

# Clinical Guidance for Evaluating Beryllium Sensitization and Chronic Beryllium Disease

IIMAC

April 23, 2015



# AMERICAN THORACIC SOCIETY DOCUMENTS



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

John R. Balmes, Jerrold L. Abraham, Raed A. Dweik, Elizabeth Fireman, Andrew P. Fontenot, Lisa A. Maier, Joachim Muller-Quernheim, Gaston Ostiguy, Lewis D. Pepper, Cesare Saltini, Christine R. Schuler, Tim K. Takaro, and Paul F. Wambach; on behalf of the ATS *Ad Hoc* Committee on Beryllium Sensitivity and Chronic Beryllium Disease

THIS OFFICIAL STATEMENT OF THE AMERICAN THORACIC SOCIETY (ATS) WAS APPROVED BY THE ATS BOARD OF DIRECTORS, June 2014

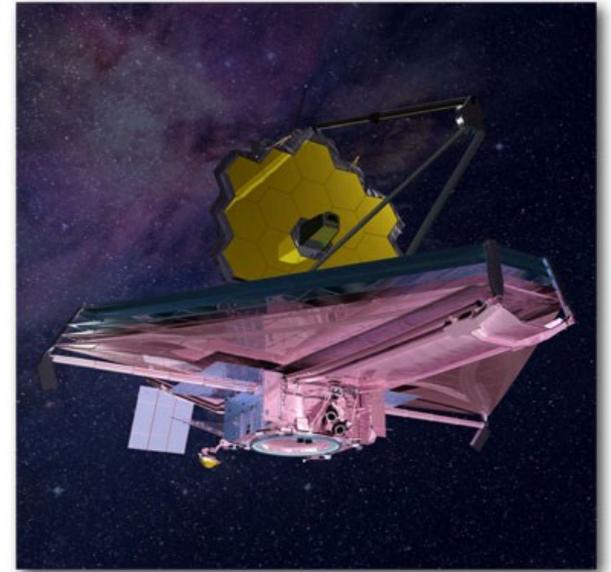
# PERIODIC TABLE OF THE ELEMENTS

1A																						8A
1 H 1.008	2A															3A	4A	5A	6A	7A	2 He 4.003	
3 Li 6.939	4 Be 9.0122											5 B 10.811	6 C 12.011	7 N 14.007	8 O 15.999	9 F 18.998	10 Ne 20.183					
11 Na 22.99	12 Mg 24.312	3B	4B	5B	6B	7B	-----8B-----				1B	2B	13 Al 26.982	14 Si 28.086	15 P 30.974	16 S 32.064	17 Cl 35.453	18 Ar 39.948				
19 K 39.102	20 Ca 40.08	21 Sc 44.956	22 Ti 47.9	23 V 50.942	24 Cr 51.996	25 Mn 54.938	26 Fe 55.847	27 Co 58.933	28 Ni 58.71	29 Cu 63.546	30 Zn 65.37	31 Ga 69.72	32 Ge 72.59	33 As 74.922	34 Se 78.96	35 Br 79.904	36 Kr 83.8					
37 Rb 85.47	38 Sr 87.62	39 Y 88.905	40 Zr 91.22	41 Nb 92.906	42 Mo 95.94	43 Tc [97]	44 Ru 101.07	45 Rh 102.91	46 Pd 106.4	47 Ag 107.87	48 Cd 112.4	49 In 114.82	50 Sn 118.69	51 Sb 121.75	52 Te 127.6	53 I 126.9	54 Xe 131.3					
55 Cs 132.91	56 Ba 137.34	57* La 138.91	72 Hf 178.49	73 Ta 180.95	74 W 183.85	75 Re 186.2	76 Os 190.2	77 Ir 192.2	78 Pt 195.09	79 Au 196.97	80 Hg 200.59	81 Tl 204.37	82 Pb 207.19	83 Bi 208.98	84 Po 210	85 At 210	86 Rn 222					
87 Fr 215	88 Ra 226.03	89** Ac 227.03	104 Rf [261]	105 Db [262]	106 Sg [266]	107 Bh [264]	108 Hs [269]	109 Mt [268]	110 [271]	111 [272]	112 [277]	114 [289]		116 [289]								

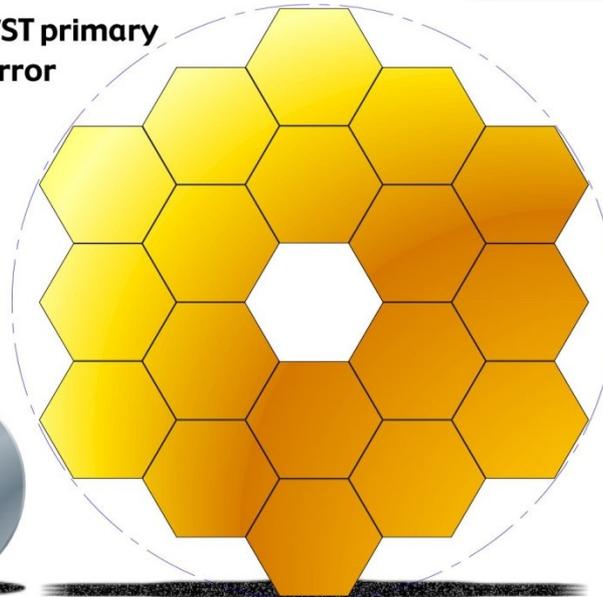
*Lanthanides	58 Ce 140.12	59 Pr 140.91	60 Nd 144.24	61 Pm 145	62 Sm 150.35	63 Eu 151.96	64 Gd 157.25	65 Tb 158.92	66 Dy 162.5	67 Ho 164.93	68 Er 167.26	69 Tm 168.93	70 Yb 173.04	71 Lu 174.97
**Actinides	90 Th 232.04	91 Pa 231	92 U 238.03	93 Np 237.05	94 Pu 239.05	95 Am 241.06	96 Cm 244.06	97 Bk 249.08	98 Cf 252.08	99 Es 252.08	100 Fm 257.1	101 Md 258.1	102 No 259.1	103 Lr 262.11

- Gaseous at room temperature
- Liquid at room temperature
- Gallium mts at 29.78 deg. C.
- Synthetic elements
- All other elements are solid at room temperature

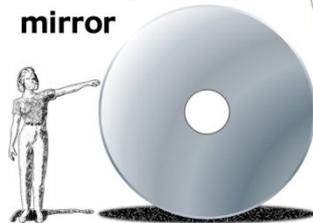
Source: [www.jwst.nasa.gov](http://www.jwst.nasa.gov)



**JWST primary mirror**



**Hubble primary mirror**



Industries	Occupations
Atomic energy/nuclear industries including power, weapons & defense	Grinders
Rod and wire and copper tubing production	Machinists
Aeronautics/aerospace	Hot press operators
Electronics & computers manufacturing	Welders
Construction/demolition	Security Guards where there is known risk of exposure
Ceramic manufacturing	Janitorial workers where there is known risk of exposure
Laboratory work	Dental hygienists, prosthetists, technicians
Recycling/Hazardous waste cleanup	Laser cutters of beryllium metals and alloys
Fiber optics	Those who worked with fluorescent lamps prior to 1951
Dental materials manufacturing and laboratories (alloys in bridges, crowns etc.)	Those who decontaminate or decommission structures where beryllium was present/used.
Bicycle and golf club manufacturing	Cleaners or rebuilders of furnaces where beryllium was present/used
Plastics injection molding	

# Exposure → BeS → CBD

- 134,000 currently exposed workers
- Ever exposed is “much greater”
- Consensus statement summarizes longitudinal cohort studies
  - Develops BeS over time (1.0-16.2%)
  - Develops CBD over time (0.0 to 11.0%)

# Be lymphocyte proliferation test

- Isolate mononuclear cells from sample
- Expose to three concentrations of Be salts incubated over two time intervals (6 combinations)
- Culture Be-stimulated, unstimulated, and + control cells in tritiated thymidine media
- Dividing cells uptake tritiated thymidine—↑ cell proliferation ↑ radioactivity
- Calculate stimulation index—ratio of measured radioactivity in stimulated vs. unstimulated cells

- Abnormal result—2 or more of 6 stimulation indices exceed threshold
- Borderline result—1 of 6 stimulation indices exceed threshold
- Some explanations for uninterpretable result:
  - Inadequate response in positive control cells
  - High measured radioactivity in unstimulated cells
  - Highly variable response in stimulated cells

Citations: 2, 9, Stange, Furman and Hilmas. 2004. The BeLPT: Relevant Issues in Be Health Surveillance. Am. J. Ind. Med. 46:453–462

# Performance Characteristics—single peripheral blood BeLPT

- (Stange, Furman and Hilmas 2004)
  - Sensitivity 0.683
  - Specificity 0.969

# Guidance—Sensitization

- Beryllium sensitization is confirmed by:
  - At least two abnormal blood BeLPT tests\* [2](#) OR
  - At least one abnormal and one borderline blood BeLPT tests\* [2](#) OR
  - At least three borderline blood BeLPT tests\*† [2](#), [11](#) OR
  - An abnormal bronchoalveolar lavage LPT if performed [2](#) OR
  - Positive skin patch test to beryllium if performed [2](#). Labor and Industries does not require skin patch testing to diagnose chronic beryllium disease due to the risk of inducing sensitization. [2](#), [4](#)

## BeS is work-related if:

1. exposure resulted from a direct occupational injury such as a puncture wound from beryllium metal, OR
2. If the exposure is not due to an occupational injury, but arises from conditions that are distinctive to the job (e.g. working in an environment where known beryllium-containing alloys, dust, vapors, or liquids are present), OR
3. Exposure undocumented, LPT shows sensitized—requires careful analysis and evaluation of potential work-relatedness

# Definitive work-related CBD requires:

- Evidence of work-related beryllium sensitization as defined above, AND
  - EITHER:
    - Lung biopsy showing granulomatous inflammation (typically noncaseating granulomas),
  - OR
    - Clinical presentation and diagnostic findings consistent with CBD, such as from imaging studies, bronchoalveolar lavage, and pulmonary function tests.

Signs, symptoms and test results of CBD can include <sup>[5, 9, 17]</sup>:

### **Per History and Physical**

- Non-productive cough
- Abnormal lung sounds (crackles)
- Chest discomfort
- Dyspnea on exertion
- Fever
- Weight loss
- Night sweats
- Fatigue
- Loss of appetite

### **Per Tests and Procedures**

- Chest x-ray or CT scans show small lung scars, hilar adenopathy (enlargement of lymph nodes in the central part of the chest), and/or most commonly reticular-nodular infiltrates
- Abnormal results from pulmonary function tests, such as restrictive, obstructive, or mixed patterns, or showing restrictive patterns or reduced carbon monoxide diffusing capacity
- Hypoxemia by arterial blood gases or oximetry, and oxygen desaturation with exercise
- Granulomas found in lung or skin tissue per biopsy
- Lymphocytosis on bronchoalveolar lavage

- In rare circumstances, following comprehensive evaluation as described above (including bronchoalveolar lavage BeLPT unless medically contraindicated), CBD may be present without a positive BeLPT test.
  - Example, false negative BAL BeLPT in cigarette smokers.<sup>16</sup>

**In rare circumstances, a diagnosis of work-related CBD may be made if four objective criteria are met:**

1. There is a known scientific or medical basis for the false negative BeLPT result, AND

**In rare circumstances, a diagnosis of work-related CBD may be made if four objective criteria are met:**

2. The patient has a clinical presentation and objective findings consistent with CBD, e.g. a lung biopsy confirming the presence of granulomas that are consistent with CBD, AND

**In rare circumstances, a diagnosis of work-related CBD may be made if four objective criteria are met:**

3. Other causes of granulomatous lung disease have been excluded, such as mycobacterial and fungal infection; hypersensitivity pneumonitis; and sarcoidosis with systemic disease and extra-pulmonary organ involvement (e.g. neurologic, ophthalmologic, cardiac, etc.), AND

**In rare circumstances, a diagnosis of work-related CBD may be made if four objective criteria are met:**

4. There is strong evidence of work-related exposure to beryllium, e.g. through a documented occupational injury, exposure monitoring demonstrating exposure distinctive to employment, or confirmed cases of work-related beryllium sensitization in similarly exposed co-workers of the individual.