

The Myeloma Patient's Guide to Understanding Your Test Results

Myeloma is a complex disease that can have different features in each patient. No single test or study is adequate to tell the whole story about a patient's status, but used together, test results give a more complete picture than any single test does. It is important for you and your doctor to understand your disease and to know which tests are best for monitoring your myeloma.

The following information is designed to help familiarize you with the various tests used in diagnosing and monitoring multiple myeloma and to help you work with your doctor in making the most of the information they provide. It is important to note that the normal lab values (a range, usually shown in parentheses next to your lab result) vary from lab to lab. If your lab result falls below the lower limit of normal or above the upper limit of normal, your reported lab value will be followed by a symbol to let you know that it is out of range (usually an "H" for high or an "L" for low). You should discuss the significance of any abnormal lab value with your physician.

Test results are the most important tools you and your hematologist/oncologist have to:

- Diagnose active multiple myeloma versus the earlier disease conditions called MGUS and asymptomatic ("smoldering") myeloma
- Assess the stage of your myeloma and the presence or absence of good or poor risk features
- Determine if you need to begin treatment
- Determine the best treatment option(s)
- Evaluate your response to treatment
- Monitor the course of your myeloma over time.

Tests for myeloma fall into several groups:

- Laboratory tests (blood and urine)
- Imaging studies (skeleton)
- Pathology studies (biopsies)
- Genetic studies (done on biopsy specimens)
- There are also tests used in special circumstances (amyloidosis, neuropathy, kidney or infectious complications). These tests are beyond the scope of this booklet because they are not used routinely.

LABORATORY TESTS

1. **Complete blood count (CBC)** gives information about the presence or absence of anemia, and/or low white cell count, and/or low platelet count.
2. **Chemistry/Metabolic Panel** provides the blood calcium level; serum creatinine as a measure of kidney function; and liver function test results.
3. **Serum Protein Electrophoresis (SPEP)** assesses the amount of abnormal (monoclonal) protein.
4. **Urine Protein Electrophoresis (UPEP)** shows the amount of monoclonal protein in the urine. Patients must collect urine for 24 hours and it is then sent to the lab for UPEP. Only monoclonal light chains, not heavy chains, are found in urine. Approximately 30% of patients have light chain protein in their urine as well as heavy and light chains in the blood. Approximately 10% of patients have myeloma cells that produce only light chains and no heavy chains.
5. **Immunofixation (IFE)** provides information as to the presence or absence of a monoclonal protein as well as the type of myeloma protein; i.e., heavy chain (G, A, D, or E); and/or light chain (kappa or lambda).
6. **Quantitative Immunoglobulins** shows the total amount of IgG, IgA, and IgM, both normal and abnormal (spike).
7. **Freelite® test (serum free light chain assay, SFLC)** is used to measure the number of free kappa or free lambda light chains (fragments of the monoclonal protein) if it is not possible to quantify heavy chains with serum protein electrophoresis, or light chains with urine protein electrophoresis. Some patients' myeloma cells secrete very little or no monoclonal protein that can be detected with SPEP or UPEP; the majority of these patients can be tested adequately with the serum free light chain assay.
8. **Routine urinalysis** can show the presence of protein and/or may indicate evidence of kidney damage or infection.
9. **Urine Immunofixation (urine IFE)** as for IFE in the serum, indicates both the presence or absence as well as the type of monoclonal protein.

IMAGING STUDIES

1. **X-rays** are the first imaging study done to search for myeloma-caused bone damage. A full skeletal x-ray survey is needed to demonstrate loss or thinning of bone (osteoporosis or osteopenia), holes in bone (lytic lesions), and/or fractures. X-rays are simple to do. Their limitations are that 30% or more of the bone must be missing before

x-ray can reveal the damage, and that damage to a bone shows up permanently on x-ray, even if there is no longer any active myeloma.

2. **CT scan or CAT Scan (Computerized Axial Tomography)** uses x-ray technology to create a three-dimensional digital image of the body. It is a much more precise study than x-ray, and can provide clear, detailed images of bone. Downsides include limited coverage of the body, and the possible need to use contrast agents that can pose problems for myeloma patients with kidney dysfunction.
3. **MRI scan (Magnetic Resonance Imaging)** is a non-invasive study that uses magnetic energy to produce a detailed two- or three-dimensional image of structures inside the body. It is useful for imaging plasmacytomas (tumors formed from massing of myeloma cells inside or outside the bone marrow); infiltration of the bone marrow by clumps of myeloma; and compression of the spinal cord. Although it is useful for detecting new disease rapidly, there is a 9-month or more lag time before an MRI will look normal after an area of myeloma has been successfully treated and is no longer active. It is an expensive study compared to x-ray and CT, takes 30-60 minutes to complete, and covers a limited area of the body.
4. **PET scan (Positron-Emission Tomography)** requires that a patient be injected with a sugar-fluorine compound (FDG, or fluoro-deoxyglucose) that is taken up by the body's actively multiplying cells. When the body is scanned, the areas with the highest concentrations of fluorine "glow," revealing "hot spots" where rapid metabolism can indicate areas of cancer cells. This scan covers the whole body, is very sensitive in detecting potential tumor activity, and is the only "real-time" imaging study. It is a valuable tool for patients who do not secrete monoclonal protein and whose myeloma is therefore difficult to assess, and for situations where x-ray, MRI, and CT do not provide enough information about potential new disease. It is, however, expensive and time-consuming, requiring 90-150 minutes to perform.
5. **PET/CT** combines PET and CT scans in one imaging study, providing information both about past damage and current cancer activity, thus enabling the doctor to study changes over time. It is a highly accurate study, but like standard PET, it is expensive and time-consuming.
6. **Bone density testing** is helpful for monitoring the bones of patients who have diffuse thinning (osteopenia or the more severe condition osteoporosis) of the bone cortex. Improvement with thickening of bone (increased density) occurs with the benefit of using bisphosphonate therapy.

PATHOLOGY STUDIES

1. **Bone marrow biopsy** is performed to assess the percentage of myeloma cells in the bone marrow and to determine how much they differ from normal plasma cells. Special testing is done on the bone marrow biopsy sample to assess prognosis based on chromosomal abnormalities. (See “Genetic Studies below.”)
2. **Other tissue biopsy** may be performed if the hematologist/oncologist is concerned about amyloidosis or extramedullary (outside the bone marrow) disease.

GENETIC STUDIES

1. **Metaphase Cytogenetics (karyotyping)** is a test in which the bone marrow biopsy specimen is placed into a special dish and allowed to grow in the laboratory. Cells are later taken from the growing sample and stained. The laboratory specialist uses a microscope to examine the size, shape, and number of chromosomes in the cell sample. The chromosomes can only be examined in this way if the cells are undergoing active cell division (metaphase). The stained sample is photographed to provide a karyotype, which shows the arrangement of the chromosomes. Certain abnormalities can be identified through the number or arrangement of the chromosomes. This test is particularly valuable for identifying higher-than-average-risk myeloma in patients with fewer than two copies of each chromosome (hypodiploidy) and in those with deletion of chromosome 13 during cell division.
2. **Fluorescence *In Situ* Hybridization (FISH)** provides researchers with a way to visualize and map the genetic material in an individual's cells, including specific genes or portions of genes. This is important for understanding a variety of chromosomal abnormalities and other genetic mutations. Unlike metaphase cytogenetic, FISH does not have to be performed on cells that are actively dividing. It is useful for defining high-risk myeloma in patients with certain chromosomal translocations and deletions, especially t(4;14) and 17p-, in which the top part of chromosome 17 is lost (missing).