Bence Jones protein

A **Bence Jones protein** is a monoclonal globulin protein found in the blood or urine. Finding this protein in the context of end-organ manifestations such as malignant bone marrow cancer, renal failure, lytic bone disease, or anemia, or large numbers of plasma cells in the bone marrow of patients can be diagnostic of multiple myeloma, in which it is present in 2/3 of cases.

The proteins are antibody immunoglobulin free light chains (paraproteins) and are produced by neoplastic plasma cells. They can be kappa (most of the time) or lambda. The light chains can be immunoglobulin fragments or single homogenous immunoglobulins. They are found in urine as they are small and hence easily cleared by the kidneys. The light chains can be detected by heating or electrophoresis of concentrated urine. Light chains precipitate when heated to 50 - 60 degrees C and redisolve at 90 -100 degrees C. These tests are essential in patients suspected of having Bence Jones proteins in their urine as these proteins do not react with the reagents normally utilized in urinalysis dipsticks. This leads to false negative results in people with Bence Jones proteins in their urine undergoing standard urinalysis. There are various rarer conditions which can produce Bence Jones proteins, such as Waldenström's macroglobulinemia and other malignancies.

The Bence Jones protein was described by the English physician Henry Bence Jones in 1847 and published in 1848. The protein was later sequenced by Frank Putnam at the laboratory of Fred Sanger in Cambridge, who was the first to report the entire sequence.

Purpose

Testing for these proteins is done to diagnose and monitor multiple myeloma and other similar diseases. Bence Jones proteins are considered the first tumor marker. A tumor marker is a substance, made by the body that is linked to a certain cancer, or malignancy.

Bence Jones proteins are made by plasma cells, a type of white blood cell. The presence of these proteins in a person's urine is associated with a malignancy of plasma cells.

Multiple myeloma, a tumor of plasma cells, is the disease most often linked with Bence Jones proteins. The amount of Bence Jones proteins in the urine indicates how much tumor is present. Physicians use Bence Jones proteins testing to diagnose the disease as well as to check how well the disease is responding to treatment.

Other diseases involving cancerous or excessive growth of plasma cells or cells similar to plasma cells can cause Bence Jones proteins in the urine. These diseases include: Waldenström's macroglobulinemia, some lymphomas and leukemias, osteogenic sarcoma, cryoglobulinemia, malignant B-cell disease, amyloidosis, light chain disease, and cancer that has spread to bone.

Description

Urine is the best specimen in which to look for Bence Jones proteins. Proteins are usually too large to move through a healthy kidney, from the blood into the urine. Bence Jones proteins are an exception. They are small enough to move quickly and easily through the kidney into the urine.

A routine urinalysis will not detect Bence Jones proteins. There are several methods used by laboratories to detect and measure these proteins. The classic Bence Jones reaction involves heating urine to 60C. At this temperature, the Bence Jones proteins will clump. The clumping disappears if the urine is further heated to boiling and reappears when the urine is cooled. Other clumping procedures using salts, acids, and other chemicals are also used to detect these proteins. These types of test will reveal whether or not Bence Jones proteins are present, but not how much is present.

A more complex procedure is done to measure the exact amount of Bence Jones proteins. This procedure (immunoelectrophoresis) is usually done on urine that has been collected for 24-hours.

Preparation

Urine is usually collected throughout a 24-hour time period. A person is given a large container in which to collect the urine. The urine should be refrigerated until it is brought to the laboratory.

Normal results

Bence Jones proteins normally are not present in the urine.

Abnormal results

Bence Jones proteins are present in 50-80% of people with multiple myeloma. People with other malignancies also can have a positive Bence Jones proteins test, but less frequently.

Certain nonmalignant diseases, such as rheumatoid arthritis, systemic lupus erythematosus, and chronic renal insufficiency, can have Bence Jones proteins in the urine. High doses of penicillin or aspirin before collecting the urine can give a false positive result.

Bence-Jones proteins are rarely found in urine, but if they are, they are usually associated with multiple myeloma. Less commonly they are present in Waldenstrom's macroglobulinemia, chronic lymphocytic leukemia, or amyloidosis.

Special considerations

Transport: Two 4.5 mL aliquots from a well-mixed 24-hour collection at 2-8°C. (Min: 4.5 mL.

Remarks: Keep refrigerated at all times. Record total volume and collection time interval on transport tube and test request

form. Random urine specimens are acceptable, but not preferred.

Unacceptable Conditions: Specimens that are not refrigerated.

Stability: Ambient: 2 hours; Refrigerated: 1 week; Frozen: 1 month

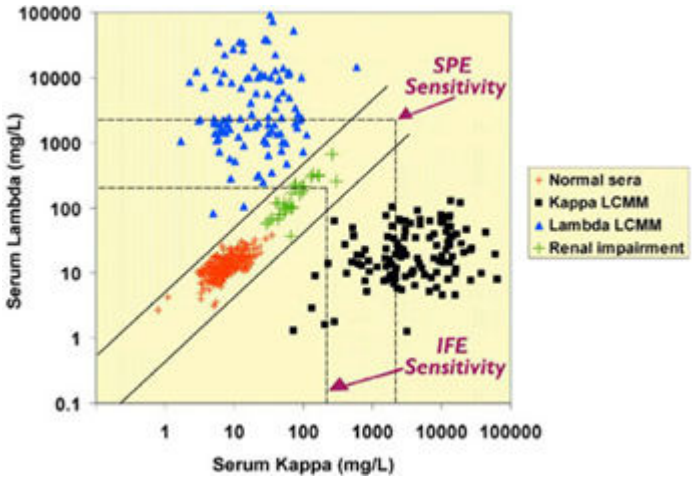
Urine immunofixation is the best test for detecting Bence-Jones proteins.

Components	**Reference Interval**
Total Protein	10-140 mg/d
Albumin, Urine	Detected
Alpha-1 Globulins, Urine	None detected
Alpha-2 Globulins, Urine	None detected
Beta Globulins, Urine	None detected
Gamma, Urine	None detected
Free Urinary Kappa Light Chains	0.14 - 2.42 mg/dL
Free Urinary Kappa Excretion/Day	By report
Free Urinary Lambda Light Chain	0.02 - 0.67 mg/dL
Free Urinary Lambda Excretion/Day	By report
Free Urinary Kappa/Lambda Ratio	2.04 - 10.37 (ratio)
IFE Interpretation	By report

Interpretive Data:
Total urinary protein is determined nephelometrically by adding the albumin and kappa and/or lambda light chains. This value may not agree with the total protein as determined by chemical methods, which characteristically underestimate urinary light chains.

Light Chain (Bence Jones) Multiple Myeloma (LCMM)

Freelite is a suitable alternative to 24-hour urine testing in the diagnosis and monitoring of light chain multiple myeloma.



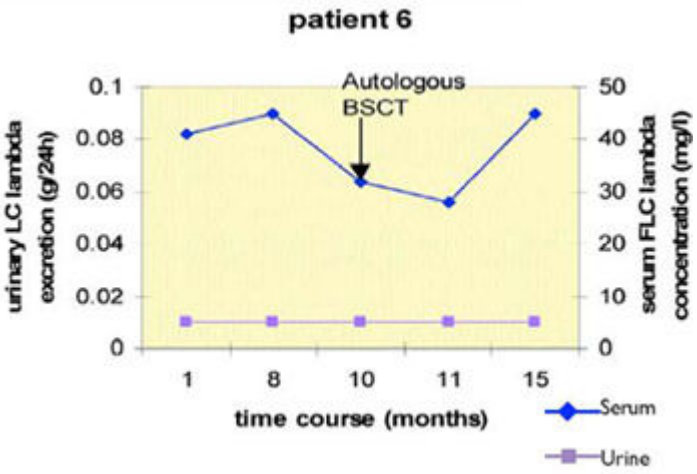
Approximately 15% of MM patients have only monoclonal free light chain and no monoclonal intact immunoglobulin secreted by the malignant clone.

These patients are difficult to diagnose as they frequently show no abnormality when tested by Serum Protein Electrophoresis (SPE).

For this reason it has been recommended that a 24 hour urine collection is tested for the presence of monoclonal free light chains.

However, urine tests for free light chains can be negative early in the disease as the capacity for reabsorption of light chains by the kidneys must be exceeded before free light chains appear in the urine.

Other contributory factors to the inherent difficulty of the urine assay are patient compliance to a 24 hour urine collection together with inaccuracy and poor precision of the technique itself.



...the serum free light chain proved sensitive enough for correlation with clinical events.

Using serum as the test medium the problems of urine assays can be overcome. In a recent study, serum measurements of free light chains were used to detect 100% of patients with LCMM.

For some patients, eg patient 6 urine free light chain concentrations are too low for reliable quantification. However, serum free light chains can be measured at all times.