Reiber diagram Reiber scheme

General:

Measurement of immunoglobulin free light chains in serum is an alternative to the analysis of Bence Jones proteins in urine.

Light chains are incorporated into immunoglobulin molecules during B-cell development and are expressed initially on the surface of pre-B-cells. Production of light chains occurs throughout the rest of B-cell development and in plasma cells, where secretion is highest.

Production of free immunoglobulin light chains in healthy individuals is approximately 500 mg/day from bone marrow and lymph node cells. There is approximately 40% excess immunoglobulin light chain production over immunoglobulin heavy chain synthesis. Possibly this is simply to allow proper conformation of the intact immunoglobulin molecules but an immunological role for the free light chains has also been proposed. There are approx. twice as many kappa producing plasma cells as lambda plasma cells. Kappa free light chains are normally monomeric, while lambda free light chains tend to be dimeric, joined by disulfide bonds. Polymeric forms of both types of free light chain can also occur.

In healthy individuals, free light chains are rapidly cleared from the blood and catabolized by the kidneys. If immunoglobulin light chains are produced in sufficient amounts to overwhelm the proximal tubules' absorption mechanisms (usually due to the presence of a plasma cell tumor) the light chains enter the distal tubules and can appear in urine. The passage of large amounts of immunoglobulin light chains through the kidneys may cause in-flammation or blockage of the kidney tubules.

The serum free light chain assay in combination with serum protein electrophoresis and serum immunofixation is sufficient to screen for pathological monoclonal plasma-proliferative disorders (MGUS, smoldering or active multiple myeloma, gammopathy) other than AL amyloidosis which re-quires all the serum tests as well as 24 h urine immunofixation electropho-resis.

A Bence Jones protein is a monoclonal light chain (paraprotein) immunoglobulin found in blood or urine, with a molecular weight of 20 kDa. The proteins are produced by neoplastic plasma cells. They can be kappa (most common) or lambda.

The detection of 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 the cases.

The light chains can be detected by heating or electrophoresis of concentrated urine. Light chains

precipitate when heated to 50-60 °C and redissolve at 90-100 °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 urine analysis stix. This leads to false negative results in patients with Bence Jones proteins.

The following tests are available:

- **Immunofixation in serum**
  Indication: Clarification of paraproteinemia, monitoring gammopathy
  Material: 2 ml serum
  TAT: 5-7 days*
  Method: immunofixation
  Note: Immunofixation electrophoresis is a highly sensitive test in detecting gammopathies.

- **Immunofixation in urine**
  Indication: Clarification of paraproteinemia, monitoring gammopathy
  Material: 10 ml urine
  TAT: 5-7 days*
  Method: immunofixation

- **Free Kappa/Lambda light chains in serum including ratio**
  Indication: Course control in monoclonal gammopathy
  Material: 2 ml serum
  TAT: 7-10 days*
  Method: turbidimetry

- **Free Kappa/Lambda light chains in urine including ratio**

Indication: Course control in monoclonal gammopathy
Material: 10 ml urine
TAT: 7-10 days*
Method: nephelometry

- **Immunofixation in CSF (oligoclonal bands, REIBER diagram)**

Indication: Suspicion of autonomous immunoglobulin formation in the CNS (e.g. in cases of multiple sclerosis), brain/blood barrier disturbance
Material: 2 ml serum + 2 ml CSF
TAT: 5-7 days*
Method: immunofixation
Preanalytics: Serum must be collected on the same day and must be sent together with CSF!

CSF protein profiles according to Felgenhauer and Reiber

Type	Interpretation
1 (C−/S−):	no bands in either CSF or serum, normal result
2 (C+/S−):	oligoclonal IgG bands in CSF but not in serum, indicating intrathecal IgG synthesis
3(C++/S+):	oligoclonal IgG bands in CSF with additional identical IgG bands in CSF and serum, also indicating intrathecal IgG synthesis
4 (C+/S+):	identical IgG bands in CSF and serum, indicating systemic immune reaction
5 (Cm/Sm):	monoclonal IgG bands in CSF and serum, indicating the presence of a systemic paraprotein
6 (Cm/S−):	monoclonal IgG band in CSF but not in serum, indicating the presence of an intrathecal monoclone; this can occur as part of the early evolution of an intrathecal oligoclonal response or represent an intrathecal paraprotein

For complete list of laboratory test offered at Freiburg Medical Laboratory, please visit
http://www.fml-dubai.com/parameter-listings/