



Tests to assess monoclonal protein

This important group of blood and urine tests is used to assess the amount and activity of myeloma. These tests measure the monoclonal protein that myeloma cells secrete into the blood and/or urine.

Serum Quantitative Immunoglobulins (QIg)

REFERENCE RANGE for patients ≥ 18 years old

IgG 767–1,590 mg/dL

IgA 61–356 mg/dL

IgD ≤ 10 mg/dL

IgE ≤ 214 mg/dL

IgM 37–286 mg/dL



QIg testing measures the total amount of each primary immunoglobulin or antibody class (also called an “isotype”) in the serum. It measures both polyclonal (normal) and monoclonal (myeloma-related) immunoglobulins.

Thus, if an increase in one of the antibody isotypes is found, further testing with electrophoresis is required. This testing can determine if the elevation is caused by the presence of monoclonal immunoglobulin protein.

QIg is often the preferred way to assess IgA protein, because IgA may be difficult to quantify with electrophoresis. **Note:** The ranges for IgD and IgE are reported differently from those for IgG, IgA, and IgM.

IgA may be difficult to quantify with electrophoresis. That’s why QIg is often the preferred way to assess IgA protein. Note: The ranges for IgD and IgE are reported differently from those for IgG, IgA, and IgM.

Isotypes of immunoglobulins

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appa

lambda

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WITHDRAW CONSENT

IgE kappa	IgE lambda
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Serum Protein Electrophoresis (SPEP)

REFERENCE RANGE

albumin 3.3–5.7 g/dL

alpha-1 0.1–0.4 g/dL

alpha-2 0.3–0.9 g/dL

beta-2 0.7–1.5 g/dL

gamma 0.5–1.4 g/dL

SPEP is one of the most important tests used to diagnose and assess the status of myeloma. It measures the amount of M-protein that is made by myeloma cells. The amount of M-protein production is linked to the number and/or activity of myeloma cells, except with non-secretory myeloma.



SPEP separates and quantifies proteins based on their electrical charge, size, and shape. As you learned above, the two types of protein in serum are albumin and globulin. Although there is only one type of albumin, there are sub-types of globulin, usually appearing on SPEP as alpha-1, alpha-2, beta-1, beta-2, and gamma globulins.

Immunoglobulin proteins are gamma globulins, and usually, M-protein produced by myeloma cells will separate out in the gamma region of the graph. The exception to this rule is IgA protein. This protein may sometimes migrate to the beta or even the alpha-2 region. If this occurs, other tests can be more useful than SPEP.

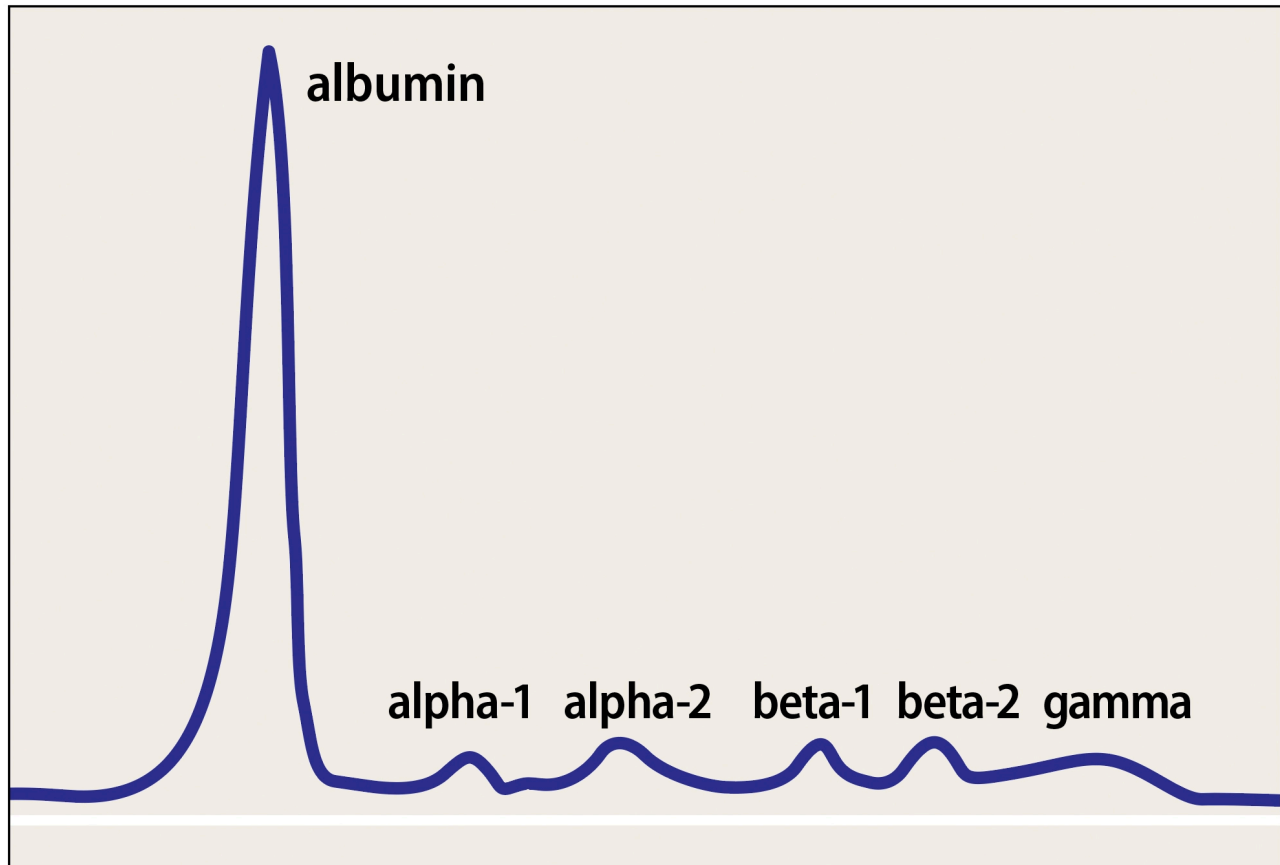
Monoclonal immunoglobulin protein appears on the results graph as a narrow spike. Because all the cells in the M-protein are identical and have the same electrical charge, they gravitate to the same small gamma region and form a narrow spike on the graph. The M-spike is the telltale indicator of myeloma protein.

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blood and is produced in the liver. When myeloma is active, it stimulates the production of certain cellular proteins (cytokines). These cytokines impede the ability of the liver to produce albumin, and the level of albumin in the serum drops. According to the [revised International Staging System \(R-ISS\)](#) ([/international-staging-system-iss-revised-iss-r-iss](#)), albumin is one of two blood proteins used to predict the behavior of myeloma cells at diagnosis. The other blood protein is serum beta-2 microglobulin (β 2-microglobulin, β 2M, or β 2M).

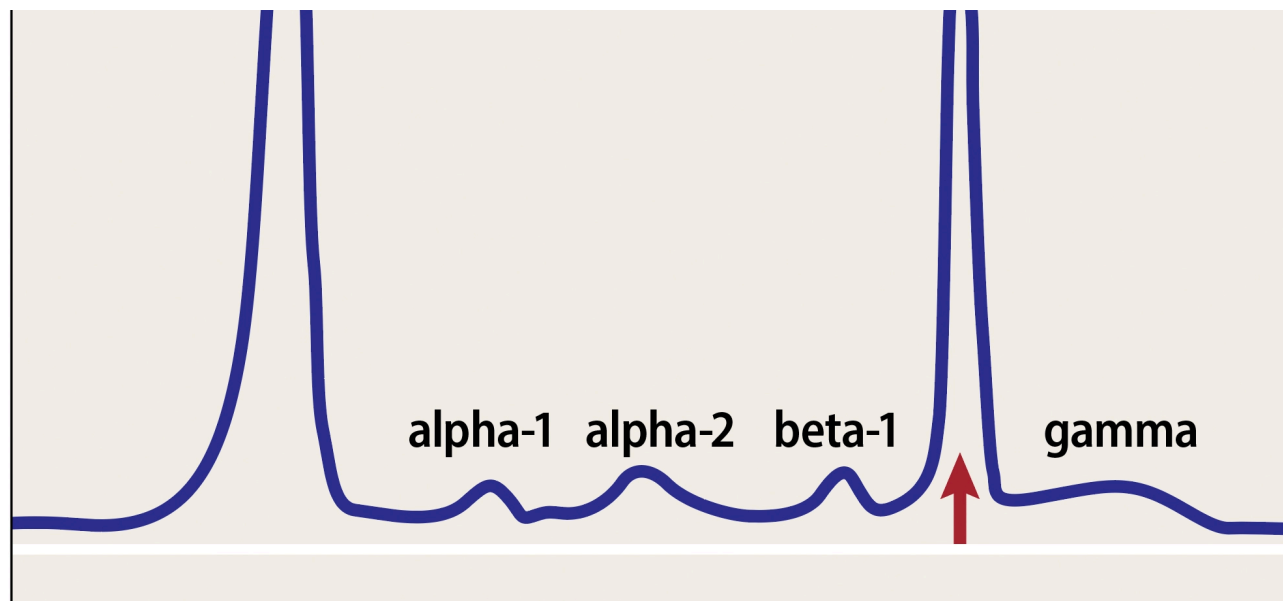
SPEP test result examples:



Normal SPEP result

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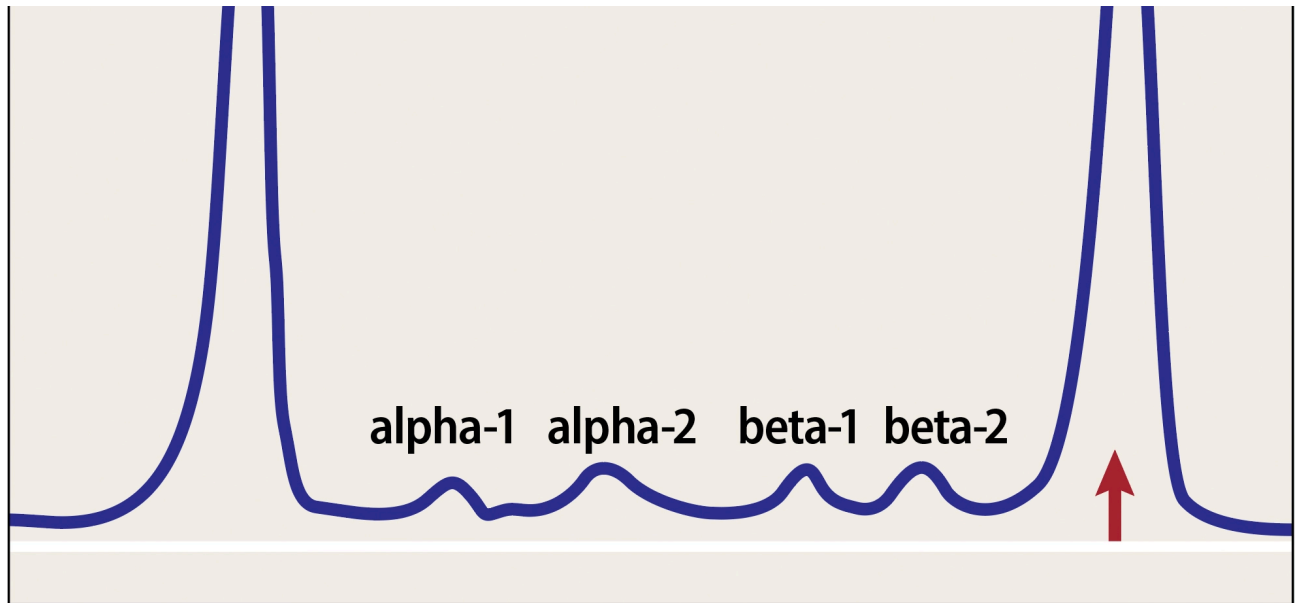


Abnormal result with myeloma cells producing the M-protein, creating an M-spike in the beta-2 region



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Abnormal result with myeloma cells producing the M-protein, creating an M-spike in the gamma region



Urine Protein Electrophoresis (UPEP)

REFERENCE RANGE

globulins in the urine no significant amount

total protein < 167 mg/24 hours

urine albumin < 5 mg/dL

Approximately 30% of myeloma patients have light chain protein in their urine as well as heavy chain protein in the blood. Approximately 15%–20% of patients have myeloma cells that produce only light chains and no heavy chains. Although fragments of heavy chain proteins can be found in the urine, intact heavy chains are too large to fit through the capillaries that send blood to the kidneys for filtration. Light chains, however, are so small and light in molecular weight (hence the name “light” chains). Because of their small size, they can easily pass t

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proteins in the urine. SPEP separates the proteins according to their size and electrical charge. Then, it quantifies the amount of light chain protein.

Immunofixation electrophoresis (IFE)

The IFE laboratory test identifies the type of M-protein (heavy chain IgG, IgA, IgD, IgE, or IgM; kappa or lambda light chain). It does not measure the amount of M-protein, so there is no reference range. Urine IFE is performed on a 24-hour urine collection.

The test result is either negative or positive for the presence of a specific type of M-protein. Serum or urine immunofixation that is negative for an M-protein is considered normal.

SPEP and IFE provide different but complementary information. You need to be aware of both the amount (SPEP) and type (IFE) of immunoglobulin protein made by your myeloma cells.



The [IMWG Uniform Response Criteria for Multiple Myeloma \(/node/2193\)](#) define complete response (CR) to therapy as:

Negative immunofixation on the serum and urine, and
disappearance of any soft tissue plasmacytomas, and
 $\leq 5\%$ plasma cells in the bone marrow.

Serum Free Light Chain (sFLC)

REFERENCE RANGE*

free kappa 3.3–19.4 mg/L

free lambda 5.71–26.3 mg/L

kappa/lambda ratio 0.26–1.65

*The reference range cited above is used by the Mayo Clinic. Your laboratory may use a different reference range.

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antibody molecules circulating in their blood, but they have fewer free light chains.

The sFLC test can show if the myeloma cells are releasing kappa free light chains at a high level and lambda light chains at a normal or lower level. The sFLC test can also show if the myeloma cells are secreting lambda free light chains at a higher level and kappa free light chains at a normal or lower level.

Some patients' myeloma cells secrete both heavy and light chains. Some secrete only heavy chains. Some secrete only light chains; this is called Bence-Jones myeloma. Some patients' myeloma cells may secrete many more light chains at relapse than they did prior to treatment.



The sFLC test is useful for patients with any type of myeloma, including low-secreting or non-secretory myeloma, and at different stages of disease, during treatment and after treatment. Your sFLC test results are a meaningful way to monitor your myeloma when the tests are tracked over time.

Do not compare your sFLC test results with other patients. The sFLC test is also used in the diagnosis and monitoring of patients with MGUS, and in monitoring patients with SMM. For more information, read the IMF's booklet [Understanding MGUS and Smoldering Multiple Myeloma \(/resource-library/understanding-mgus-smoldering-myeloma\)](/resource-library/understanding-mgus-smoldering-myeloma) .

Possible sFLC test results

Kappa/Lambda ratio	Kappa	Lambda	Interpretation
(0.26 - 1.65)	(3.3-19.4 mg/L)	(5.7-26.3 mg/L)	

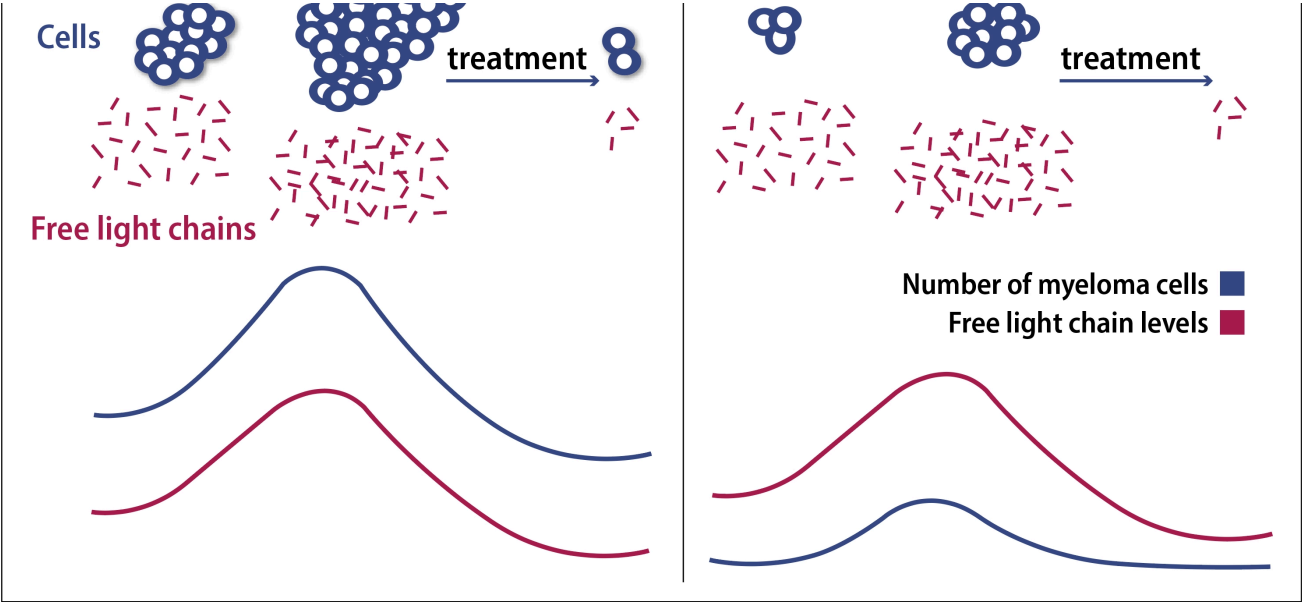
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Low	Normal	High	Monoclonal lambda free light chains.
Normal	High	High	Plasma cells of both light chain types are secreting antibodies (possible infection, autoimmunity, or kidney damage).
Normal	Low	Low	General immense suppression (possibly due to chemotherapy or for other reasons).
High	Normal	Low	Possible low-level monoclonal kappa free light chains or immune suppression of lambda.
Low	Low	Normal	Possible low-level monoclonal lambda free light chains or immune suppression of kappa.
"Slightly" High	"Slightly" high	Normal or "slightly" high	Possible kidney damage ("slightly" = up to approximately 3.1).

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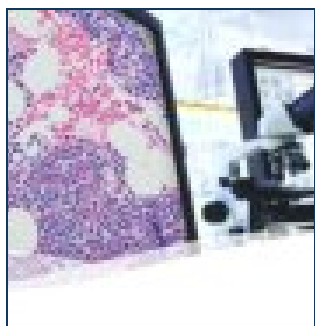
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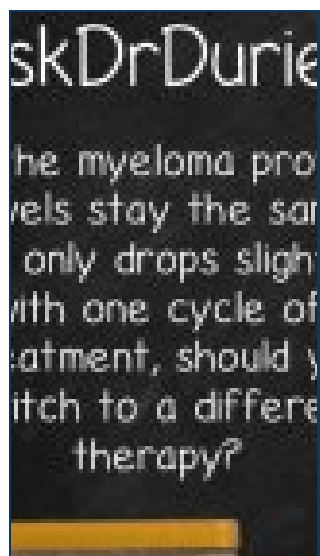
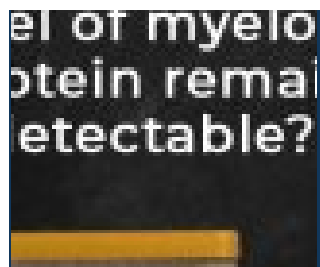


Does the M-spike cor
the amount of myelo
protein in the body?

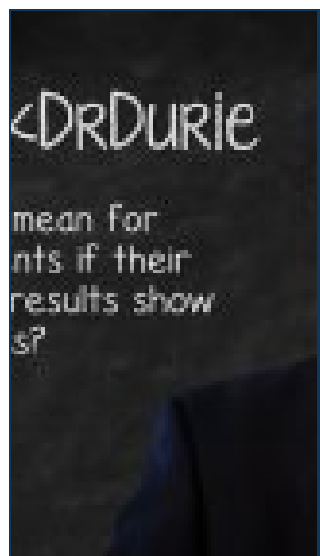
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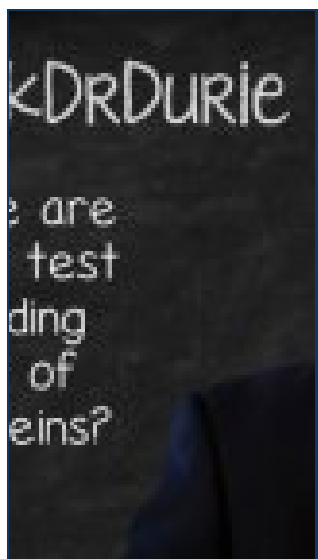
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Comprised of leading medical researchers, hematologists, oncologists, oncology-certified nurses, medical editors, and medical journalists, our team has extensive knowledge of the multiple myeloma treatment and care landscape.

Additionally, the content on this page is medically reviewed by myeloma physicians and healthcare professionals.

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