Waldenstrom Macroglobulinemia Early Detection, Diagnosis, and Staging

Detection and Diagnosis

Catching cancer early often allows for more treatment options. Some early cancers may have signs and symptoms that can be noticed, but that is not always the case.

- Can Waldenstrom Macroglobulinemia Be Found Early?
- Signs and Symptoms of Waldenstrom Macroglobulinemia
- How Is Waldenstrom Macroglobulinemia Diagnosed?

Stages and Outlook (Prognosis)

After a cancer diagnosis, staging provides important information about the extent of cancer in the body and anticipated response to treatment.

- How Is Waldenstrom Macroglobulinemia Staged?
- Survival Rates for Waldenstrom Macroglobulinemia

Questions to Ask About Waldenstrom Macroglobulinemia

Here are some questions you can ask your cancer care team to help you better understand your cancer diagnosis and treatment options.

- Questions To Ask About Waldenstrom Macroglobulinemia

Can Waldenstrom Macroglobulinemia Be Found Early?
Waldenstrom macroglobulinemia (WM) is not common, and at this time there are no widely recommended screening tests to look for this disease in people without symptoms.

Still, many cases of WM are found early, either when people go to the doctor because of symptoms they are having, or when they have blood tests done for other reasons. The best way to find this cancer early is to see your doctor if you have signs or symptoms that might be caused by this disease.

- References

Last Medical Review: July 19, 2018 Last Revised: July 19, 2018


See all references for Waldenstrom Macroglobulinemia

Last Medical Review: July 19, 2018 Last Revised: July 19, 2018

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When WM does cause symptoms, some of them can be like those seen with other types of non-Hodgkin lymphoma (NHL). For example, weight loss, fever, night sweats, and swollen lymph nodes can be seen in many types of NHL.

Other WM symptoms are caused by the large amounts of abnormal IgM antibody (M protein) made by the cancer cells:

• In hyperviscosity syndrome, too much of the M protein in the blood can cause it to become too “thick.” (This is not the kind of thickness that can be treated with drugs known as blood thinners.) When the blood gets too thick, it has trouble moving through blood vessels. This can cause problems such as poor circulation to the brain, which can lead to symptoms like those from a stroke.
• If the M protein only thickens the blood in cooler parts of the body (like in the tip of the nose, ears, fingers, and toes), it is called a cryoglobulin. Cryoglobulins can cause pain or other problems in these areas if a person is exposed to cooler temperatures.
• A condition called amyloidosis can occur when a part of the IgM antibody (called the light chain) builds up in organs like the heart and kidneys. This buildup can lead to heart and kidney problems.

Not all people with WM develop hyperviscosity, cryoglobulins, or amyloidosis.

**Common symptoms of WM**

**Weakness:** This is one of the most common symptoms of WM. It can be caused by anemia (too few red blood cells), which can happen when the WM cells crowd out normal cells in the bone marrow. Some people also feel weak when the blood thickens from the buildup of the abnormal protein.

**Loss of appetite:** Some people with WM lose their appetite.

**Fever, sweats, weight loss:** WM, like other lymphomas, can cause fevers (without an infection), drenching night sweats, and weight loss (without trying). These are called B symptoms.

**Neuropathy:** In some people with WM, the abnormal antibody can attack and damage nerves outside the brain. This can lead to numbness or a painful “pins and needles” sensation in the feet and legs, which is called neuropathy.

**Less common signs and symptoms of WM**
**Enlarged lymph nodes:** These usually appear as lumps under the skin around the neck, in the groin, or in the armpits. Enlarged lymph nodes are usually about 1 or 2 inches (2.5-5 cm) across. They are seen less often in WM than in most other lymphomas.

**Swollen abdomen (belly):** WM can sometimes make the spleen or liver bigger, making the belly look swollen. In the upper part of the abdomen, the liver is on the right and the spleen on the left. When the spleen gets larger, it can press on the stomach, which makes people feel full when they eat even a small amount.

**Circulation system symptoms:** In hyperviscosity syndrome, the thickened blood causes poor brain circulation, leading to problems like headache, confusion, and dizziness. It can also cause symptoms like those seen with a stroke, including slurred speech and weakness on one side of the body. Patients with these symptoms should contact their doctor right away.

**Abnormal bleeding:** High levels of abnormal antibody can damage blood vessels, which can lead to problems like nosebleeds and bleeding gums.

**Vision problems:** Bleeding around the small blood vessels inside the eyes or poor circulation in these vessels caused by thickened blood might lead to blurred vision or blind spots.

**Kidney problems:** High levels of the M protein can damage the kidneys directly or through the development of amyloidosis. When the kidneys don’t work well, excess salt, fluid, and body waste products stay in the blood. This can cause symptoms like weakness, trouble breathing, and fluid buildup in body tissues.

**Heart problems:** High levels of the M protein can damage heart tissue directly or through the development of amyloidosis, in which the protein builds up in the heart muscle. This weakens the heart, affecting its ability to pump blood. In addition, because the blood of people with WM is thicker than normal, their hearts have to work harder to pump blood throughout the body. This strain can wear down the heart muscle, leading to a condition called **congestive heart failure.** Symptoms can include heart palpitations, feeling tired and weak, cough, shortness of breath, rapid weight gain, and swelling in the feet and legs.

**Infections:** The high levels of abnormal antibody in WM can slow the body’s normal antibody production. This makes it harder for the body to fight infections.

**Digestive symptoms:** In some people with WM, the buildup of the M protein in the intestines can lead to problems such as diarrhea, poor absorption of vitamins, or
gastrointestinal bleeding (seen as blood in the stools or dark stools).

**Sensitivity to cold:** In people with cryoglobulins, exposure to cold temperatures can lead to pain, itching, a bluish color, or even sores on the tip of the nose, ears, fingers, or toes due to reduced blood flow to these areas.

- **References**


See all references for Waldenstrom Macroglobulinemia

Last Medical Review: July 19, 2018 Last Revised: July 19, 2018

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**Tests for Waldenstrom Macroglobulinemia**

Waldenstrom macroglobulinemia (WM) is often found when a person goes to see their doctor because of symptoms they are having, or because they just don’t feel well and
go in for a checkup. Sometimes it’s found in people without symptoms when they have blood tests done for some other reason.

If signs or symptoms suggest that a person might have WM, exams and tests will be done to be sure. The most important tests will look for abnormal proteins in the blood and abnormal cells in the bone marrow. Because WM is a type of lymphoma, like other lymphomas it can invade the bone marrow, lymph nodes, and other organs.

**Medical history and physical exam**

Your doctor will want to get a thorough medical history, including information about your symptoms, possible risk factors, family history, and other medical conditions.

Next, the doctor will examine you, paying special attention to your lymph nodes and other areas of your body that might be involved, including the eyes, nerves, spleen, and liver. The doctor might also look for signs of infection, which can cause many of the same symptoms.

If the doctor suspects that WM (or another type of lymphoma) might be causing your symptoms, the next step probably will be to order blood tests. You might also be referred to a hematologist, a doctor who specializes in diseases of the blood, or an oncologist, a doctor who specializes in cancer.

**Lab tests**

WM might be suspected if your doctor finds you have low blood cell counts or unusual protein levels on blood tests. If so, your doctor may order a blood test called serum protein electrophoresis to find out what the abnormal proteins are. It is usually only after these tests are done that a biopsy of either the bone marrow or a lymph node is considered.

**Blood cell counts**

The complete blood count (CBC) is a test that measures the levels of red blood cells, white blood cells, and platelets. If lymphoma cells occupy too much of the bone marrow, these blood levels may be low.

**Immunoglobulin levels**
This test measures the levels of the different antibodies (immunoglobulins) in the blood – IgA, IgE, IgG, and IgM – to see if any are abnormally high or low. In WM the level of IgM is high but the IgG level is often low.

**Electrophoresis**

The abnormal immunoglobulin made in WM is an IgM antibody. This antibody is monoclonal, meaning that it is many copies of the exact same antibody. Serum protein electrophoresis (or SPEP) is a test that measures the total amount of immunoglobulins in the blood and finds any monoclonal immunoglobulin. Another test, such as immunofixation electrophoresis, is then used to determine the type of antibody that is abnormal (IgM or some other type).

Finding a monoclonal IgM antibody in the blood is needed to diagnose WM. This abnormal protein in WM is known by many different names, including monoclonal immunoglobulin M, IgM protein, IgM spike, IgM paraprotein, M protein, and M-spike. High levels of other types of monoclonal immunoglobulins, like IgA or IgG, are seen in different disorders (like multiple myeloma and some other lymphomas).

Sometimes pieces of the IgM protein are excreted by the kidneys into the urine. These proteins can be detected with a test called urine protein electrophoresis (or UPEP).

**Viscosity**

Viscosity is a measure of how thick the blood is. If the IgM level is too high, the blood will become thick ( viscous) and can’t flow freely (think about pouring honey compared to pouring water).

**Cryocrit**

This test measures the blood levels of cryoglobulins (proteins that clump together in cool temperatures and can block blood vessels).

**Cold agglutinins**

Cold agglutinins are antibodies that attack and kill red blood cells, especially at cooler temperatures. These dead cells can then build up and block blood vessels. A blood test can be used to detect these antibodies.

**Beta-2 microglobulin (2M)**
This test measures another protein made by the cancer cells in WM. This protein itself
doesn’t cause any problems, but it’s a useful indicator of a patient’s prognosis (outlook).
High levels of 2M are linked with a worse outlook.

Biopsies

The symptoms of WM and non-Hodgkin lymphoma (NHL) are not distinctive enough for
a doctor to know for certain if a person has one of them, based on symptoms alone.
Most symptoms can also be caused by non-cancerous problems like infections or by
other kinds of cancers. Blood tests can help point to the correct diagnosis, but a biopsy
(removing samples of affected tissue to look at under a microscope) is the only way to
be sure. Several types of biopsies might be used.

Bone marrow aspiration and biopsy

This is the most important type of biopsy for WM, and is needed to confirm the
diagnosis. It can be done at the doctor’s office or at the hospital.

The bone marrow aspiration and biopsy are usually done at the same time. The
samples are taken from the back of the pelvic (hip) bone, although in some cases they
may be taken from the sternum (breast bone) or other bones.

- In bone marrow aspiration, you lie on a table (either on your side or on your belly).
The doctor cleans the skin over the hip and then numbs the area and the surface of
the bone by injecting a local anesthetic. This may briefly sting or burn. A thin, hollow
needle is then inserted into the bone, and a syringe is used to suck out a small
amount of liquid bone marrow. Even with the anesthetic, most patients still have
some brief pain when the marrow is removed.
- A bone marrow biopsy is usually done just after the aspiration. A small piece of
bone and marrow is removed with a slightly larger needle that is pushed down into
the bone. This may also cause some brief pain.

Once the biopsy is done, pressure is applied to the site to help stop any bleeding. There
will be some soreness in the biopsy area when the numbing medicine wears off. Most
patients can go home right after the procedure.

The bone marrow samples are then sent to a lab, where they are tested to see if they
have lymphoma cells (see below). For a diagnosis of WM, at least 10% of the cells in
the bone marrow must be lymphoplasmacytoid lymphoma cells.
Fine needle aspiration (FNA) biopsy

In an FNA biopsy, the doctor uses a very thin, hollow needle with a syringe to withdraw a small amount of tissue from a tumor or lymph node. This type of biopsy is useful for sampling lymph nodes to see if they are enlarged because of cancer or an infection. FNA can help diagnose some lymphomas, but WM is usually diagnosed with a bone marrow biopsy.

For an FNA on an enlarged node near the surface of the body, the doctor can aim the needle while feeling the node. If the enlarged node (or tumor) is deep inside the body, the needle can be guided while it is seen on a computed tomography (CT) scan or ultrasound (see the descriptions of imaging tests later in this section).

The main advantage of FNA is that it does not require surgery and can often be done in a doctor’s office. The main drawback is that in some cases it might not get enough tissue to make a definite diagnosis of lymphoma. However, advances in lab tests (discussed later in this section) and the growing experience of many doctors with FNA have improved the accuracy of this procedure.

Excisional or incisional biopsy

For these types of biopsies, a surgeon cuts through the skin to remove an entire lymph node or tumor (excisional biopsy) or just a small part of a large tumor or lymph node (incisional biopsy). These biopsies are rarely needed in people with WM because the diagnosis is usually made with a bone marrow biopsy. They are used more often for other types of lymphoma.

If the area to be biopsied is near the skin surface, this can be done using local anesthesia (numbing medicine). If the area is inside the chest or abdomen, general anesthesia or deep sedation is used (where the patient is asleep). These types of biopsies almost always provide enough tissue to diagnose the exact type of lymphoma.

Fat pad fine needle aspiration

This type of biopsy may be used in some people with WM to check for amyloid. In this procedure, a thin, hollow needle with a syringe attached is inserted into an area of fat (usually under the skin of the abdomen/belly). A small amount of fat is removed and sent to the lab for testing.

Lab tests on biopsy specimens
All biopsy specimens are looked at in the lab by a pathologist – a doctor with special training in using lab tests to diagnose diseases. In some cases, a hematopathologist, a doctor with further training in diagnosing blood and lymph node diseases, might also look at the biopsy. The doctors look at the size and shape of the cells and how they are arranged. Sometimes just looking at the cells doesn’t provide a clear answer, so other lab tests are needed.

**Immunohistochemistry**

In this test, a part of the biopsy sample is treated with special man-made antibodies that attach to cells only if they contain specific proteins. These antibodies cause color changes in the cells, which can be seen with a microscope. This test may help tell different types of lymphoma from one another and from other diseases.

**Flow cytometry**

In this test, cells are treated with special man-made antibodies. Each antibody sticks only to certain types of cells. The cells are then passed in front of a laser beam. If the cells now have antibodies attached to them, the laser will make them give off light, which is measured and analyzed by a computer.

This is the most common test for **immunophenotyping** – classifying lymphoma cells according to the proteins (antigens) on their surfaces. Different types of lymphocytes have different antigens on their surface. These antigens also change as each cell matures.

This test can help show if a lymph node is swollen because of lymphoma, some other cancer, or a non-cancerous disease. It has become very important in helping doctors determine the exact type of lymphoma so they can select the best treatment.

**Cytogenetics**

Doctors use this technique to look at the chromosomes (long strands of DNA) inside lymphoma cells. Cells (usually from the bone marrow) are first grown in the lab. Then the chromosomes are stained and looked at closely. Because it takes time for the cells to start dividing, this test can take a few weeks.

In some lymphomas, the cells may have too many chromosomes, too few chromosomes, missing parts of chromosomes (called deletions), or other abnormalities. These changes can help identify the type of lymphoma.
Molecular genetic tests

Molecular tests such as fluorescent in situ hybridization (FISH) and polymerase chain reaction (PCR) are not usually needed to diagnose WM, but they are sometimes used to diagnose other types of NHL. These tests look at the cells’ DNA without having to grow the cells in the lab first. The tests can give results in less time than cytogenetics and can be done on cells from different sources (like lymph nodes, blood, and bone marrow). They are generally used to look for specific chromosome or gene changes, not just any change.

More testing information

See Testing Biopsy and Cytology Specimens for Cancer to learn more about tests used to diagnose cancer and what the results can tell you.

Imaging tests

Imaging tests use x-rays, magnetic fields, sound waves, or radioactive particles to produce pictures of the inside of the body. These tests are not needed to diagnose WM, but one or more of them might be done to help show how much disease and where it is in the body.

Chest x-ray

An x-ray might be done to look at the chest for enlarged lymph nodes.

Computed tomography (CT) scan

The CT scan is an x-ray that makes detailed cross-sectional images of your body. Unlike a regular x-ray, CT scans can show the detail in soft tissues (such as internal organs). This scan can help show if any lymph nodes or organs in your body are enlarged. CT scans are useful for looking for signs of lymphoma in the chest, abdomen, and pelvis.

CT-guided needle biopsy: CT scans can also be used to guide a biopsy needle into a suspicious area. For this procedure, the patient lies on the CT scanning table while the doctor moves a biopsy needle through the skin and toward the area. CT scans are repeated until the needle is in the right place. A biopsy sample is then removed and sent to the lab.
Magnetic resonance imaging (MRI) scan

This test is rarely used in WM, but if your doctor is concerned about the brain or spinal cord, MRI is very useful for looking at these areas.

Ultrasound

Ultrasound can be used to look at lymph nodes near the surface of the body or to look inside your abdomen for enlarged lymph nodes or organs such as the liver, spleen, and kidneys. (It can’t be used to look at organs or lymph nodes in the chest because the ribs block the sound waves.) It is sometimes used to help guide a biopsy needle into an enlarged lymph node.

Positron emission tomography (PET) scan

A PET scan can be helpful in spotting small collections of cancer cells. It is even more valuable when combined with a CT scan (PET/CT scan).

PET scans also can help tell if an enlarged lymph node contains lymphoma or not. It can help spot small areas that might be lymphoma, even if the area looks normal on a CT scan. These tests can be used to tell if a lymphoma is responding to treatment. They can also be used after treatment to help decide whether an enlarged lymph node still contains lymphoma or is merely scar tissue.

References


For most types of cancer, determining the stage is very important. The stage of a cancer describes how much cancer is in the body. It helps determine how serious the cancer is and how best to treat it. Doctors also use a cancer’s stage when talking about survival statistics.

There is no standard staging system for Waldenstrom macroglobulinemia (WM) based on the extent of the disease in the body because this hasn’t been shown to be important when looking at outcomes or deciding on treatment.

Instead, doctors look at other factors, such as age, blood cell counts, the amount of immunoglobulin (IgM) in the blood, and the level of another protein in the blood called beta-2 microglobulin (2M). People with lower levels of IgM and 2M tend to do better than those with higher levels. People with WM who are older, are anemic (based on a low blood hemoglobin level), or have a low blood platelet count tend to have a poorer outlook.
Experts have used these factors to develop a system that helps predict prognosis (outlook) for patients with WM. It is called the International Prognostic Scoring System for Waldenstrom Macroglobulinemia (ISSWM). This system takes into account the factors that seem to predict a poorer outcome, such as:

- Older than 65
- Blood hemoglobin level 11.5 g/dL or less
- Platelet count 100,000/mcL or less
- Beta-2 microglobulin more than 3 mg/L
- Monoclonal IgM level more than 7 g/dL

Except for age, each of these factors is worth a single point. The points are added to make a score, which is used to divide patients into 3 risk groups:

- The low-risk group includes patients 65 or younger who have no more than 1 point.
- The intermediate-risk group includes those who are older than 65 with 2 or fewer points, and those younger than 65 who have 2 points.
- The high-risk group includes those of any age who have at least 3 points.

These groups can be used to help predict survival (discussed in more detail in Survival Rates for Waldenstrom Macroglobulinemia).

**References**


See all references for Waldenstrom Macroglobulinemia

Last Medical Review: July 19, 2018 Last Revised: July 19, 2018
Survival Rates for Waldenstrom Macroglobulinemia

Survival rates are often used by doctors as a way of discussing a person’s outlook.

Survival rates tell you what percentage of people with the same type and stage of cancer are still alive a certain length of time (usually 5 years) after they were diagnosed. These numbers can’t tell you how long you will live, but they may help give you a better understanding about how likely it is that your treatment will be successful.

What is a 5-year survival rate?

Statistics on the outlook for a certain type and stage of cancer are often given as 5-year survival rates, but many people live longer – often much longer – than 5 years. The 5-year survival rate is the percentage of people who live at least 5 years after being diagnosed with cancer. For example, a 5-year survival rate of 90% means that an estimated 90 out of 100 people who have that cancer are still alive 5 years after being diagnosed.

Relative survival rates are a more accurate way to estimate the effect of cancer on survival. These rates compare people with cancer to people in the overall population. For example, if the 5-year relative survival rate for a specific type and stage of cancer is 90%, it means that people who have that cancer are, on average, about 90% as likely as people who don’t have that cancer to live for at least 5 years after being diagnosed.

But remember, survival rates are estimates – your outlook can vary based on a number of factors specific to you.

Cancer survival rates don’t tell the whole story

Survival rates are often based on previous outcomes of large numbers of people who had the disease, but they can’t predict what will happen in any particular person’s case. There are a number of limitations to remember:
• The numbers below are among the most current available. But to get 5-year survival rates, doctors look at people who were treated at least 5 years ago. As treatments are improving over time, people who are now being diagnosed with Waldenstrom Macroglobulinemia may have a better outlook than these statistics show.

• The statistics below are based on the stage of the cancer when it was first diagnosed. In the case of Waldenstrom Macroglobulinemia, the "stage" is called a prognostic score. The statistics do not apply to cancers that come back later or spread, for example.

• Besides the cancer stage or prognostic score, many other factors can affect a person's outlook, such as age and overall health, and how well the cancer responds to treatment.

Your doctor can tell you how these numbers may apply to you, as he or she is familiar with the aspects of your particular situation.

According to the National Cancer Institute's SEER database (based on people diagnosed between 2001 and 2010), the overall relative 5-year survival of people with WM is about 78%.

The group that created the International Prognostic Scoring System for Waldenstrom Macroglobulinemia (ISSWM) used data from about 600 patients with WM who were diagnosed and treated before January 2002 to develop their risk groups:

<table>
<thead>
<tr>
<th>ISSWM risk group</th>
<th>5-year survival rate</th>
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<tr>
<td>Low</td>
<td>87%</td>
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<tr>
<td>Intermediate</td>
<td>68%</td>
</tr>
<tr>
<td>High</td>
<td>36%</td>
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**Median survival**

Median survival is another way to look at survival. It is the length of time at which half of the patients in a group are still alive, and half have died. By definition, half of the patients live longer than the median survival. The group that developed the ISSWM used data from WM patients diagnosed and treated before January 2002 and found the following:

<table>
<thead>
<tr>
<th>ISSWM risk group</th>
<th>Median survival*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>12 years</td>
</tr>
<tr>
<td>Intermediate</td>
<td>8 years</td>
</tr>
<tr>
<td>High</td>
<td>3.5 years</td>
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</tbody>
</table>
Median survival is measured from the point that treatment is started.

In the last decade (2001-2010), the median overall survival for all WM groups has improved to just over 8 years compared to 6 years in the previous decade (1991-2000).

- **References**


[See all references for Waldenstrom Macroglobulinemia](#)

Last Medical Review: July 19, 2018 Last Revised: October 17, 2018

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**Questions To Ask About Waldenstrom Macroglobulinemia**

It is important for you to have honest, open discussions with your cancer care team. They want to answer all of your questions, no matter how trivial you might think they are. Here are some questions to consider:

**When you’re told you have Waldenstrom macroglobulinemia**
• Where is the cancer located?
• Will I need other tests before we can decide on treatment?
• Do I need to see any other doctors or health professionals?
• If I’m concerned about the costs and insurance coverage for my diagnosis and treatment, who can help me?
• Do you recommend starting treatment now or waiting until later on?

When deciding on a treatment plan

• What are my treatment options?
• What do you recommend and why?
• Is a stem cell transplant an option for me? What are the pros and cons of this treatment?
• How much experience do you have treating this type of cancer?
• Should I get a second opinion? How do I do that? Can you recommend someone?
• What would the goal of the treatment be (to reduce symptoms, lower IgM levels, etc.)?
• How quickly do we need to decide on treatment?
• What should I do to be ready for treatment?
• How long will treatment last? What will it be like? Where will it be done?
• What risks or side effects are there to the treatments you suggest? Are there things I can do to reduce these side effects?
• How might treatment affect my daily activities? Can I still work full time?
• What are the chances the cancer will recur (come back) with these treatment plans?
• What will we do if the treatment doesn’t work or if the cancer recurs?
• What if I have transportation problems getting to and from treatment?

During treatment

Once treatment begins, you’ll need to know what to expect and what to look for. Not all of these questions may apply to you, but asking the ones that do may be helpful.

• How will we know if the treatment is working?
• Is there anything I can do to help manage side effects?
• What symptoms or side effects should I tell you about right away?
• How can I reach you on nights, holidays, or weekends?
• Do I need to change what I eat during treatment?
• Are there any limits on what I can do?
• Can I exercise during treatment? If so, what kind should I do, and how often?
• Can you suggest a mental health professional I can see if I start to feel overwhelmed, depressed, or distressed?
• What if I need social support during treatment because my family lives far away?

After treatment

• Do I need a special diet after treatment?
• Are there any limits on what I can do?
• What other symptoms should I watch for?
• What kind of exercise should I do now?
• What type of follow-up will I need after treatment?
• How often will I need to have follow-up exams and imaging tests?
• Will I need any blood tests?
• How will we know if the cancer has come back? What should I watch for?
• What will my options be if the cancer comes back?

Along with these sample questions, be sure to write down some of your own. For instance, you might want more information about recovery times. Or you may want to ask about available clinical trials.

Keep in mind that doctors aren’t the only ones who can give you information. Other health care professionals, such as nurses and social workers, can answer some of your questions. To find out more about speaking with your health care team, see The Doctor-Patient Relationship.

• References
See all references for Waldenstrom Macroglobulinemia

Last Medical Review: July 19, 2018 Last Revised: July 19, 2018

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