

Waldenström Macroglobulinemia: Questions and Answers

Key Points

- Waldenström macroglobulinemia is a rare type of slow-growing, non-Hodgkin lymphoma (cancer that begins in the cells of the immune system). It causes overproduction of a protein called monoclonal immunoglobulin M (IgM or “macroglobulin”) antibody (see Question 1).
- Symptoms include weakness, swollen lymph nodes, severe fatigue, nose bleeds, weight loss, and visual and neurological problems; some patients do not have symptoms (see Question 4).
- Waldenström macroglobulinemia is diagnosed using bone marrow biopsy and blood tests; other techniques may also be used (see Question 5).
- Treatments for Waldenström macroglobulinemia in patients with symptoms may include plasmapheresis, chemotherapy, and/or biological therapy (see Question 6).
- People with Waldenström macroglobulinemia are encouraged to enroll in clinical trials (research studies) that explore new treatments (see Question 7).

1. What is Waldenström macroglobulinemia?

Waldenström macroglobulinemia (WM) is a rare, indolent (slow-growing) non-Hodgkin lymphoma (cancer that begins in the cells of the immune system). WM is also called lymphoplasmacytic lymphoma. It starts in white blood cells called B lymphocytes or B cells.

B cells are an important part of the body’s immune system. They form in the lymph nodes, spleen, and other lymphoid tissues, including bone marrow (the soft, spongy tissue inside bones). Some B cells become plasma cells, which make, store, and release antibodies. Antibodies help the body fight viruses, bacteria, and other foreign substances.



Lymphoplasmacytic cells are cells that are in the process of maturing from B cells to plasma cells. In WM, abnormal lymphoplasmacytic cells multiply out of control, producing large amounts of a protein called monoclonal immunoglobulin M (IgM or “macroglobulin”) antibody. High levels of IgM in the blood cause hyperviscosity (thickness or gumminess), which leads to many of the symptoms of WM (see Question 4).

2. How often does Waldenström macroglobulinemia occur?

WM is a rare cancer; about 1,500 new cases occur annually in the United States. The incidence of WM is higher in males and higher in whites than in African Americans. Incidence increases sharply with age. The median age at diagnosis is 63 (half of the cases are diagnosed before age 63, and half are diagnosed after age 63) (1).

3. What are the possible causes of Waldenström macroglobulinemia?

The exact cause of WM is not known. However, scientists believe that genetics may play a role in WM, because the disease has been seen to run in families (1).

4. What are the symptoms of Waldenström macroglobulinemia?

Some patients do not have symptoms. For those who do have symptoms, the most common ones are weakness, severe fatigue, bleeding from the nose or gums, weight loss, and bruises or other skin lesions. Severely high levels of IgM can lead to hyperviscosity syndrome, in which the blood becomes abnormally thick. Symptoms of this syndrome include visual problems (e.g., blurring or loss of vision) and neurological problems (e.g., headache, dizziness, vertigo). During a physical exam, a doctor may also find swelling of the lymph nodes, spleen, and/or liver (2).

5. How is Waldenström macroglobulinemia diagnosed?

Initial diagnosis of WM is based on blood test and bone marrow biopsy results. Blood tests are used to determine the level of IgM in the blood and the presence of proteins, or tumor markers, that can indicate WM. For the biopsy, a sample of bone marrow (soft, sponge-like tissue in the center of most bones) is removed, usually from the back of the pelvis bone, through a needle for examination under a microscope. The pathologist (a doctor who identifies diseases by studying cells and tissue under a microscope) looks for certain types of lymphocytes (white blood cells) that indicate WM (1). Flow cytometry (a method of measuring cell properties using a light-sensitive dye and laser or other type of light) is often used to look at markers on the cell surface or inside the lymphocytes.

Additional tests may be recommended to confirm the diagnosis. A computed tomography (CT or CAT) scan uses a computer linked to an x-ray machine to create pictures of areas inside the body. This test may be used to evaluate the chest, abdomen, and pelvis, particularly swelling of the lymph nodes, liver, and/or spleen (1). A skeletal

survey (x-rays of the skeleton) can help distinguish between WM and a similar plasma cell cancer, multiple myeloma (1).

6. How is Waldenström macroglobulinemia treated?

At this time, there is no known cure for WM. However, several treatment options are available to prevent or control the symptoms of the disease.

Patients who do not have symptoms of WM are usually monitored without being treated; these patients often live for many years before requiring treatment (2). Patients with symptoms are usually treated with chemotherapy. Biological therapy (treatment that stimulates the immune system to fight cancer) is also used to treat WM (3). Promising results have been seen with biological therapy and chemotherapy in combination. An example of combination therapy uses rituximab and fludarabine (4). Patients with high levels of IgM and hyperviscosity syndrome may undergo plasmapheresis. In this procedure, blood from the patient is removed and circulated through a machine that separates the plasma (which contains the antibody IgM) from other parts of the blood (red blood cells, white blood cells, and platelets). The red and white blood cells and platelets are returned to the patient, along with a plasma substitute (4). Plasmapheresis is often followed by chemotherapy.

Because WM is rare, some doctors may suggest treatments that have been effective in some cases but are not considered standard treatment and/or are under study in clinical trials (research studies). Some of these treatments include (4):

- **High-dose chemotherapy with autologous stem cell transplantation**—blood-forming stem cells (cells from which all blood cells develop) are harvested (removed) and stored, then given back to the patient following high-dose chemotherapy. The harvested cells may be treated before transplantation to get rid of cancer cells. The transplanted cells travel to the bone marrow and begin to produce new blood cells.
- **Splenectomy**—surgery to remove the spleen. This procedure has been used in WM patients who have a significantly enlarged spleen. Occasionally, WM patients who have had this procedure have experienced remissions (decrease in or disappearance of signs or symptoms of cancer) lasting for many years. The remissions are believed to be due to the removal of a major source of IgM production.
- **Thalidomide and bortezomib**—drugs used to treat multiple myeloma, a disease similar to WM. Side effects of thalidomide include constipation, weakness, and peripheral neuropathy (a problem in nerve function that causes pain, numbness, tingling, swelling, and muscle weakness). Both agents are currently being studied in clinical trials for WM.

7. Are clinical trials (research studies) available? Where can people get more information about clinical trials?

Yes. The National Cancer Institute (NCI), a component of the National Institutes of Health, is sponsoring clinical trials that are designed to find new treatments and better ways to use current treatments. Before any new treatment can be recommended for general use, doctors conduct clinical trials to find out whether the treatment is safe for patients and effective against the disease. Participation in clinical trials may be a treatment option for patients with WM.

People interested in taking part in a clinical trial should talk with their doctor. Information about clinical trials is available from the NCI's Cancer Information Service (CIS) (see below) at 1-800-4-CANCER and in the NCI booklet *Taking Part in Cancer Treatment Research Studies*, which can be found at <http://www.cancer.gov/publications> on the Internet. This booklet describes how research studies are carried out and explains their possible benefits and risks. Further information about clinical trials is available at <http://www.cancer.gov/clinicaltrials> on the NCI's Web site. The Web site offers detailed information about specific ongoing studies by linking to PDQ[®], the NCI's comprehensive cancer information database. The CIS also provides information from PDQ.

Selected References

1. Munshi NC, Anderson KC. Plasma cell neoplasms. In: DeVita VT Jr., Hellman S, Rosenberg SA, editors. *Cancer: Principles and Practice of Oncology*. Vol. 2. 7th ed. Philadelphia: Lippincott Williams and Wilkins, 2004.
2. Richardson P, Hideshima T, Anderson KC. Multiple myeloma and related disorders. In: Abeloff MD, Armitage JO, Niederhuber JE, Kastan MB, McKenna WG, editors. *Clinical Oncology*. 3rd ed. London: Churchill Livingstone, 2004.
3. Gertz MA, Anagnostopoulos A, Anderson K, et al. Treatment recommendations in Waldenstrom's macroglobulinemia: Consensus panel recommendations from the Second International Workshop on Waldenstrom's Macroglobulinemia. *Seminars in Oncology* 2003; 30(2):121-126.
4. Dimopoulos MA, Kyle RA, Anagnostopoulos A, Treon SP. Diagnosis and management of Waldenstrom's macroglobulinemia. *Journal of Clinical Oncology* 2005; 23(7):1564-1577.

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Related NCI materials and Web pages:

- National Cancer Institute Fact Sheet 5.2, *Computed Tomography (CT): Questions and Answers* (<http://www.cancer.gov/cancertopics/factsheet/Detection/CT>)
- National Cancer Institute Fact Sheet 5.18, *Tumor Markers: Questions and Answers* (<http://www.cancer.gov/cancertopics/factsheet/Detection/tumor-markers>)
- National Cancer Institute Fact Sheet 7.2, *Biological Therapies for Cancer: Questions and Answers* (<http://www.cancer.gov/cancertopics/factsheet/Therapy/biological>)
- National Cancer Institute Fact Sheet 7.49, *Targeted Cancer Therapies: Questions and Answers* (<http://www.cancer.gov/cancertopics/factsheet/Therapy/targeted>)
- *Biological Therapy: Treatments That Use Your Immune System To Fight Cancer* (<http://www.cancer.gov/cancertopics/biologicaltherapy>)
- *Chemotherapy and You: Support for People With Cancer* (<http://www.cancer.gov/cancertopics/chemotherapy-and-you>)
- Taking Part in Cancer Treatment Research Studies (<http://www.cancer.gov/clinicaltrials/Taking-Part-in-Cancer-Treatment-Research-Studies>)
- Non-Hodgkin Lymphoma Home Page (<http://www.cancer.gov/cancertopics/types/non-hodgkins-lymphoma>)

For more help, contact:

NCI's Cancer Information Service

Telephone (toll-free): 1-800-4-CANCER (1-800-422-6237)

TTY (toll-free): 1-800-332-8615

LiveHelp[®] online chat: <https://cissecure.nci.nih.gov/livehelp/welcome.asp>

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