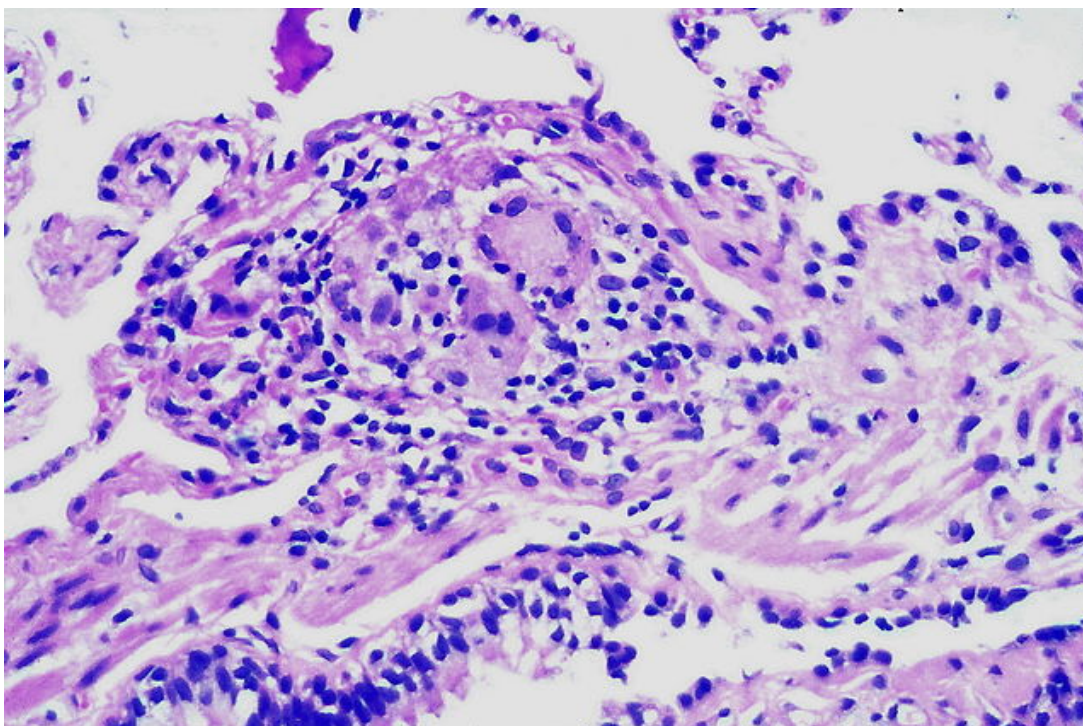


## Berylliosis — Symptoms and Treatment

[See online here](#)

**Inhalation of Beryllium (Be) dust, or its vapors or compounds, or subcutaneous implantation of Beryllium can lead to either acute or chronic beryllium disease, also known as berylliosis. It can affect genetically susceptible individuals or workers exposed to the fumes or vapors of the metal. It was first described by Hardy and Tabershaw in 1946. Beryllium can cause either an immediate acute form of illness or insidious chronic berylliosis.**



### Types of Berylliosis

Berylliosis is an occupational disease and **can affect the lungs as acute berylliosis or chronic berylliosis**. It is commonly associated with aerospace and nuclear industry workers.

#### Acute berylliosis

Acute berylliosis occurs due to **chemical irritation caused by the metal Beryllium**. It is characterized by sudden onset with rapid progression of **cough** and **dyspnea** due to a non-specific inflammatory pneumonitis. Occasionally, it may also involve the skin or the eyes. However, after the introduction of the **Be-exposure standards in 1949**, the occurrence of acute berylliosis has decreased remarkably.

## Chronic berylliosis

Chronic berylliosis occurs insidiously and progresses slowly over several years after initial exposure to Beryllium. It is characterized by **inflammatory granulomas in the subcutaneous tissues and liver**, with scarring and subsequent [interstitial pulmonary fibrosis](#).

## Epidemiology of Berylliosis



[Image](#): "Big crystalline fragment of Beryllium." by Alchemist-hp = Alchemist-hp (pse-mendelejew.de) - Own work. License: [CC BY-SA 3.0](#)

Of the individuals exposed to Beryllium, approximately 2—5 % may develop a **hypersensitivity granulomatous disease**, a condition known as chronic beryllium disease (CBD). The condition is commonly seen in workers exposed to high levels of Beryllium. The general population is rarely affected by this condition as the ambient Beryllium levels in the air are normally less than 0.03 ng/m<sup>3</sup>.

Adults are the most commonly affected individuals, although children with secondary exposure have also been reported to suffer from this condition. Berylliosis has no sex predilection with males and females being equally affected. No racial predisposition has been reported, although genetic susceptibility to the disease has been observed.

The estimated mortality rate of CBD ranges between 5.8 to 38 %. The reasons for this huge variability in mortality rates of CBD are unknown. The main morbidities of CBD are progressive decline in lung volume and diffusing capacity, pulmonary fibrosis, respiratory failure, and cor pulmonale.

## Pathophysiology and Presentation of Berylliosis

Beryllium is a **rare earth metal, which can form alloys with several other metals**. It was earlier used in fluorescent lights and is currently used in electronics, aerospace, dental alloys, ceramics and metal extraction industries.

Workers become exposed to Be by inhaling fumes or dust, or through contact with the

metal with skin. Following inhalation and over a period of time, **Beryllium acts as a hapten, or class II-restricted antigen**, stimulating the proliferation and accumulation of helper T-cells with a delayed hypersensitivity type reaction.

This initiates cellular events like changes in pulmonary permeability, production of pro-inflammatory cytokines and growth factors, which eventually lead to the formation of granulomas. Gradually, with the progression of the disease, the granulomas evolve to form fibrous nodules with subsequent impairment of pulmonary function.

The genetic susceptibility to Be is linked to HLA-DPB1 alleles, which possess a glutamic acid at the 69<sup>th</sup> position on the beta chain. Workers with the mutation in the Glu69 HLA-DPB1 position have a higher incidence of Beryllium sensitization and chronic berylliosis.

## Presentation of berylliosis

The rate of progression from Be sensitization to berylliosis cannot be predicted, although it may vary from 6 to 8 %. Symptoms may start within weeks to decades after initial exposure to the metal.

Initial symptoms may be innocuous and include **cough** and difficulty in breathing. There may be inspiratory rales on pulmonary auscultation, lymphadenopathy, cutaneous dermatitis or rash and hepatosplenomegaly. Other symptoms may include weight loss, chest pain, fever and joint aches.

## Differential Diagnosis of Berylliosis

Several conditions and diseases can mimic the signs and symptoms of berylliosis:

1. **Sarcoidosis**: This multisystem disease may resemble berylliosis, except that patients with sarcoidosis will not provide a history of exposure to Beryllium.
2. **Idiopathic pulmonary fibrosis**: Symptoms such as dyspnea and persistent dry cough may resemble those of berylliosis.
3. **Hypersensitivity pneumonitis**: Exposure to allergens or hard metals like cobalt, titanium dioxide or chromium can lead to chronic inflammation with extensive pulmonary scarring and thickening of pulmonary tissues with symptoms similar to those of berylliosis.
4. **Tuberculosis**: Tb is associated with caseating granulomas of histopathology versus the non-caseating granulomas seen in berylliosis.

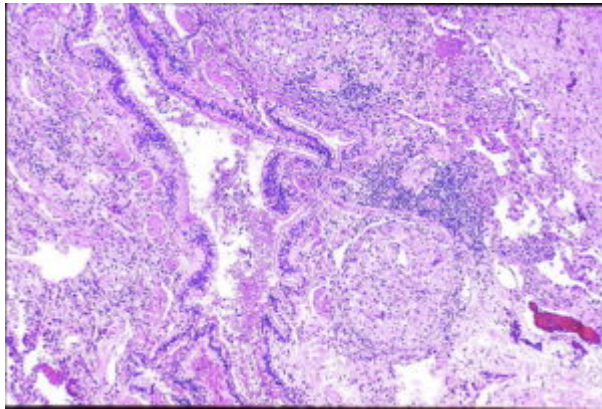
## Workup of Berylliosis

The workup consists of a thorough patient history with **details and duration of Be exposure, blood BePLT, bronchoscopy with bronchoalveolar lavage fluid, beryllium lymphocyte proliferation test (BePLT), pulmonary CT scan and biopsy of lung granulomas.**

Blood BePLT is the test of choice to diagnose Be-sensitization or berylliosis. The test, which is performed in a few specialized laboratories, consists of exposing mononuclear cells from peripheral blood to beryllium salts in vitro. A positive test is indicated by the proliferation of the cells in the presence of Be.

Chest radiographs appear normal in most patients although hilar lymphadenopathy and increased interstitial markings may be noted in some cases.

High-resolution CT scan is more useful than chest radiographs. Findings on CT scan include:



[Image](#): "Microscopic image of chronic berylliosis." by Yale Rosen from USA - Chronic berylliosis Uploaded by CFCF. License: [CC BY-SA 2.0](#)

- Upper lobe fibrosis
- Pulmonary nodules
- Diffuse interstitial fibrosis
- Traction bronchiectasis
- Interlobular septal thickening
- Hilar and mediastinal lymphadenopathy
- Occasional ground glass changes.

[Pulmonary function tests](#) including **spirometry, DLCO (diffusing capacity for carbon monoxide), lung volumes as well as [arterial blood gases](#) and cardiopulmonary exercise test** are performed to monitor disease progression. Spirometry may show restrictive or obstructive patterns or both. DLCO tends to decrease over the course of the disease. Abnormalities may be detected in gas exchange during exercise, and it is the most sensitive test.

Laser microprobe mass spectrographic analysis (LAMMS) is used to detect Be in lung biopsy specimens, but this test is only available in a few centers.

Bronchoscopy with bronchoalveolar lavage (BAL) and transbronchial biopsies is used to confirm the diagnosis. BePLT test is also performed on BAL cells. Bronchoscopy can be repeated if the findings of the first bronchoscopy are negative.

Open lung biopsy is warranted in rare cases when the diagnosis cannot be confirmed even after a repeat bronchoscopy.

Histopathology shows non-necrotizing (non-caseating) granulomas similar to the ones seen in [sarcoidosis](#).

## Diagnostic Criteria for Chronic Beryllium Disease

**For the accurate diagnosis of CBD, we suggest to use the following diagnostic criteria:**

- Evidence of beryllium exposure
- Evidence of an immune response to beryllium, i.e. positive responses in blood or bronchoalveolar lavage fluid in the beryllium lymphocyte proliferation tests

- Histopathological evidence consistent with CBD, i.e. non-necrotizing granulomas

## Treatment and Prognosis of Berylliosis

Preventive strategies form the crux of managing berylliosis. The mainstay of treatment is **advising patients with chronic berylliosis to avoid further exposure to Be**. Corticosteroids with regular monitoring of pulmonary function tests and high-resolution tomography may help to assess the progression of the disease. Oral corticosteroids, if started early in CBD, might not only halt the progression of the disease but actually induce some regression in CBD pathology.

However, once pulmonary fibrosis develops, even corticosteroids cannot reverse the disease. Methotrexate is an option for those patients who do not respond to corticosteroids. **Lung transplantation is the only known treatment** which can help to alleviate end-stage disease.

Affected individuals may have presentations ranging from no symptoms to severe symptoms, pulmonary dysfunction and death. Although the [lungs](#) are primarily affected, other organs like the [liver](#), extra-pulmonary lymph nodes, skin, salivary glands, myocardium, skeletal muscle, bones and [kidneys](#) may also be involved.

## Prevention of Berylliosis

This occupational disease can be prevented with **continuous monitoring of exposure, timely tests of beryllium sensitization and regular medical evaluation of workers for chronic berylliosis**. Workers can be advised to change their work clothing and shoes, shower and change into their civilian (non-work) clothes to decrease the risk of carrying the Be dust on their body back to their homes and families.

## References

[Chronic beryllium lung disease](#) via radiopaedia.org

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