AMERICAN THORACIC SOCIETY DOCUMENTS

An Official American Thoracic Society Statement: Diagnosis and Management of Beryllium Sensitivity and Chronic Beryllium Disease

Executive Summary

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Rationale: Beryllium continues to have a wide range of industrial applications. Exposure to beryllium can lead to sensitization (BeS) and chronic beryllium disease (CBD).

Objectives: The purpose of this statement is to increase awareness and knowledge about beryllium exposure, BeS, and CBD.

Methods: Evidence was identified by a search of MEDLINE. The committee then summarized the evidence, drew conclusions, and described their approach to diagnosis and management.

Main Results: The beryllium lymphocyte proliferation test is the cornerstone of both medical surveillance and the diagnosis of BeS and CBD. A confirmed abnormal beryllium lymphocyte proliferation test without evidence of lung disease is diagnostic of BeS. BeS with evidence of a granulomatous inflammatory response in the lung is diagnostic of CBD. The determinants of progression from BeS to CBD are uncertain, but higher exposures and the presence of a genetic variant in the HLA-DP β chain appear to increase the risk. Periodic evaluation of affected individuals can detect disease progression (from BeS to CBD, or from mild CBD to more severe CBD). Corticosteroid therapy is typically administered when a patient with CBD exhibits evidence of significant lung function abnormality or decline.

Conclusions: Medical surveillance in workplaces that use beryllium-containing materials can identify individuals with BeS and at-risk groups of workers, which can help prioritize efforts to reduce inhalational and dermal exposures.

Contents

Overview

Many workers are exposed to beryllium throughout the world, and sensitization to the metal continues to occur. To address this problem, an international committee of experts was convened to write a statement about beryllium sensitization (BeS) and chronic beryllium disease (CBD). After thoroughly reviewing the literature, the committee summarized the relevant evidence, drew conclusions, and described their usual approach to diagnosis and management.

- The beryllium lymphocyte proliferation test (BeLPT) is used for medical surveillance and the diagnosis of BeS and CBD. A BeLPT is considered "abnormal" if two or more of the six stimulation indices exceed the normal range. A test is typically considered "borderline" if only

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one of the six stimulation indices exceeds the normal range.

- A diagnosis of BeS in beryllium-exposed workers undergoing medical surveillance can be based on two abnormal blood BeLPTs, one abnormal and one borderline blood BeLPT, or one abnormal bronchoalveolar lavage (BAL) BeLPT. Workers identified as having BeS are evaluated for CBD.
- Pulmonary function testing (PFT) and chest imaging (either a chest radiograph or chest computed tomography scan) are typically performed when the BeLPT is diagnostic of BeS. Bronchoscopy with transbronchial biopsy is performed on a case-by-case basis. The following considerations favor performing bronchoscopy: (*1*) absence of contraindications, (*2*) evidence of pulmonary function abnormalities, (*3*) evidence of abnormalities on chest imaging, and (*4*) personal preference of the patient.
- The diagnosis of CBD is based on the demonstration of both BeS and granulomatous inflammation on lung biopsy. Depending up the clinical setting, feasibility of certain diagnostic tests, and degree of diagnostic certainty needed, probable CBD can be diagnosed based on differing diagnostic criteria, including a clinical presentation consistent with CBD, a history of beryllium exposure, evidence of BeS (e.g., abnormal BeLPT), radiographic findings, lung histology, BAL findings, and PFT abnormalities.
- Periodic evaluation (every 1–3 yr) is performed to determine if an individual with BeS has progressed to CBD. It includes a symptom review, physical examination, and PFT, followed by a chest computed tomography scan if pulmonary function has deteriorated and bronchoscopy on a case-by-case basis.
- Corticosteroid therapy is initiated when a patient with CBD exhibits significant lung function abnormality or decline. Steroid-sparing agents are considered if significant side effects occur.
- Medical surveillance in workplaces that use beryllium-containing materials can identify individuals with BeS and at-risk groups of workers, which can help prioritize efforts to reduce inhalational and dermal exposures. The BeLPT is the cornerstone of medical surveillance. Individuals with beryllium exposure who do not have BeS at the time of initial evaluation remain at future risk and may benefit from periodic BeLPTs.

Introduction

Beryllium is a naturally occurring element that is extracted from ores and processed into metal, oxides, alloys, and composite materials. The major applications of beryllium are in automotive electronics, telecommunications, computers, aerospace, and defense equipment (Table 1 in the full-length version, which is available online only). Industrial use of beryllium, such as machining metal parts, can lead to BeS and CBD (1). In the United States, it has been estimated that up to 134,000 workers are currently exposed to beryllium (2); presumably, the number of ever-exposed individuals is much greater. Internationally, CBD has been reported in many countries (3–10). Despite its prevalence, BeS and CBD may be unrecognized because workers are unaware of their exposure and/or physicians are unaware of beryllium-related health effects. This statement reviews current knowledge about BeS and CBD, including its diagnosis, management, and prevention.

Methods

The chair of the committee was selected by the leadership of the American Thoracic Society. Committee members were selected to participate based on their expertise in BeS and/or CBD. Prospective members of the committee were required to disclose all financial interests relevant to the subject matter of the statement. Disclosures were reviewed by the American Thoracic Society prior to appointment of the committee, and appointments were made according to American Thoracic Society policies for management of conflicts of interest. In addition, individuals with conflicts of interest related to the subject matter of the statement acknowledged those conflicts in a face-to-face meeting, stated that they would not bias their participation on the committee, and were not assigned to work on sections of the document that addressed issues related to their conflict.

Committee members independently searched the medical literature through December 2012 using MEDLINE. Bibliographies of the selected studies were also searched. Selected studies were appraised, discussed, and summarized. The literature searches, study selections, and appraisals were author directed. They did not conform to the standards of a systematic review. Structured discussions were used to determine the committee members' usual approach to the diagnosis and management of BeS and CBD. Variations in clinical practice were infrequent and minor; therefore, the approach described reflects the committee's collective clinical experience in occupational health programs.

The committee's work was supported by the U.S. Department of Energy, the National Institute for Occupational Safety and Health, and American Thoracic Society. The methods used to develop this statement are summarized in Table 1.

Epidemiology

The BeLPT is the primary screening tool for BeS and CBD (11–13) and, therefore, the test used for most epidemiological studies. Cross-sectional studies of workers in various U.S. industries found that the prevalence of BeS ranged from 0.9 to 14.6%, and the prevalence of CBD ranged from 0.0 to 7.8% (12, 14–26, 37, 106) (Table 1 in the full-length version, which is available online only). Longitudinal cohort studies showed that 1.0 to 16.2% of exposed workers developed BeS and 0.0 to 11.0% developed CBD (27–33, 35, 36, 45). Table 2 provides the estimated prevalence of BeS and CBD associated with various jobs or work processes.

Higher estimates of total and respirable beryllium concentration were associated with BeS (highest-exposure job worked, average exposure) and CBD (cumulative exposure) in a study of exposure–response relationships performed in a manufacturing plant (37). However, the body of evidence pertaining to exposure–response relationships has been inconsistent. No association was found in some studies, whereas the association did not reach statistical significance in other studies (i.e., the effect would have been clinically important if real, but the confidence intervals were wide due to relatively few events and included no effect) (16, 17, 38). The absence of a definitive relationship between the airborne beryllium level and the risk of BeS and CBD raises the possibility that other routes (e.g., dermal), genetic susceptibility, and/or other factors may be important in determining sensitization to beryllium and/or CBD (34, 39–52).

Pathogenesis

Engagement of a surface T-cell receptor with a major histocompatibility complex (MHC) II molecule on the surface of antigen-

Table 1. Methods

	Yes	No
Panel assembly		
Included experts from relevant clinical and nonclinical disciplines	X	
Included individual who represents patients and society at large		X
Included methodologist with appropriate expertise		X
Literature review		
Performed in collaboration with a librarian		X
Searched multiple electronic databases		X
Reviewed reference lists of retrieved articles	X	
Evidence synthesis		
Applied prespecified inclusion and exclusion criteria		X
Evaluated included studies for sources of bias	X	
Explicitly summarized benefits and harms		N/A
Used PRISMA to report systematic review		N/A
Used GRADE to describe quality of evidence		N/A
Generation of recommendations		
Used GRADE to rate the strength of recommendations		N/A

Definition of abbreviations: GRADE = Grading of Recommendations Assessment, Development and Evaluation; N/A = not applicable; PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

presenting cells in the presence of beryllium activates beryllium-specific $CD4^+$ T cells, inducing an oligoclonal expansion specific for both beryllium and compartmentalization to the lung (53–55) (Figure 1). Noncaseating granulomas develop (56–59), which usually include multinucleated giant cells. The morphology of the granuloma may vary from a loosely formed collection of a few epithelioid histiocytes with scattered lymphocytes to a well-formed one. The distribution of granulomas is similar to sarcoidosis: the subpleura, adjacent to bronchovascular bundles, and within interlobular septae. Beryllium-containing particles may be demonstrated within CBD granulomas (60–62).

Genetic susceptibility contributes to the development of BeS and the progression of BeS to CBD (63). Multiple studies have confirmed that polymorphism of the HLA-DP β_1-chain gene is associated with susceptibility to beryllium-induced disease (65–73). As an example, *HLA-DPB1* alleles coding for a glutamic acid residue at position 69 of the β-chain (Glu^{69}) are strongly associated (i.e., odds ratios consistently >10) with an increased risk of both BeS and CBD. The magnitude of the risk for CBD varies among the Glu69 alleles.

Diagnostic Criteria

BeLPT

The blood BeLPT is the primary diagnostic tool for identifying BeS (11–13, 35, 74–77). Lymphocytes are isolated from heparinized peripheral venous blood or BAL fluid and then placed in culture in the presence and absence of beryllium sulfate, across a three-log range of salt concentrations. Cell proliferation is measured by the incorporation of tritiated thymidine into dividing cells at two different time points (after Day 4 or 5 and Day 6 or 7 in culture). Positive control samples are incubated with nonspecific mitogens, such as phytohemagglutinin A or concanavalin A, or antigens, such as tetanus toxoid or *Candida albicans*. Results are expressed as a stimulation index (SI), which is the ratio of the counts per minute of radioactivity in cells stimulated with beryllium salts divided by the counts per minute in unstimulated cells (78).

A BeLPT is considered "abnormal" if two or more of the six stimulation indices exceed the normal range, "borderline" if one of the six stimulation indices exceeds the normal range, and "normal" if all six stimulation indices are in the normal range (79). A BeLPT is considered "uninterpretable" if it cannot be determined whether it is abnormal, borderline, or normal. This can occur when there are high radioactivity counts in the unstimulated control cells, low radioactivity counts in the positive control cells, or high variability across the beryllium-exposed wells. The BeLPT is usually repeated to confirm the initial results (77, 80). Borderline results are typically repeated by splitting the repeat samples and then sending them to two different laboratories (79).

There is no gold standard for BeS, so receiver operating characteristics for the BeLPT can only be estimated. CBD based on histology or two abnormal BeLPTs has been used as the standard from which to estimate receiver operating characteristics. The BeLPT appears to be highly specific for the detection of BeS (77, 80–82), although estimates of its sensitivity vary widely (13, 14, 17, 22, 27, 77, 83–85). In an analysis of U.S. Department of Energy surveillance data (77), a single BeLPT detected BeS (defined as two abnormal BeLPTs) with a sensitivity of 68.3% and a specificity of 96.9%. Reanalysis using a modified approach (i.e., the repeat blood sample was split between two laboratories and an initial abnormal test was considered to have been confirmed if the repeat test had an abnormal or borderline result) found that the BeLPT had both a high sensitivity and specificity (81, 82). An enhanced approach (i.e., both the initial and repeat blood samples were split and the criterion for BeS was at least one abnormal test and one borderline test) improved sensitivity of the BeLPT to 88% without sacrificing specificity (81).

An alternative test for the presence of a beryllium-specific immune response is the beryllium patch test. Use of the patch test is primarily historic, because it can lead to sensitization in beryllium-naive individuals (86).

Diagnostic Criteria for BeS

Individuals who have evidence of a beryllium-specific immune response without beryllium-related lung disease are considered to have BeS without CBD (76, 78, 87). A beryllium-specific immune response is confirmed by demonstration of any of the following: two abnormal peripheral blood BeLPTs, one abnormal and one borderline peripheral blood BeLPT, one abnormal BAL BeLPT, or a positive skin patch test (88). Some individuals believe that three borderline peripheral blood BeLPTs may also indicate sensitization (89).

Diagnostic Criteria for CBD

A diagnosis of CBD is based on confirmation of an immune response to beryllium and granulomatous inflammation on lung biopsy (88, 90). Depending on the clinical setting, feasibility of certain diagnostic tests, and degree of diagnostic

Table 2. Process-related Risk of Beryllium Sensitization and Chronic Beryllium Disease by Type of Industry

Industry (Reference)	Job or Process	BeS (%)	CBD (%)
Nuclear weapons facility (14)*	Machinists	4.7	N/A
	Metallurgical operator	4.6	
Beryllia ceramics (22)	Dry pressing	15.8	15.8
	Process development/engineering	13.6	13.6
	Ventilation maintenance	11.1	11.1
Beryllia ceramics (15)†	Lapping‡	20.0	N/A
	Machining	14.3	
Beryllium metal, alloy, and oxide production (16)§	Ceramics production	11.6	9.0
	Be metal pebble plant‖	13.4	5.2
	Analytic laboratory¶	20.0	4.0**
Beryllia ceramics (17)†,††	Lapping	21.1	N/A
	Machining	17.5	
	Forming	15.6	
	Firing	14.9	
Nuclear weapons facility (28)*	Beryllium machinists	11.9	8.5
	Health physics	11.9	4.8
	Construction trade	10.0	2.6
Copper-beryllium alloy finishing (20)	Point and chamfer‡‡	21.4	21.4
	Wire pickling and annealing	12.5	10.3
	Wire drawing	13.6	9.5
Beryllium metal, alloy, and oxide production (37)§,§§	Be metal pebbles plant/Be oxide	26.9	5.0**
	Alloy melting and casting	14.8	5.2
	Maintenance	18.0	2.4**

Definition of abbreviations: BeS = beryllium sensitization; CBD = chronic beryllium disease; N/A = not applicable.
Results presented are significant at the $P < 0.10$ or lower level. Adapted by permission from Reference 34.
*Same facility (14, 28).
†Same facility (15, 17).
‡Lapping is a machining operation in which two surfaces are rubbed together with a liquid containing an abrasive grit.
§Same facility (16, 37).
‖All ceramics workers removed from this analysis.
¶All ceramics and pebble plant workers removed from this analysis.
**Results not significant.
††Results are for longer-term workers (employed ⩾6 yr; first surveyed in 1992 but none had BeS at that time).
‡‡Chamfer (here) is the process of putting a beveled edge on a rod.
§§Results are for shorter-term workers (employed ⩽6 yr).

certainty needed, probable CBD can be diagnosed based on differing diagnostic criteria, including a clinical presentation consistent with CBD, a history of beryllium exposure, evidence of BeS (e.g., abnormal BeLPT), radiographic findings, lung histology, BAL findings, and PFT abnormalities. For example, when BeS is confirmed but a lung biopsy is not done or is not possible, a probable diagnosis of CBD can be based on either imaging consistent with sarcoidosis or BAL lymphocytosis (88, 90). It should be recognized that certain diagnostic findings (e.g., an abnormal BeLPT, lung granulomas) lead to greater diagnostic certainty than others (e.g., nonspecific interstitial changes on chest radiographs or pulmonary function deficits).

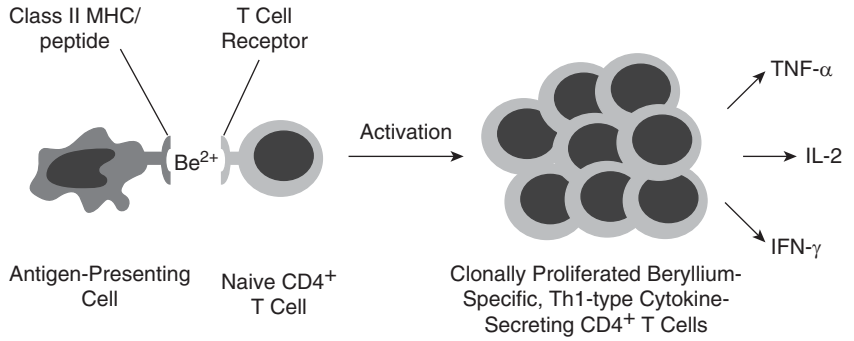

Figure 1. Immune response to beryllium. After the inhalation of beryllium-containing particulates, antigen-presenting cells expressing the major histocompatibility complex (MHC) molecule, HLA-DP, with a glutamic acid at amino acid position 69 of the β-chain present beryllium to $CD4^+$ T cells. This results in T-cell activation, proliferation, and Th1-type cytokine production (e.g., IFN-γ, IL-2, and tumor necrosis factor [TNF]-α). IFN-γ and TNF-α promote macrophage accumulation, activation, and aggregation, which lead to the development of granulomatous inflammation and eventually lung fibrosis.

Evaluation

Clinical Manifestations of BeS and CBD

BeS and CBD are increasingly identified by workplace surveillance programs when individuals are relatively asymptomatic, with normal lung function and chest imaging (19, 76, 78, 91), although progression to severe CBD still occurs (92, 93). Symptom onset is insidious in CBD

and may include exertional dyspnea, fatigue, cough, and chest discomfort (92, 94–96). Patients with early disease typically have a normal physical examination, although inspiratory crackles may develop as the disease progresses (22, 90). Symptoms and signs may emerge many years after cessation of exposure to beryllium.

PFT can show obstruction, restriction, a mixed process, and/or an isolated reduction of the diffusing capacity for carbon monoxide. Obstruction is the most common abnormality (97–99). Normal PFT is also common, especially among individuals who have subclinical disease identified by BeLPT (99). Cardiopulmonary exercise testing may detect ventilatory and gas exchange abnormalities (99).

Chest radiographs in CBD are similar to those of sarcoidosis, except mediastinal and hilar lymphadenopathy are less common and are usually accompanied by parenchymal opacities (100). Computed tomography (CT) scans generally reveal nodules clustered together around bronchi, within interlobular septa, or in the subpleural region. Ground-glass opacities, bronchial wall thickening, and thickening of interlobular septa are also seen (100–104). In advanced disease, honeycombing, subpleural cysts, calcification, and conglomerate masses may be found.

The lung is the primary organ affected by CBD. Extrathoracic organ involvement occurs (92, 94–96), but it is rare and generally unimportant clinically (Table 3).

Table 3. Clinical Differences between Sarcoidosis and Chronic Beryllium Disease

Clinical Finding	CBD	Sarcoidosis
Beryllium lymphocyte proliferation test	Abnormal	Normal
Ophthalmologic	Conjunctivitis only	Conjunctivitis, uveitis, retinal involvement
Erythema nodosum	No	Yes
Lupus pernio	No	Yes
Onset	Insidious	Acute or insidious
Neurologic involvement	None	Can involve the central or peripheral nervous system
Cardiac involvement	Rare	Occasional
Hepatic involvement	Occasional	Common
Isolated hilar adenopathy	Very rare	Common
Extrapulmonary manifestations without pulmonary involvement	No	Yes

Definition of abbreviation: CBD = chronic beryllium disease.

Diagnostic Evaluation for BeS and CBD

When a patient presents with possible beryllium exposure, sarcoidosis, or interstitial lung disease, a thorough occupational history is obtained. This history includes questions regarding work in industries with known beryllium use (Table 5 in the full-length version, which is available online only). Because the latency between exposure and disease can be long, potential beryllium exposure should be assessed throughout the patient's lifetime (17, 27, 29, 34, 35). The diagnosis should be considered in any individual with a history of working in a beryllium-using industry, because CBD has been reported in individuals with seemingly minimal exposures (14, 16, 21, 22, 27, 35, 64). A history of exposure to beryllium is not necessary to make the diagnosis of BeS or CBD.

Diagnostic testing begins with a BeLPT. For those patients with BeS according to the BeLPT (see diagnostic criteria for BeS above), PFT and chest imaging (either a chest radiograph or chest CT scan) are performed. The sensitivity and specificity of these tests for CBD are less than that of tissue sampling via bronchoscopy with transbronchial biopsy because pulmonary function and radiographic abnormalities usually do not emerge until the parenchymal disease has progressed. The decision of whether or not to perform bronchoscopy in patients with BeS is made on a case-by-case basis.

Criteria favoring bronchoscopy include: (*1*): absence of contraindications, (*2*) evidence of pulmonary function abnormalities, (*3*) evidence of abnormalities on chest imaging, and (*4*) personal preference of the patient. Patients with a negative bronchoscopy remain at risk for the subsequent development of disease and require ongoing follow-up (35). Tissue sampling is controversial in patients with BeS who have no pulmonary function or radiographic abnormalities. Arguing for tissue sampling is the observation that a significant percentage (14–100%) of patients with BeS have CBD on histologic examination of lung tissue at the time of their initial evaluation (35), and confirmation of CBD determines disease status and guides subsequent management. Arguing against tissue sampling is that treatment will not be initiated until the patient develops lung function abnormalities (105).

The bronchoscopic procedure typically includes both BAL and transbronchial biopsies. BAL fluid is sent for the following: mycobacterial and fungal stains and cultures, a differential cell count to detect lymphocytic alveolitis, and a BeLPT. A large-volume lavage (e.g., four 30–60 ml aliquots in each of the two subsegments of the middle lobe or lingula for a total of 240–480 ml) is performed to obtain sufficient viable lymphocytes for the BeLPT (11, 90, 105). The BAL fluid is rapidly processed so that cells can be shipped to the laboratory without delay. BAL typically reveals a lymphocytosis in CBD, with lymphocyte values greater than 20% (76, 107).

Transbronchial biopsies are performed to obtain tissue to look for granulomas and/or mononuclear interstitial infiltrates, which are consistent with CBD. The number of lung tissue pieces needed for a definitive evaluation for CBD has not been studied, but an approach similar to that used for sarcoidosis seems reasonable (59). Histochemical studies for fungal and mycobacterial organisms should be performed on the tissue specimens to rule out infectious granulomatous disease.

Other diseases may present similarly and should be considered whenever CBD is suspected. These include sarcoidosis, tuberculosis, atypical mycobacterial infections, hypersensitivity pneumonitis, granulomatous disease due to other metals (e.g., aluminum or titanium), and idiopathic pulmonary fibrosis. CBD is differentiated from these diseases by the presence of a beryllium-specific immune response.

Natural History and Management

Natural History and Management of BeS

Two overlapping case series reported that the rate of progression from BeS to CBD is as high as 8.8% over a period of up to 20 years (35, 109). However, other studies have found little or no evidence of progression from BeS to CBD (69, 112). Whether or not continued exposure increases the risk of progression from BeS to CBD is uncertain. However, the possibility that it may be a contributing factor (36) is supported by the observations that nuclear weapons workers have an increased risk of CBD with higher cumulative exposures (110, 111), machinists may have a higher risk of progression (35), and individuals who work in low-exposure settings are less likely to have CBD at the time of their initial evaluation (17, 23). Some individuals with BeS never develop CBD (35, 40). Based on the limited evidence, it seems prudent for workers with BeS to avoid all future occupational exposures to beryllium, even though wage and job loss can occur when a worker is medically precluded from further exposure to beryllium (88).

Periodic medical evaluation (every 2–3 yr, or yearly if there is concern for disease progression) is performed to determine if an individual with BeS has progressed to CBD (106). Evaluation includes a symptom review, physical examination, and PFT. These are followed by a chest CT scan if pulmonary function has deteriorated and bronchoscopy on a case-by-case basis (35, 87, 88, 108, 109, 112).

Natural History and Management of CBD

Patients with CBD generally demonstrate a faster decline in lung function than individuals with BeS alone (109), although the natural history of CBD is variable (40, 87, 92, 93, 95, 97, 105, 109, 112). Patients may be initially asymptomatic, with some remaining symptom-free and others progressing to clinically significant disease. Alternatively, patients may be symptomatic at presentation and experience a gradual downhill course. Spontaneous reversal is rare (92, 97, 113).

Patients with CBD are followed at least annually, with the frequency dictated by the severity of disease and the need for treatment. Those with severe disease, rapidly progressive disease, or a need for pharmacological therapy are seen more frequently.

Risk factors for progression of CBD need further investigation. There is limited evidence that removal of the worker from exposure will result in improvement (114). Medical therapy of CBD is directed at suppressing the immune response to beryllium and subsequent granuloma formation and fibrosis. The decision to initiate treatment is based on symptoms and PFT results and not solely on the radiographic findings. Patients with a significant abnormality or decline in lung function typically receive pharmacological therapy.

Systemic corticosteroids are used as first-line therapy unless there is a contraindication (115). Treatment of CBD (including the steroid dose and regimen) is based on the approach used in sarcoidosis, given the clinical, histopathologic, and radiographic similarities of the diseases (116). Prednisone is generally started at 20 to 40 mg daily or every other day for 3 to 6 months, with the exact duration determined by how long it takes to maximize the improvement in lung function. The dosage may then be reduced gradually using PFT to assess for evidence of relapse. Relapse often occurs, prompting the dosage to be increased to the level that previously stabilized or improved pulmonary function. Lifetime treatment with corticosteroids is often necessary, but a dose reduction is generally tried every 2 to 3 years.

A randomized trial evaluating the effects of corticosteroids in CBD has never been performed, but observational evidence suggests that they are beneficial (10, 92, 114, 117, 118, 119), with improvement of pulmonary function, radiographic abnormalities, respiratory symptoms, and functional status. If significant side effects are experienced, steroid-sparing therapy is considered (e.g., methotrexate, azathioprine, cyclophosphamide, mycophenolate, and infliximab).

Immunosuppressive therapy is accompanied by supportive and preventive therapies, as indicated for other types of interstitial lung disease. Lung transplantation has been used in a few patients with end-stage CBD, but its effectiveness is unknown. Workers' compensation programs typically recognize CBD as a compensable occupational illness.

Prevention

Controlling exposure to beryllium is advocated by occupational health experts for any facility that uses beryllium-containing products (1). The goals of a control program are to limit inhalation and dermal exposures as much as possible and reduce the number of employees who are directly or indirectly exposed. This may be achieved (listed in descending order of effectiveness) by elimination or substitution, engineering controls (e.g., process confinement, local ventilation), personal protective equipment, and administrative changes (e.g., exclusions from certain jobs). Recent work that resulted from a collaboration of National Institute for Occupational Safety and Health with the United States' primary producer of beryllium products suggests that a rigorous and comprehensive approach to workplace control of exposure to beryllium can successfully reduce the incidence of BeS (31–33). If BeS can be prevented or reduced, then it is reasonable to expect that CBD might also be prevented or reduced.

Reduction of exposure concentration is unlikely to prevent all cases of BeS or CBD (34). Medical surveillance in workplaces that use beryllium-containing materials can identify workers with BeS so that they can be managed as described above. The BeLPT is used for medical surveillance of beryllium-exposed workers (1). Individuals with beryllium exposure who do not have BeS at the time of initial evaluation generally undergo periodic BeLPTs because they remain at future risk.

Additional benefits of medical surveillance include defining at-risk groups of workers, identifying hazardous jobs and processes, and prioritizing efforts to reduce inhalational and dermal exposures. Prevalence and incidence of BeS may be examined by risk factors such as job, task, or area by questionnaire or linking to administrative data. If process and exposure-related risks identified by surveillance are linked to preventive actions that reduce exposure, such as additional exposure controls, BeS and CBD may be reduced or prevented.

Preventive efforts do not have to wait until BeS or CBD is identified. Interventions can be directed at preventing cases through a comprehensive approach to improved control of exposures. Environmental monitoring data, if available, can be used to target areas and processes for interventions. ■

This official statement was prepared by an *ad hoc* subcommittee of the Environmental, Occupational, and Population Health Assembly.

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EDITOR'S NOTE: This document is a Clinical Statement and not a Clinical Practice Guideline, meaning that evidence-based recommendations for patient care are not provided and are beyond the scope of the document. The goal of a Statement is to discuss relevant evidence and describe how the expert co-authors apply the evidence in their clinical practices.

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