Beryllium Lymphocyte Proliferation Test (Be-LPT)

Background Information

Beryllium (Be) is a lightweight metal that can cause acute or chronic disease that may be asymptomatic. Occupational exposure typically is responsible for this but for the most part it occurs in individuals carrying certain HLA alleles such as *HLA-DPB1* in 83%-97% of individuals with chronic Be disease (CBD). CBD is much more common than the acute disease nowadays which is typically a chronic non-caseating granulomatous inflammation in individuals who develop Be-specific, cell-mediated immunity (typically CD4+ T cells). It is estimated that circa 140,000 workers in the United States are exposed to Be every year. Depending on the nature of the exposure and the HLA type, CBD will develop in up to 16% of exposed subjects thus CBD remains an important public and occupational health issue. Be-sensitized individuals may remain asymptomatic for life but ca. 6-8% develop CBD every year.[1]

Testing for an individual's sensitivity to Be is performed with an in vitro lymphocyte proliferation test (LPT). This is used not only as a screening assay but also as a part of the diagnostic criteria for CBD.

Clinical Indications

Be is a lightweight metal with high melting point, high strength and good electrical conductivity. As a result, beryllium has become widely used in a variety of industrial applications, such as thermal coating, nuclear reactors, rocket heat shields, micro-circuits, brakes, X-ray tubes, golf clubs, ceramics, and dental plates. Frequently, it is formulated as an alloy or an oxide.

Correlation between the clinical status of CBD (chronic beryllium disease) and in vitro responses to Be in an LPT was developed.[2] An elevated blood Be-LPT result may indicate Be sensitization but definitive diagnosis of CBD requires lung biopsy in the context of compatible signs and symptoms and radiological findings, therefore, as a follow-up step, individuals may undergo pulmonary evaluation, including bronchoscopy, trans-bronchial biopsy or BAL collection for BAL Be-LPT. This is important in the differential diagnosis of CBD as sarcoidosis can clinically mimic CBD. Extra-pulmonary CBD may also be occasionally seen such as cutaneous nodules.

Methodology

The blood lymphocyte proliferation test for Be sensitization (Be-LPT) is measured by radioactive ^{3}H-thymidine uptake in a cell culture system on two different days after exposure to a range of Be sulfate to re-stimulate effector memory CD4+ T cells in peripheral blood. As a control, a common mitogen, phytohemagglutinin (PHA) and also Candida antigen are used to ensure acceptable and normal T cell proliferative responses. Emitted beta rays are counted by a beta counter instrument in count per minute (CPM) and stimulation index (SI) is calculated and reported out along with an interpretive comment. The results are reviewed by staff.

Interpretation

The S.I. for PHA should be ≥50.0 and the S.I. for *Candida albicans* should be ≥2.0 to indicate normal T-cell function.

If all six Be indices are less than 3.0, this signifies a normal result meaning no evidence of Be sensitization.

Ratios of greater than or equal to 3.0 in two or more Be indices constitutes an abnormal response that is compatible with Be hypersensitivity.

References

1. McCanlies EC, Kreiss K, Andrew M, Weston A. 2003. HLA-DBP1 and chronic beryllium disease: a HuGE review. *Am. J Epidemiology*. 157:388-398.

2. Deodhar SD, Barna BP, Van Ordstrand HS. 1973. A study of the immunologic aspects of chronic berylliosis. *Chest*. 63:309-313.

3. Barna BP, Culver DA, Yen-Lieberman B, Dweik RA, Thomassen MJ. Clinical application of Beryllium Lymphocyte Proliferation Testing. *Clin and Diag Lab Immunol*. 2003;10:990-994.

4. U. S. Department of Labor, Occupational Safety and Health Administration. Directorate of Science, Technology and Medicine Office of Science and Technology Assessment, Safety and Health Information Bulletin, September 2, 1999.

Test Overview

Test Name	LPT to Beryllium, Blood
Reference Range	PHA Stim Index: ≥50.0 SI Beryllium 1.0 uM D5: < 3.0 SI Beryllium 1.0 uM D6: < 3.0 SI Beryllium 10 uM D5: < 3.0 SI Beryllium 10 uM D6: < 3.0 SI Beryllium 100 uM D5: < 3.0 SI Beryllium 100 uM D6: <3.0 SI *Candida albicans*: ≥ 2.0 SI
Methodology	^{3}H-thymidine uptake in cell culture
Specimen Requirements	30 mL whole blood in three 10 mL Heparized (sodium) green top tubes. Deliver specimen to laboratory within 48 hours of collection. Specimen must be received by 3 p.m. Monday–Thursday and by 12 p.m. Friday.
Ordering Mnemonic	BLDBE
CPT Codes	86353

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