while one reported never having used Be or Be containing products. The lab that had not been known to work with Be did not have any samples with quantifiable Be concentrations. The other two labs reported that they had worked with Be in the past, but had almost completely stopped working with the metal in the past 8 years. Nonetheless, 91% of the samples from these labs had quantifiable Be concentrations. In addition, 45% of the samples taken at these two dental labs exceeded 0.2 μg/100 cm^2 with 50% of the 6 samples exceeding 3 μg/100 cm^2 at one of the labs.

Machine/electronics shops also exhibited a high proportion (87%) of samples with quantifiable Be. Two of the samples (13.3%) yielded results of 299 μg/100 cm^2 and 32 μg/100 cm^2. The samples were collected near grinders and sanders where copper containing Be had reportedly been ground within the last two years. Auto repair shops also had a relatively high proportion (65%) of samples with quantifiable Be, but only one sample out of 20 contained Be concentrations above 0.2 μg/100 cm^2

Low proportions of samples with quantifiable Be were found at the other study sites including: 30% of the samples from machine shops not associated with electronic shops, 20% of samples from hog confinements, 20% of samples from food processing co-ops, 20% of the samples from restaurants, 10% of the samples from schools, and 10% of samples from flower shops. None of the samples taken from the electronics shops, the computer recycling shop, or bars, where cigarette smoking had occurred, had quantifiable Be concentrations.

Discussion

This pilot survey provides a small snapshot into the potential widespread occurrence of Be at worksites where workers are generally not considered to be at risk from exposure to commercial Be containing products. The proportion of wipes in this survey that had quantifiable Be levels above the LOQ was 46%, as compared to 72% in the study conducted by Sanderson et al. (9). However, the sampling results from the Sanderson et al. study were highly influenced by the high number of samples with detectable Be concentrations from one workplace, a paper processing site. Overall, the proportion of samples that contained Be concentrations above the DOE reference limit of 0.2 μg/100 cm^2 for release of items to the public was very similar in this study (12%) as compared to the Sanderson et al. study (7%).

The ceramics shop, coal burning power plant, fertilizer co-op, and one of the three dental labs exhibited the highest proportions of Be concentrations exceeding 0.2 μg/100 cm^2. One interesting finding was that the management at some of the study sites including the auto repair shops, ceramic shop, feed/fertilizer shop, and fertilizer co-op that exhibited a greater proportion of quantifiable Be concentrations reported that they were not aware that their workers may have been working with materials containing Be.

Three different sites, including a machine/electronic shop, one of the dental labs, and a fertilizer co-op, exhibited levels that exceeded the DOE's 3.0 μg/100 cm^2 reference level (see Table I). The management at the machine/electronic shop and the dental lab were the only sites that reported awareness of working with commercial Be products in the past, while the management of the fertilizer co-op did not report any known Be-related work (Table II). It is not surprising that workers who do not work with commercial Be products containing greater than 0.1% Be are not aware of their potential Be exposure from products or materials containing naturally occurring Be. Dental lab management had the greatest awareness of the potential risks of working with Be likely because the use of Be in the dental field is widely known. Management at the three labs self-reported correctly, based on the study findings that they had worked with the metal. The management at the coal-burning power plant also reported that they previously had detected Be in their dust samples. No workers at any of the worksites were observed wearing respiratory protection at the time of the survey.

In addition to knowing when personal protective equipment is required or if decontamination of the work area is needed, it is essential that workers who are exposed to respirable airborne Be particles are aware of their potential for exposure as this information is often vital for a proper diagnosis of CBD (17). While the data indicate that there is the potential for Be exposure at some work environments that are not generally considered at risk for Be exposure; it is not clear from these results what the risk might be to these workers for developing CBD from these exposures. However, it has been previously documented that exposures to even low levels of Be or exposures over a short period of time (e.g., genetically-susceptible individuals with brief exposures, bystander exposure, etc.) can lead to sensitization and CBD (18-24). In addition, since the samples were collected from deposits on elevated surfaces whenever possible, it is likely that at least some the particles accumulated through airborne deposition may have been available for inhalation at some point in time depending on their size. However, the authors are not aware of any valid method to extrapolate surface sample data to airborne concentrations or to sensitization risk.

There are several limitations of this study. First, while Be was detected in surface wipe samples, the sampling method collects all forms (e.g., various physicochemical properties, various size fractions, etc.) of Be that may vary in their ability to cause Be-related adverse health effects. Second, surface wipe samples were intentionally taken from areas with a large amount of dust accumulation which were generally estimated to be years to decades old. Therefore, it was impossible from this study to determine if the Be deposition occurred over extended periods of time or from short term or singular events. In addition, site-specific housekeeping practices can markedly affect time based accumulation. Third, even though sampling was performed by only two of the authors within a 3-week period, there may have been slight differences in pressure applied while sampling, or differences in the effectiveness of the method to efficiently collect dust based on varying surfaces (e.g., irregular, porous, or rough surfaces). Finally, because the selection of work locations was based on convenience sampling and a low number of samples per worksite, the generalizability of the findings of this study is not known.

Santo Thomas (25) previously stressed that physicians should explore possible exposure to beryllium in work environments where the potential for Be exposure may not be well documented, while acknowledging that the limited availability of the BeLPT restricts its routine use in cases of suspected Be exposure. In addition, the strict time requirement, of less than 24 hours, between time of blood draw and set up of the sample at one of the four labs that currently perform BeLPTs in the U.S. reduces the willingness of physicians to order the test.

Because of the potential for occupational Be exposures occurring at a wide range of work sites that was suggested in this study, the authors recommend focused testing of beryllium sensitivity in cohorts with a high prevalence of sarcoidosis. For example, the highest concentration (i.e., 6.1 $\mu g/100\ cm^2$) of Be measured in this limited survey was at a fertilizer co-op. Deubelbeiss et al. (26) has previously reported that the prevalence of sarcoidosis was higher than expected in regions with intense agriculture where there is an increased use of mineral fertilizers. Rather than performing wide-scale surveys for beryllium in occupations not thought to be at risk from Be exposure, from a cost effectiveness viewpoint, a more appropriate research approach may be to increase BeLPT testing in case-series of sarcoidosis patients who worked in specific industries (e.g., fertilizer-exposed workers) and perform testing for beryllium sensitization.

References

1. Henneberger P, Goe S, Miller W, Doney B, Groce D. Industries in the United States with airborne beryllium exposure and estimates of the number of current workers potentially exposed. J Occup Environ Hyg 2004; 1:648-659.
2. IARC, International Agency for Research on Cancer, Monographs on the Evaluation of Carcinogenic Risks to Humans. A review of human carcinogens: arsenic, metals, fibres, and dusts, beryllium and beryllium compounds. vol. 100C; 2012. Available at: http://monographs.iarc.fr/ENG/Monographs/vol100C/mono100C-7.pdf. Accessed May 16, 2013.
3. Field RW, Withers BL. Occupational and environmental causes of lung cancer, Clinics in Chest Medicine 2012; 33(4):681-703.
4. Samuel G, Maier LA. Immunology of chronic beryllium disease. Curr Opin Allergy Clin Immunol 2008; 8:126–134.
5. Tinkle SS, Antonini JM, Rich BA, et al. Skin as a route of exposure

and sensitization in chronic beryllium disease. Environ. Health Perspect 2003; 111(9): 1202–208.
6. Newman LS, Mroz MM, Balkissoon R, Maier LA. Beryllium sensitization progresses to chronic beryllium disease: a longitudinal study of disease risk. Am J Respir Crit Care Med. 2005; 1;171(1):54-60.
7. Federal Register, Office of Federal Register, Chronic Beryllium Disease Prevention Program, Federal Register 64(235) (December 8, 1999), pp. 68854-68914.
8. US EPA. (2005). World Trade Center Residential Dust Cleanup Program. United States Environmental Protection Agency, Region 2 New York City Response and Recovery Operations, New York, NY.
9. Sanderson W, Leonard S, Ott D, Fuortes L, Field RW. Beryllium surface levels in a military ammunition plant. J Occup Environ Hyg 2008; 5(7): 475-481.
10. Fireman E, Haimsky E, Noiderfer M, Priel I, Lerman Y. Misdiagnosis of sarcoidosis in patients with chronic beryllium disease. Sarcoidosis Vasc Diffuse Lung Dis 2003; 20: 144–148.
11. Müller-Quernheim J, Gaede KI, Fireman E, Zissel G. Diagnoses of chronic beryllium disease within cohorts of sarcoidosis patients, Eur Respir J. 2006 ;27(6):1190-5.
12. Sprince NL, Kazemi H, Hardy HL. Current (1975) problem of differentiating between beryllium disease and sarcoidosis. Ann NY Acad Sci 1976; 278: 654-664.
13. Stange AW, Furman FJ, Hilmas DE. The beryllium lymphocyte proliferation test: Relevant issues in beryllium health surveillance. Am J Ind Med 2004; 46(5): 453-462.
14. IDNR, Iowa Department of Natural Resources, The Iowa State-Wide Trace Element Soil Sampling Project: Design and Implementation, A Report of the Iowa Component of the United States Geological Survey, National Geochemical Survey, Iowa Department of Natural Resources, Prepared by Robert D. Rowden, Geologist, Iowa Geological and Water Survey, Iowa City, IA. 2010.
15. Dragun J and Chiasson A. 1991. Elements in North American Soils. Hazardous Materials Control Resources Institute, Greenbelt, MD, U.S.
16. NIOSH, National Institute for Occupational Safety and Health. 1994. Elemental Analysis (Method 7300), Cincinnati, OH: NIOSH Manual of Analytical Methods (NMAM), 4th ed. DHHS/NIOSH Pub. No. 94-113.
17. Newman LS, Rose CS, Maier LA. Sarcoidosis, N Engl J Med 1997; 336(17): 1224-1234.
18. Eisenbud M, Wanta R, Dustan C. Non-occupational berylliosis. J Ind Hyg Toxicol 1949; 31:282-294.
19. Newman L, Kreiss K. Nonoccupational beryllium disease masquerading as sarcoidosis: identification by blood lymphocyte proliferative response to beryllium. Am Rev Respir Dis 1992; 145(5):1212-1214.
20. Kreiss, K, Wasserman S, Mroz M, Newman L. Beryllium disease screening in the ceramics industry. J Occup Med 1993; 35: 267-274.
21. Stange A, Furman F, Hilmas D. Rocky Flats beryllium health surveillance. Environ Health Persp 1996; 104(Suppl 5): 981-986.
22. Barna BP, Culver DA, Yen-Lieberman B, Dweik RA, Thomassen MJ. Clinical application of beryllium lymphocyte proliferation testing. Clin Diagn Lab Immuno 2003;10(6):990–994.
23. Schuler CR, Kent MS, Deubner DC, Berakis MT, McCawley M, Henneberger PK, Rossman MD, Kreiss K. Process-related risk of beryllium sensitization and disease in a copper-beryllium alloy facility. Am J Ind Med 2005; 47: 195-205.
24. McCleskey TM, Buchner V, Field RW, Scott BL. Recent advances in understanding the biomolecular basis of chronic beryllium disease: a review, Reviews on Environmental Health 2009; 24(2):75-115.
25. Santo Tomas, L.H. Beryllium hypersensitivity and chronic beryllium lung disease. Current Opinion in Pulmonary Medicine 2009; 15(2): 165–169.
26. Deubelbeiss U, Gemperli A, Schindler C, Baty F, Brutsche MH. Prevalence of sarcoidosis in Switzerland is associated with environmental factors. Eur Respir J 2010; 35: 1088–1097.