

# History of Beryllium Disease

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# **Chemical Pneumonitis in Workers Extracting Beryllium Oxide**

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- **3 cases with presumed chemical pneumonitis**
- **Diffuse infiltrates, fever, shortness of breath**
- **Occurred during exposure to beryllium**
- **Resolved with removal from exposure**

**VanOrdstrand, Hughes, and Camody. Cleveland Clinic Q. 1943: 10, 10-18.**

# Delayed chemical pneumonitis in workers exposed to beryllium compounds

- Chronic granulomatous pneumonitis
- Skin, liver, spleen, lymph node, renal, and muscle involvement
- Occurred long after exposure has ceased
- No spontaneous remissions

Hardy and Tabershaw. J. Indus. Hyg. & Toxicology.  
1946, 28: 197

# Community Cases of CBD

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**Dutra FR. Am. J. Path. 1948; 24:1137-52**

**2 Cases that lived 1 and 5 miles from  
plant**

**DiNardi, VanOrdstrand, Carmody. Am. J.  
Med. 1949; 7:345-355**

**6 cases that lived near the Lorain Plant**

# Recommendations for safe levels in the workplace and community

## ➤ Radiologic survey of Lorain community

- ✓ 10,000 x-rays
- ✓ 11 cases detected
- ✓ Correlation with airborne levels

Eisenbud, et al. J. of Indus. Hyg. And Tox. 1949;  
31:282-294

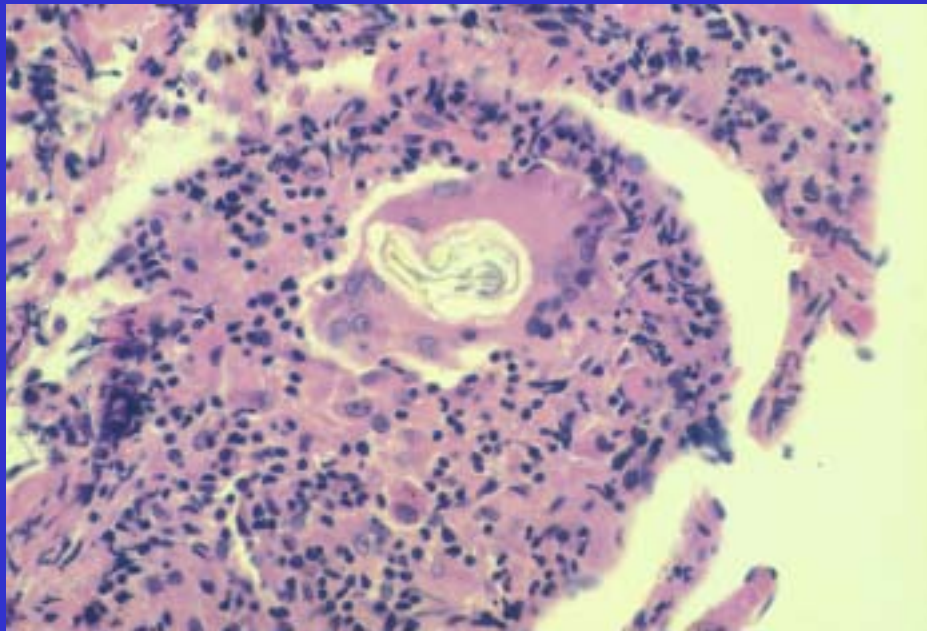
## ➤ Establishment of workplace and community levels of beryllium

Eisenbud. Environmental Research 1982; 27: 78-88

# Skin lesions in < 5%



# Typical trans-bronchial biopsy in CBD



**Epithelioid granuloma**

**Multinucleated Giant  
cell**

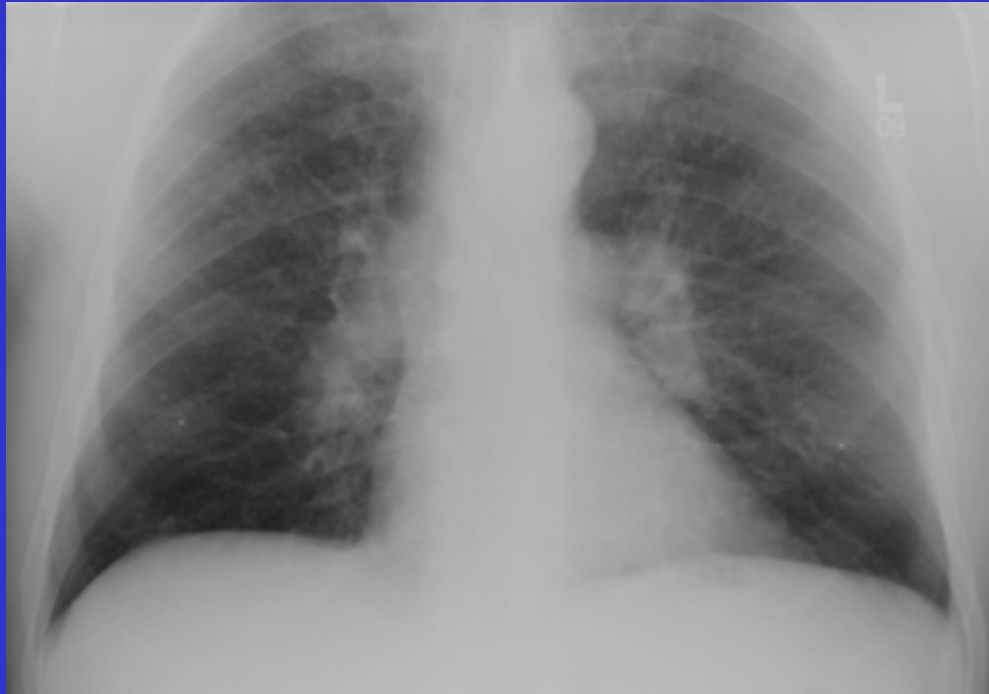
**Schumann body**

**Lymphocytic  
infiltrates**

# Classic Pathology of CBD

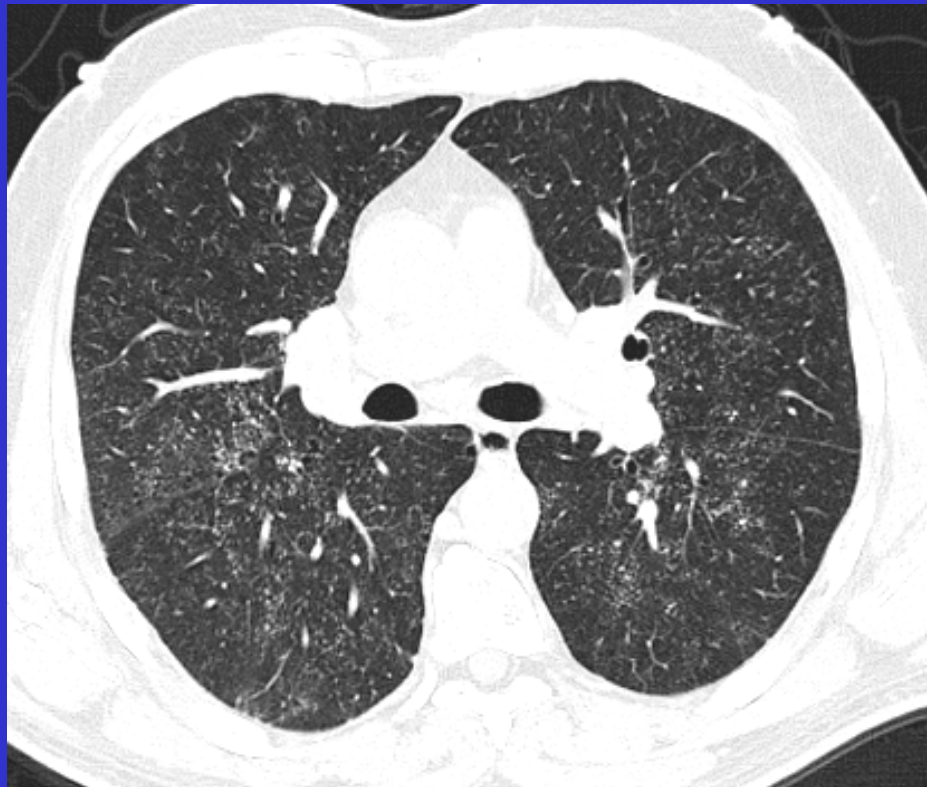
<b>Histological Classification</b>	<b>Group IA</b> (55/124 ~ 44%)	<b>Group IB</b> (44/124 ~ 35%)	<b>Group II</b> (25/124 ~ 20%)
<b>Interstitial Cellular Infiltrates</b>	<b>Moderate to Marked</b>	<b>Moderate to Marked</b>	<b>Slight or absent</b>
<b>Granuloma formation</b>	<b>Poorly formed or absent</b>	<b>Well formed</b>	<b>Numerous and well formed</b>
<b>Calcific inclusions</b>	<b>Variable</b>	<b>Variable</b>	<b>Few or absent</b>

# Chest Radiographs



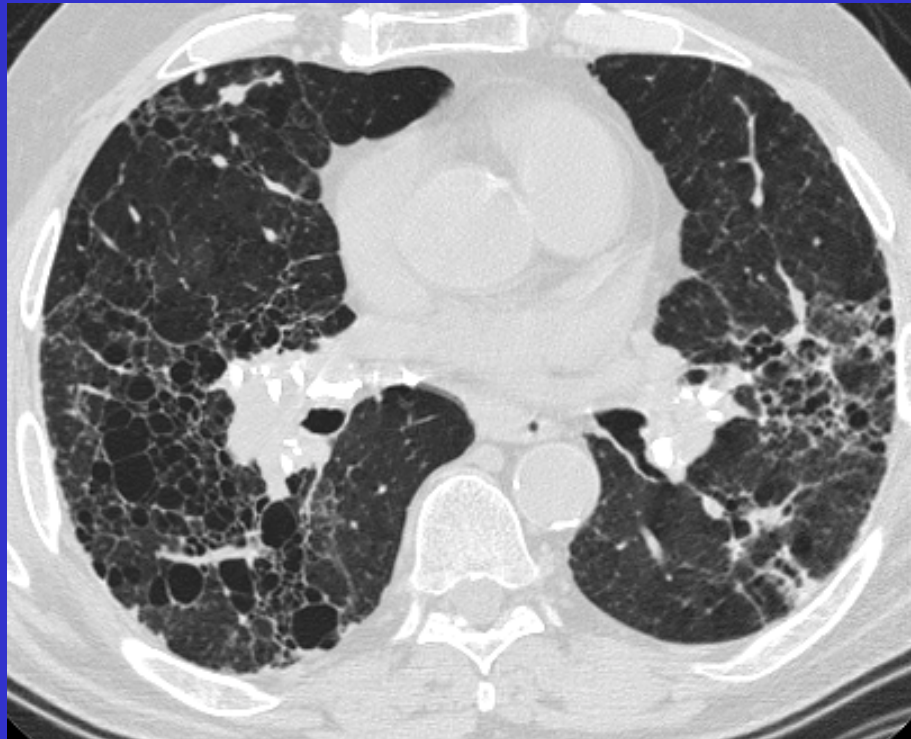
**Bilateral hilar  
adenopathy and  
fine nodular  
upper lobe  
infiltrates in  
CBD**

# Chest CTs



**Diffuse fine  
nodular disease  
and adenopathy**

# CBD can lead to end stage lung disease

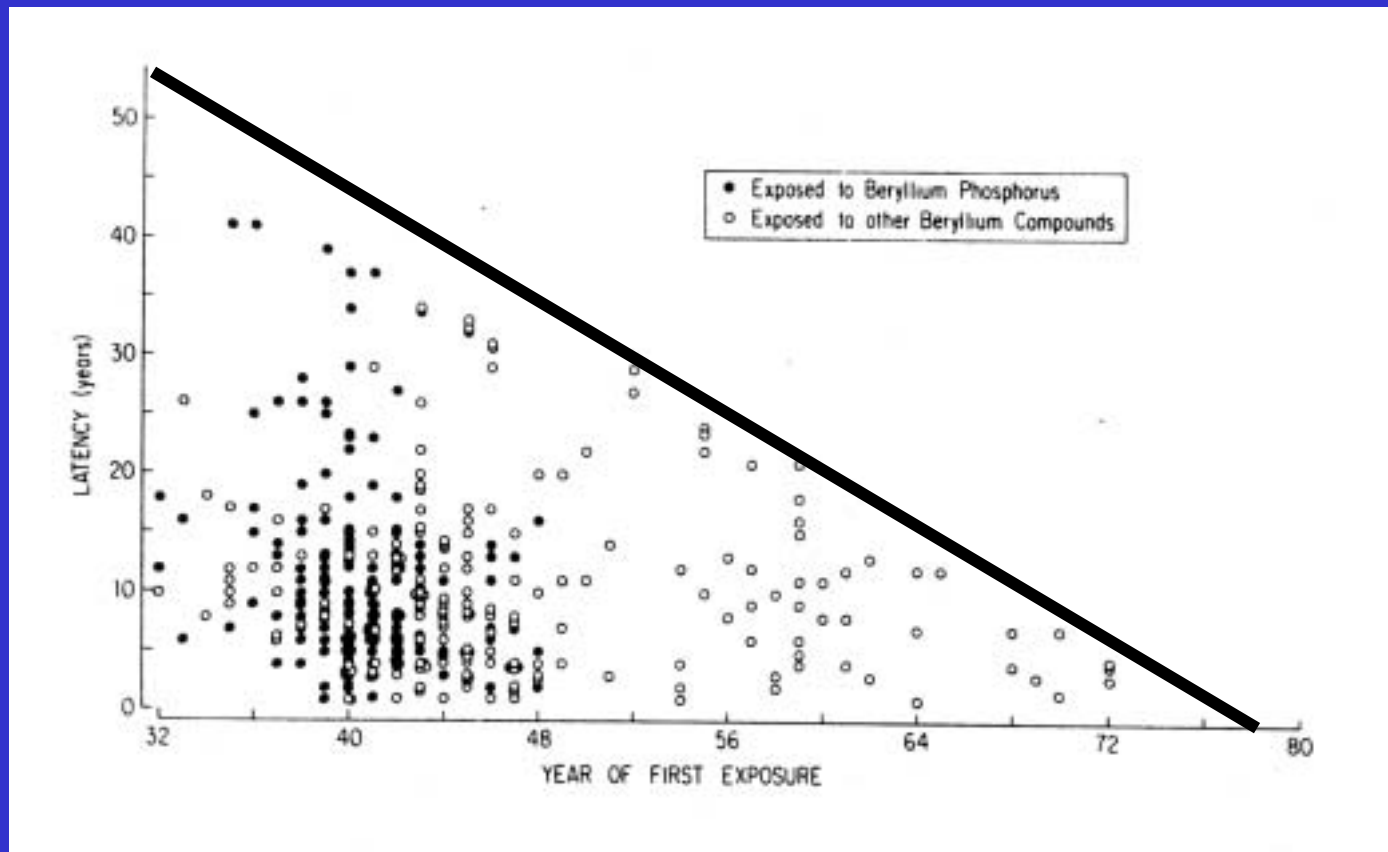


**Cyst formation**

**Distortion of  
airways**

**Large calcified  
nodes**

# CBD can occur years after first exposure



# Beryllium Case Registry Criteria

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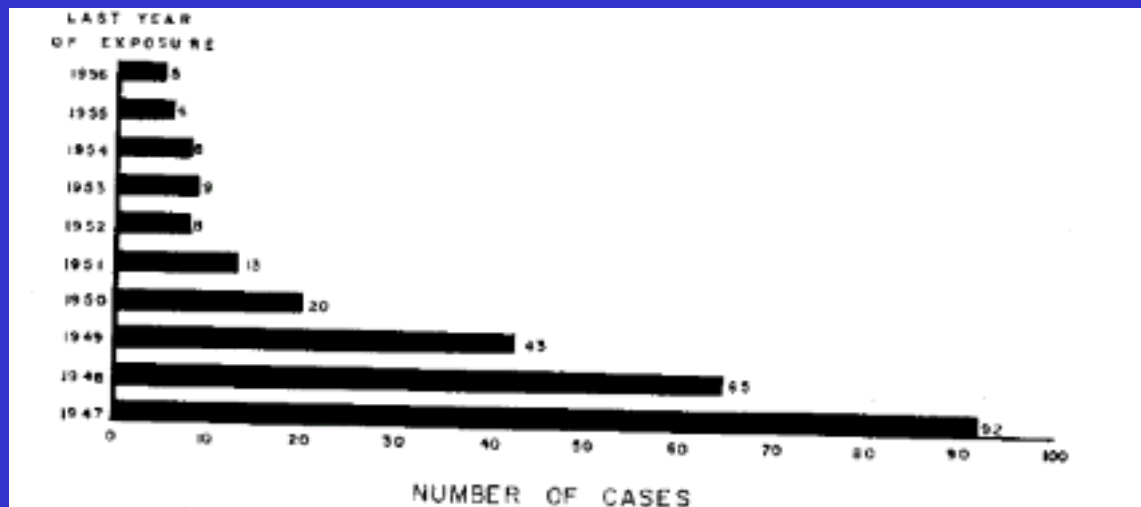
- 1. History of Exposure**
- 2. Elevated tissue/urinary levels of beryllium**
- 3. History of a chronic respiratory disease**
- 4. Abnormal pulmonary function**
  - ✓ Obstructive, restrictive or abnormal Dlco
- 5. Abnormal chest radiograph**
  - ✓ Fibronodular upper lobe infiltrates
- 6. Abnormal pathology**

# Beryllium disease was thought to be controlled.

In 1980, less than 1 case/year was being discovered.

These cases were often attributed to accidents.

The incidence rate/ton of be production was less than 0.001 where previously it had been 5-10.



# Pathogenesis of CBD was unknown

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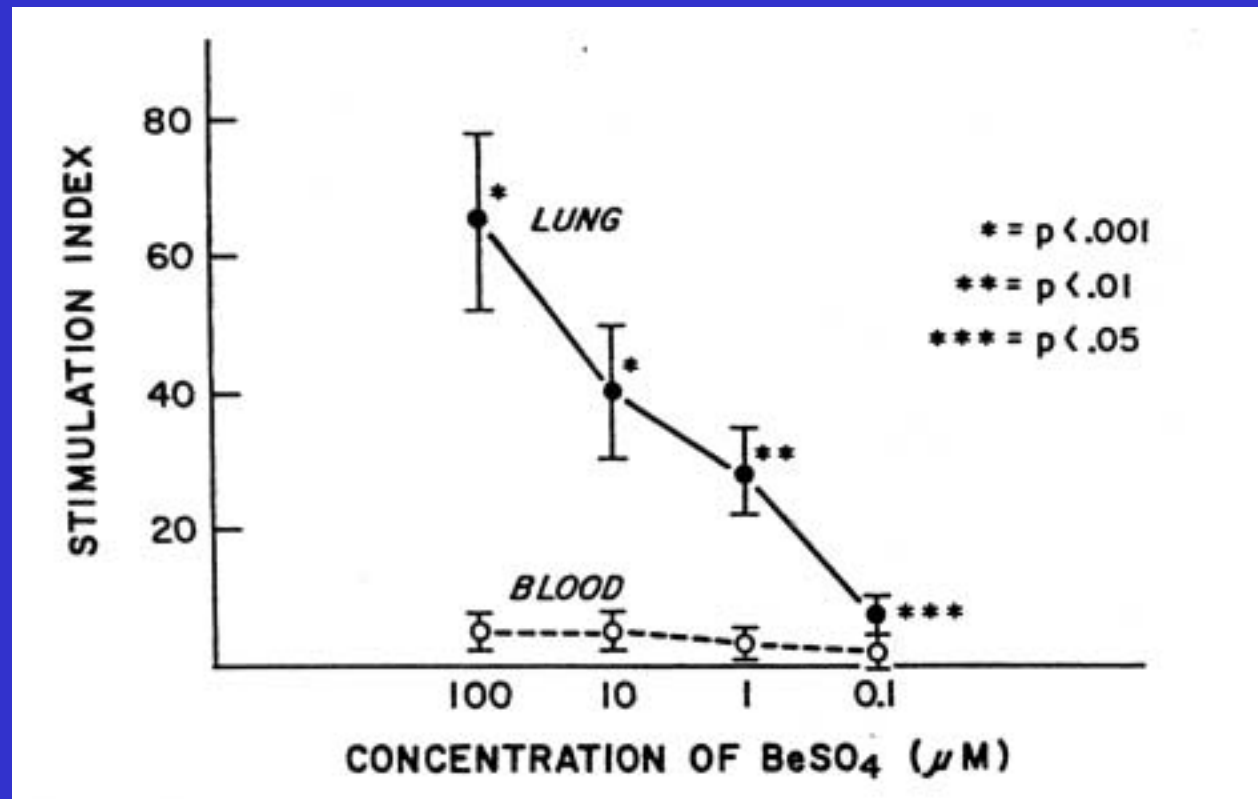
## ➤ Delayed Toxicity

- ✓ Acute Disease
- ✓ Animal Studies

## ➤ Hypersensitivity

- ✓ Low prevalence < 5%
- ✓ No clear cut dose-response relationship
- ✓ Granulomatous reaction
- ✓ Delayed skin test reactivity (Patch Test)

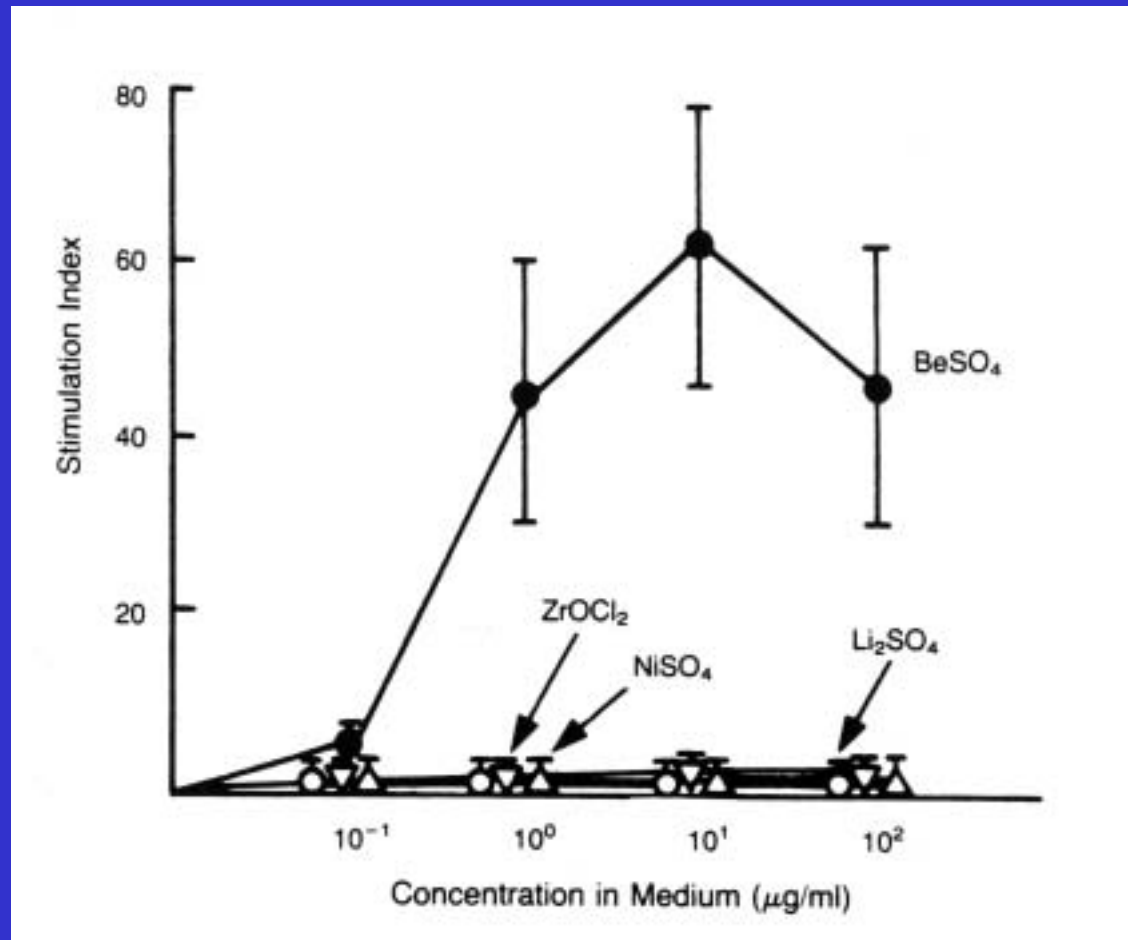
# Accumulation of Be specific cells in the BAL fluid



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Rossmann et al. Ann Intern Med 1988; 108:687-693

# There is no known cross-reactivity to Be



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Saltini et al, NEJM 1989; 320: 1103

# **CBD is due to a hypersensitivity to beryllium.**

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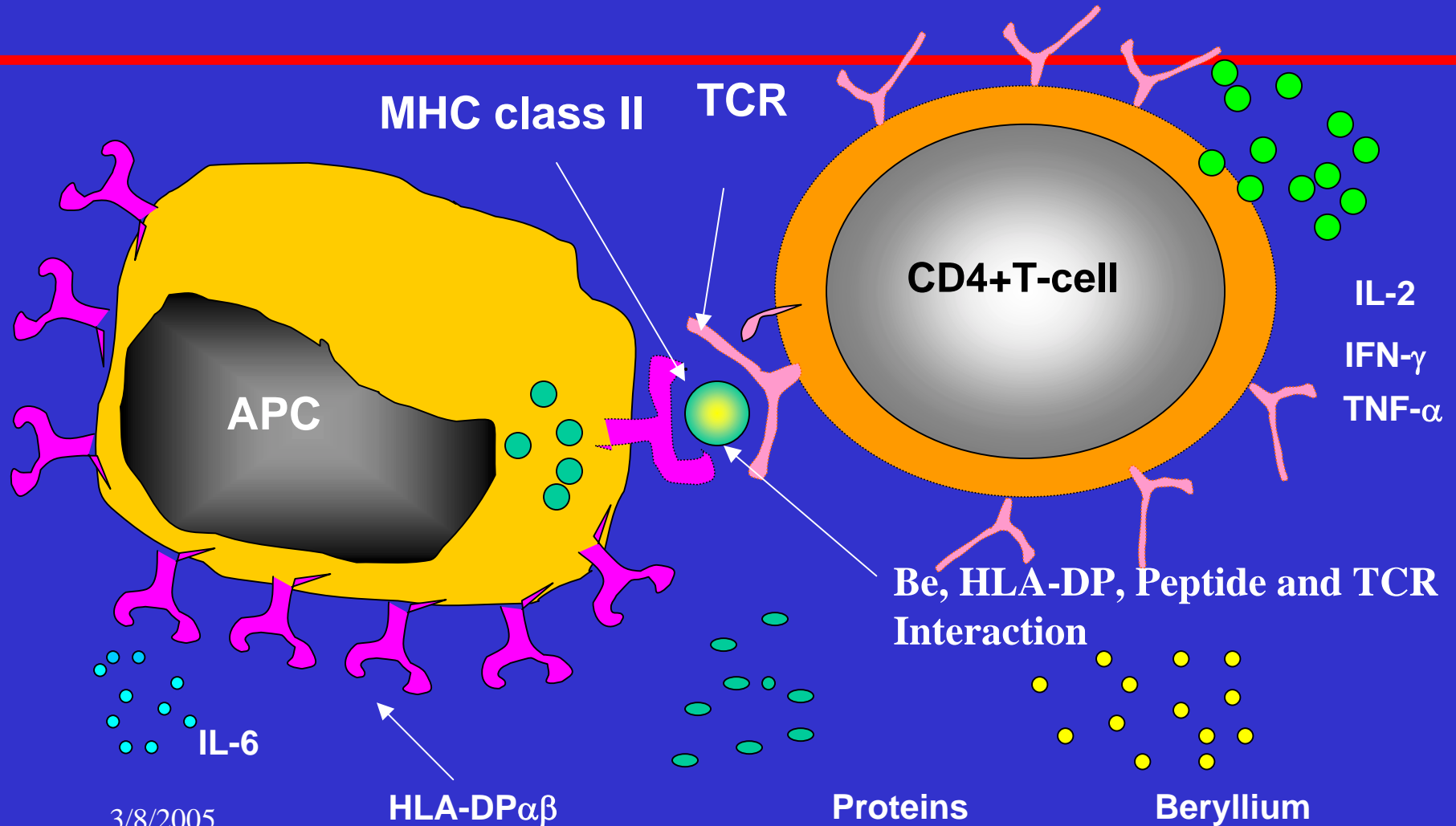
## Epidemiological evidence

- 1. Low attack rate ~ 5%**
- 2. No clear cut dose-reponse relationship**
- 3. Granulomatous reaction**
- 4. Delayed skin reactivity**

## Immunological evidence

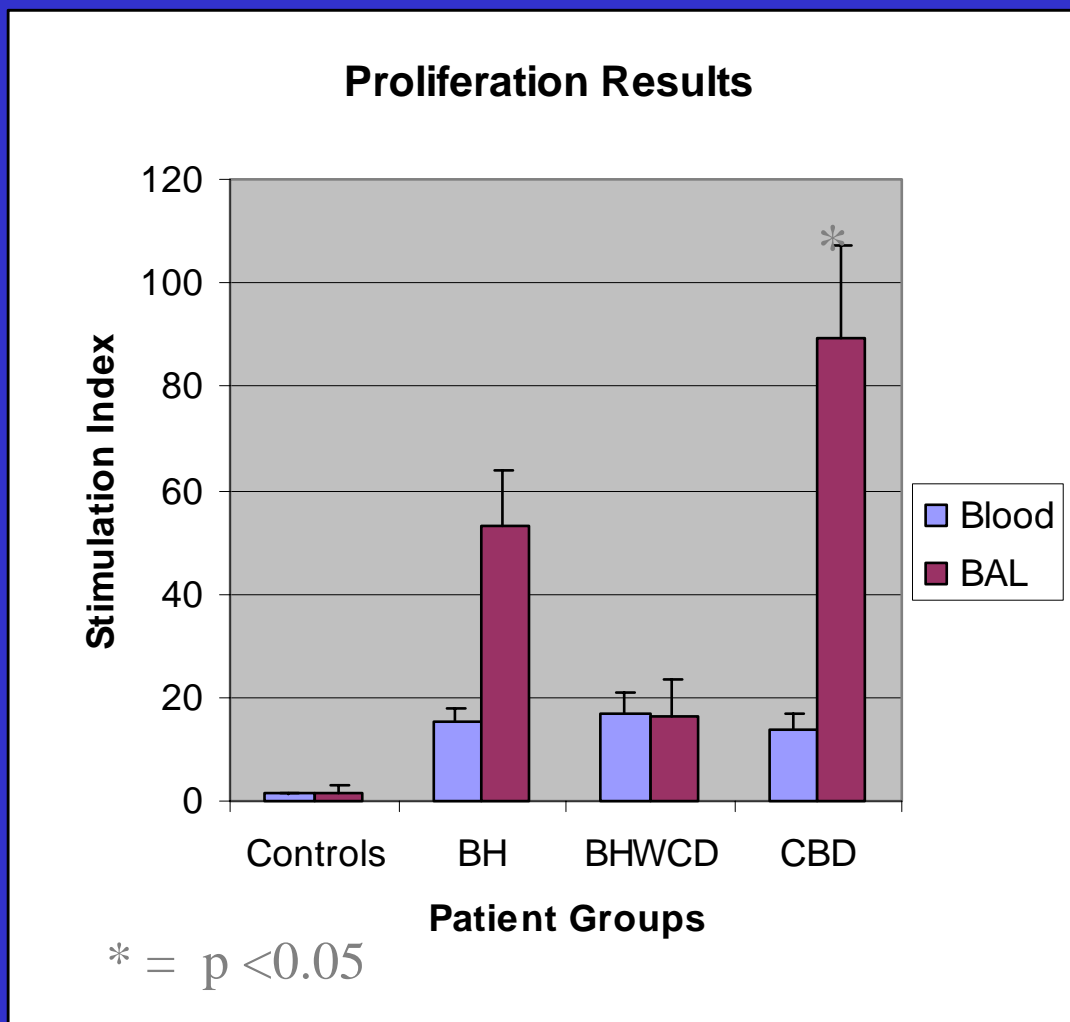
- 1. Increased CD4+ T cells in the lung**
- 2. Positive Be LPT in all individual**
- 3. Increased Be specific cells in the lungs**

# Immunopathogenesis of Berylliosis



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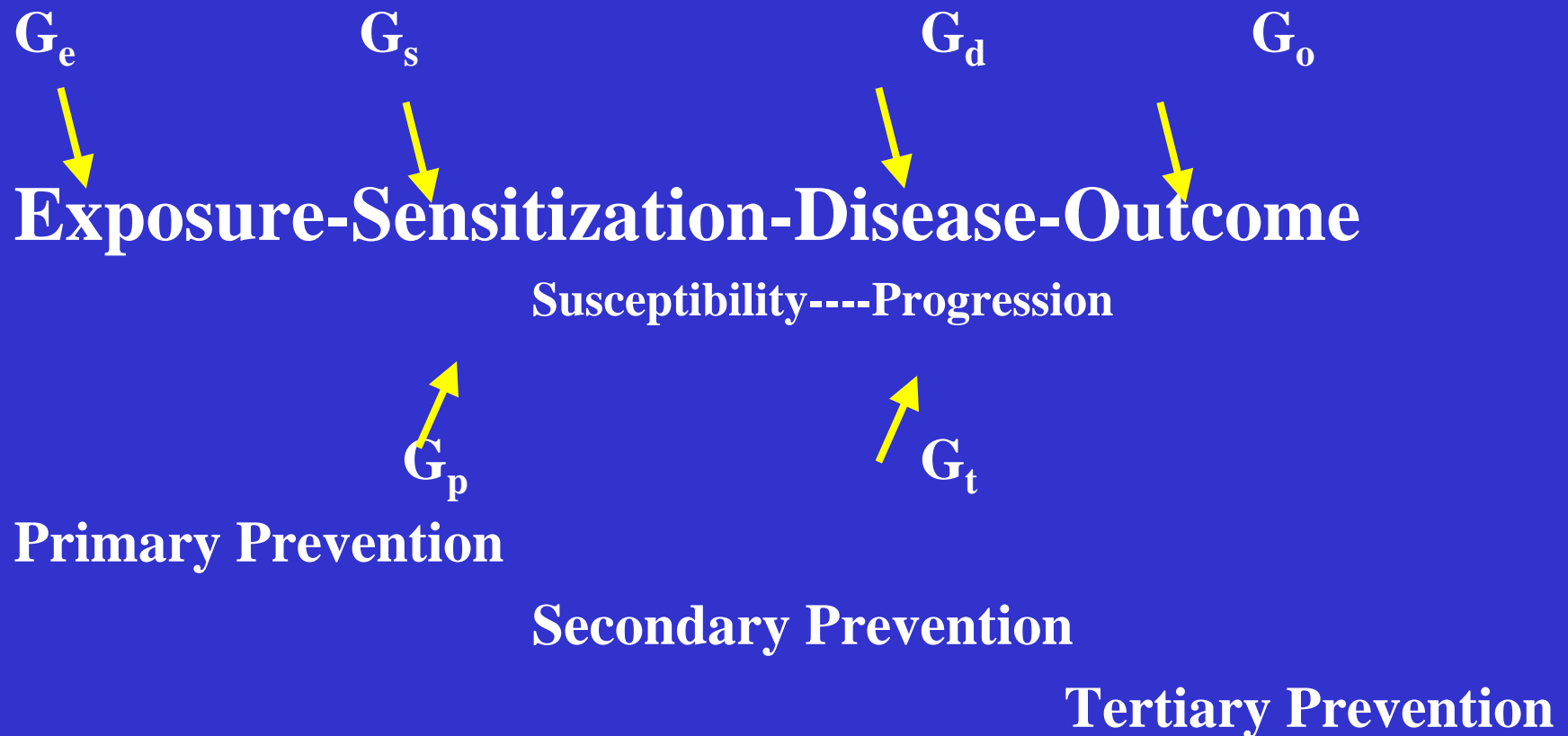
# Patients with CBD have higher BAL Beryllium Specific Proliferation



# Implications of Immunologic Testing

- **Proved CBD was a hypersensitivity disease**
  - ✓ Used diagnostically
  - ✓ Screen for disease
- **Genetic predisposition**
  - ✓ Only a proportion of the exposed population will get sick
- **Positive test for hypersensitivity proved exposure**
  - ✓ Could use immunologic testing to determine excessive exposure - surveillance

# Possible Genetic Interactions



# **Workers at risk for beryllium disease?**

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**Production and maintenance workers in:**

**beryllium extraction plants**

**basic beryllium plants producing**

**Metallic beryllium, beryllium alloys, beryllium oxide powders**

**Foundries melting beryllium alloys**

**Beryllium machine shops**

**Operations involving**

**Grinding, welding, BeO furnace cleaning, Laser cutting, heat treatment of beryllium alloys, chemical milling of beryllium**

**Decommission and decontamination of former beryllium sites**

**Dental technicians working with bridges or crowns containing beryllium**

**Jewelers working with beryllium alloys**

*3/8/2005*

# **Immunologic Screening could identify previously unrecognized CBD**

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**1533 former workers were screened from 2  
plants**

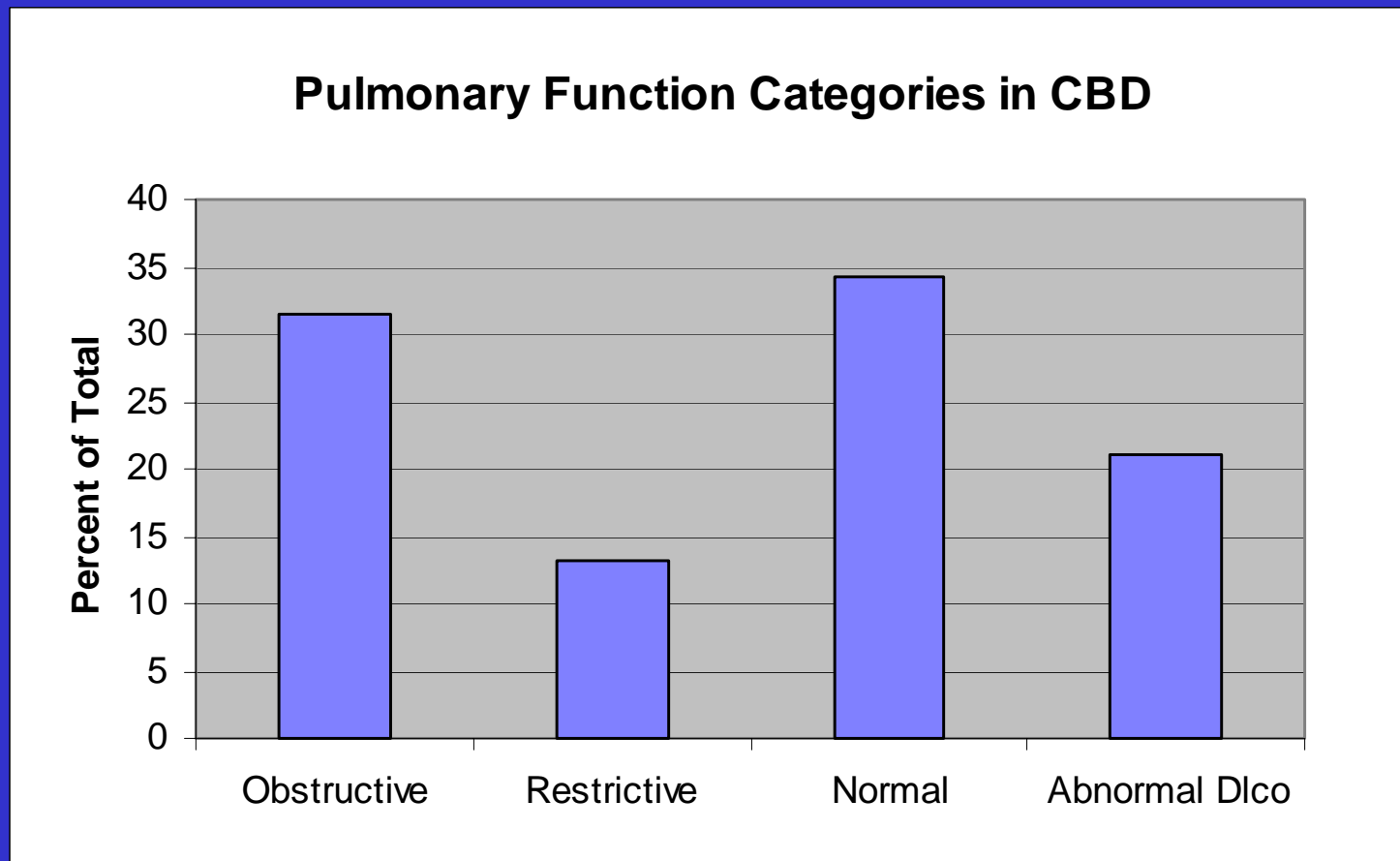
**19 cases of previously diagnosed CBD identified**

**37 newly diagnosed cases of CBD**

**Prevalence of CBD = 3.65% (56/1533 )**

**Prevalence of unrecognized CBD = 2.41% (37/1533)**

# Over 65% of Unrecognized CBD had Significant Pulmonary Function Abnormalities.



# **Immunologic screening has increased the detection the CBD**

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## **DOE former worker programs**

### **1. Former Worker Program (FWP)**

**13 Site specific projects**

### **2. Former beryllium worker medical surveillance program (BMSP)**

**Managed by ORISE**

## **Private Industry**

# CBD can also occur in communities surrounding beryllium plants from air pollution

READING EAGLE

Sunday, May 14, 2000 • C3

## Neighbors also suffer from beryllium ailment

■ One has died, and class-action litigation is planned, seeking a monitoring program to identify and help residents diagnosed with the disease.

By Tony Lucia  
Eagle Staff

Dolores B. Dondore never set foot in the beryllium-processing plant in Tuckerton, nor any other facility.

But since 1993, she has lived about half a mile from the facility, which has gone through several changes in ownership in that time and now is owned by NGK Metals Corp.

She was diagnosed with chronic beryllium disease a year ago.

Since then, she and her husband, Richard C. Dondore, have filed a suit seeking damages against NGK Metals and its predecessors in the Eastern District U.S. District Court in Philadelphia.

Her illness also seems to suggest that - no matter the precautions that were or were not taken by plant owners over the years - some amount of beryllium dust escaped into the area beyond the facility.

A lawsuit now is being readied to seek a testing program for neighbors who never worked in the plant, and have never had the testing provided for workers.

Indeed, a study undertaken by the Pennsylvania Department of Health and funded by the National Institutes of Health in 1989 found more cases of beryllium disease in the neighborhood of the plant than among those who

actually worked there.

A prior study, published in 1987 by Drs. George W. Chamberlin, W. Paul Jennings and Jan Lieben, separately found that of 20 Reading-area individuals with beryllium disease at the time, four worked at the plant, five had contact with contaminated clothing from plant workers, two lived in the immediate neighborhood, and the other nine lived four or more miles away, suggesting widespread contamination.

As part of the 1989 study, researchers also randomly sampled tissue from the lungs of 20 individuals from the Tuckerton/Muhlenberg Township area who had died in a nearby hospital, which was not identified in the study.

Of those 20 individuals, all but one, a 3-year-old child, contained higher concentrations of beryllium than those autopsied in a control group - a hospital 70 miles away.

Also, air sampling taken at 20 sites throughout the area found that concentrations of beryllium in the air were "on many occasions" higher than the government's recommended limit.

It's uncertain how many cases of chronic beryllium disease have been found among neighbors since those studies.

The Dondores' daughter, Linda

Dondore, who lives with her parents, said she has gone door to door in the community, conducting an informal survey on chronic beryllium disease.

She said she found dozens of individuals suffering from the disease, and many others who hadn't been diagnosed but had symptoms of the disease.

Ruben Honik, a lawyer with the Philadelphia firm of Golomb and Honik who is representing the Dondores, said his firm has identified numerous cases of chronic beryllium disease in the community around the plant and said it is planning class action litigation.

He said the object of that action would be the establishment of a monitoring program to identify and add those in the Muhlenberg Township area who may already have or may contract chronic beryllium disease.

Many more residents who had no workplace exposure to beryllium are beginning to be identified not only in the Reading area but throughout the nation, Honik said.

In part, the reason we're seeing them now is that the worst industrial hygiene these plants had was from the '50s to the '70s," Honik said. "Hygiene changed fairly dramatically in the '70s, but mainly in the '80s."

"Particulate matter that used to come out from these plants changed when they tightened hygiene through things like stack emissions, the way they sealed in the factory, changes in the way

workers would be required to shower and change clothes at the facility."

For instance, in the late 1960s, the company instituted a policy under which clothing worn in the plant was collected before work was left and cleaned in a special facility.

"By the '90s," Honik said, "most plants realized the airborne risks and began to improve hygiene. You may not see many cases in 20 years, but we're now seeing the results of the poor hygiene of the past."

Honik said that due to a wealth of medical and industrial studies on the effects of beryllium conducted over the last 40 years, there is now no question that an individual does not have to be in the work place to contract chronic beryllium disease.

In fact, Honik, who also represents Mary L. Russo (see related story, page C2), a worker at the plant in 1967-68, said it's also possible she could have contracted the disease from living within a 4-mile radius of the NGK plant for many years.

Russo recalled that a large, uncovered pile of dust was kept outside on the plant property, then owned by Beryllium Corporation of America.

At that time, beryllium ore was processed at the plant, and Russo said she believed the pile con-

tained byproducts of that process.

"Substantial quantities of beryllium dust were put into the environment," Honik said. "Airborne sampling ascertained there was beryllium in the general environment outside the plant, and certainly those homes in the area were bombarded for years with quantities of beryllium."

Dolores Dondore was not able to be interviewed for this article, but Linda Dondore said her mother is taking it as well as can be expected.

"My mom's a fighter," she said. "She just wishes that the owners and the stockholders of NGK and prior plant owners could get inside her body so they'd know what it

feels like."

Linda Dondore said the test has been tested for chronic beryllium disease.

"The doctor's exact words were, 'You are negative now. If you feel any of the symptoms, you know what to do,'" she recalled.

"I guess now I'm still really angry because I was really naive," Dondore said. "I guess the whole community is. I'm infuriated that today, it still goes on."

"There's no reason to me that any business should be killing its workers, let alone residents."

"There's no excuse for it, not with the technology that's out there today."

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# **Immunologic testing can also detect community acquired CBD**

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**Eight new cases of CBD recognized  
between 1999-2002.**

**Two cases misdiagnosed as sarcoidosis in  
the 1970's**

**Four cases diagnosed 17 to 44 years after  
leaving neighborhood.**

# Total number of newly reported cases of CBD since 1990

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**FWP = 28**

**BMSP = 102**

**Private cases in literature = 104**

**Our survey = 56**

**Total cases = 290**

# **CBD remains an important and probably under recognized disease.**

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**Up to 136,000 exposed workers in the US.**

*Henneberger, Journal of Occupational and Environmental Hygiene, 1: 648–659*

**5% of exposed workers may develop CBD.**

**Possibly – 6,800 cases**

**CBD is misdiagnosed as sarcoidosis.**

# Laboratory and Collaborators

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## Rossman Laboratory

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