

Understanding Paraprotein in Myeloma

Understanding the medical language surrounding myeloma can be difficult, it doesn't help that the medical profession uses complex words and often has a number of words to describe the same thing. Many of you will have heard the words paraprotein, m protein, antibodies, immunoglobulins and light chains when speaking with the treating team or doing your own research.

This fact sheet aims to help you understand these complex concepts as it is important to understand how myeloma is categorised, how response to treatment is assessed and how myeloma is monitored over time.

Myeloma and the plasma cell

Plasma cells are made in the bone marrow and form part of the immune system. Their usual function is to make antibodies to fight infections against invading bacteria or viruses. These antibodies then attach to the bacteria or virus by finding a surface protein or 'antigen' to bind to. This then signals other immune cells to remove the invading bacteria or virus and overcome/eliminate the infection. Antibodies are also referred to as immunoglobulins.

Myeloma is a cancer of the plasma cells. When plasma cells become cancerous, they make abnormal antibodies in large quantities that serve no useful function. These abnormal antibodies can be found and measured in the blood and are referred to as paraprotein or m protein. Most people with myeloma will have a paraprotein in their blood, but some do not. Those without paraprotein will most likely have light chain myeloma or non-secretory myeloma.

Understanding immunoglobulins (antibodies)

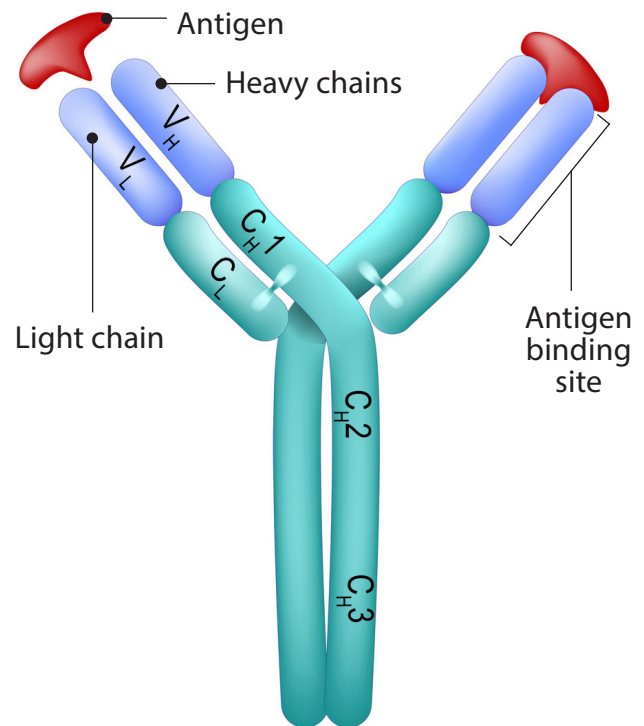
There are many different proteins in the body and the blood, the most common being albumin and immunoglobulins. Immunoglobulins are molecules made up of 2 heavy chains and 2 light chains (see figure 1).

There are five types of heavy chains; IgG, IgA, IgM, IgD and IgE and two types of light chains; Kappa and Lambda. Each immunoglobulin is made up of 1 type of heavy chain and 1 type of light chain. Each diagnosis of myeloma is labelled according to the type of immunoglobulin that has become abnormal eg IgG Kappa. Sometimes only light chains become abnormal and break away from the heavy chain and reproduce on their own. We then label the myeloma according to the type of light chain eg. Lambda light chain myeloma.

Some people may over produce two different immunoglobulins eg. IgG Kappa and IgA Lambda. These are then measured as two different paraproteins and is referred to as bi-clonal myeloma.

IMMUNOGLOBULIN

figure 1



Each immunoglobulin has their own role to play in the immune system as outlined in the table below.

Immunoglobulin Type	Usual Function
IgG	Most common immunoglobulin. Attaches itself to germs and mobilises the immune system to kill the germ.
IgA	Accumulates in mucous membranes and responds first to infection of these tissues
IgM	First response to sight of infection in the blood
IgD	Occurs in low levels in the blood. Thought to help IgM
IgE	Responsible for allergic reactions

Usual Function of Light Chains (Kappa and Lambda)

- Light chains help to make the antibody specific for a specific antigen or infection. Eg measles
- In myeloma the light chains can detach from the heavy chains and be more abundant than normal (light chain myeloma)
- Also called Bence Jones proteins because they were discovered in the urine by a doctor called Henry Bence Jones in 1845
- Light chain proteins can pass through the kidneys but can also get stuck, causing kidney damage

It is important to note that the presence of paraprotein in the blood is not always caused by myeloma. Monoclonal Gammopathy of Uncertain Significance (MGUS) produces small amounts of paraprotein without causing any problems. Not all people with MGUS go on to develop myeloma however we know that all people with myeloma once had MGUS but it may not have been detected at the time. In fact, there is only a 1% chance per year of MGUS progressing to myeloma and many people with MGUS never develop myeloma. Monoclonal Gammopathy of Renal Significance (MGRS) is a disease that can cause significant damage to the kidneys. A rise in IgM immunoglobulin can cause a rare form of lymphoma called Waldenström macroglobulinaemia. Light chain amyloidosis is a condition where the light chains change their shape and get stuck in tissues such as the nerves, heart and kidneys. Amyloidosis can occur on its own or with myeloma as well.

Monitoring myeloma with the paraprotein and light chains

For those that produce a paraprotein, it is often the easiest way to keep track of the myeloma's activity. When myeloma is active, we will see a rise in paraprotein and when myeloma is responding to treatment, we will see a decrease in paraprotein. It is important to note that a small rise in paraprotein will not always mean that more treatment is needed straight away. It is normal for the paraprotein to fluctuate slightly and the doctor will be monitoring the trend closely. The paraprotein result can also differ slightly if processed in different laboratories. Keeping tests with the same pathology service is recommended for accurate comparisons.

Paraprotein measurements are done regularly at intervals (eg monthly or three monthly) to see how well the treatment is working and to check that the myeloma is remaining stable during periods between treatments.

In those that overproduce light chains, the same approach will be taken to monitor the myeloma's activity. Unlike paraprotein, everyone will have some light chains in their blood. It is only when they increase above normal levels that monitoring is required.

The doctor will also be assessing other levels in the blood and any other symptoms that might be present as the paraprotein is only one feature of the disease.

Assessing response to treatment

The doctor will use the International Myeloma Working Group's Response Criteria to assess the response to treatment, that is, how well is the treatment working against the myeloma. This is done by comparing the blood and/or urine level of paraprotein or light chains before treatment to certain timepoints during treatment, typically once each cycle of treatment has been completed.

If no paraprotein is detected after treatment or light chains return to normal levels, it is considered a complete response (CR). If the paraprotein has fallen and is still detectable and stable after treatment it is considered a partial response (PR). A stable low level of paraprotein maintained over time is often described as plateau phase. The term 'plateau' phase is used because a graph of the paraprotein results appears flat like a plateau.

For those with non-secretory myeloma it may be necessary to measure response to treatment with bone marrow biopsies or scans.

It is possible for myeloma to become active again without producing a paraprotein. This is why it's so important to report any new symptom such as pain to the doctor for investigation.



For more information about myeloma and treatments, please see our book, *Myeloma a Comprehensive Guide* and our range of other resources. They can be found at www.myeloma.org.au or contact head office e: support@myeloma.org.au t: 03 9428 7444 (AEDT) for hard copies