WALDENSTROM'S MACROGLOBULINEMIA

A PATIENT'S GUIDE

WMFC

Waldenstrom's Macroglobulinemia Foundation of Canada

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Highlighted text indicates there is a Canadian clarification added in the appendix.

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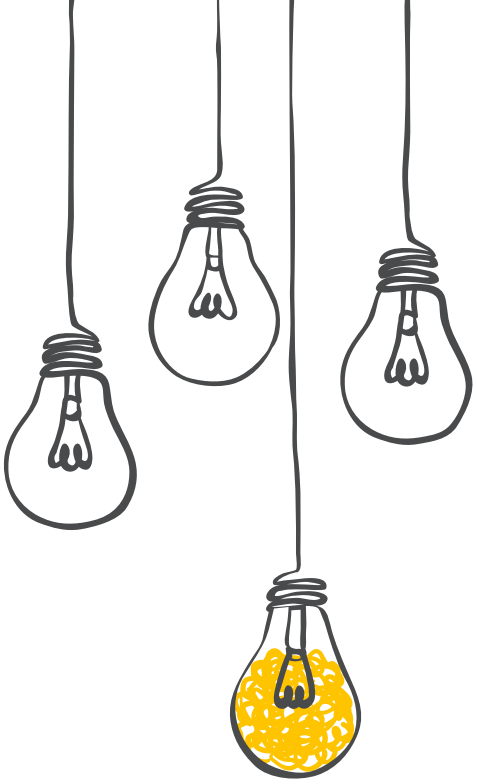
Medical Disclaimer: The information presented here is intended for educational purposes only. It is not meant to be a substitute for professional medical advice. Patients should use the information provided in full consultation with and under the care of a physician with experience in the treatment of Waldenstrom's Macroglobulinemia. We discourage the use by a patient of any information contained herein without disclosure to his or her medical specialist.

What is Waldenstrom's macroglobulinemia (WM)?

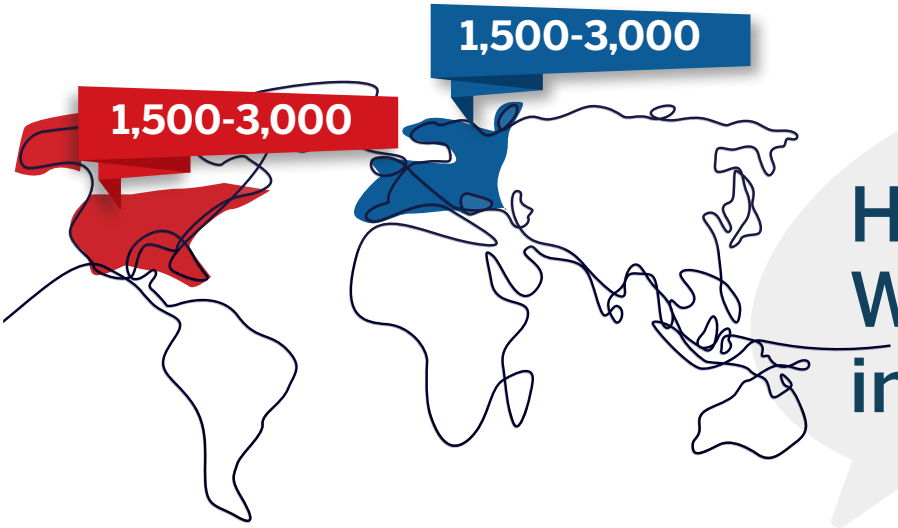
- WM is a type of blood cancer in which too much of a specific abnormal protein – an antibody (or immunoglobulin) called IgM – is produced. IgM is the largest of all the antibodies, called a macroglobulin. Generally, IgM is a "first responder" to infections. The abnormal IgM protein is normally not present in healthy people (and is also called an M-protein or paraprotein).
- In the case of WM, the abnormal WM cells do not undergo programmed cell death. Instead, they accumulate in the bone marrow. This can crowd out normal bone marrow cells that make new red blood cells, leading to anemia, and also crowd out production of other cells that protect us from infection.
- These abnormal WM cells can also grow outside the bone marrow and cause enlargement of the lymph nodes and spleen, or proliferate in the lung space, brain or spine.
- The WM cells and the excess IgM can damage cells and organs in the body, causing symptoms such as fatigue, numbness, tingling and weakness.
- The excess IgM also circulates in the blood. Because of IgM's large size, the blood can become very thick, a condition known as hyperviscosity. This can lead to blood vessels bursting, causing bleeding in the retina or brain. IgM can also deposit in organs, like the kidney, and affect their function.
- Some patients with WM can have symptoms that are directly related to the IgM protein itself, such as amyloidosis, cryoglobulinemia, cold agglutinin hemolytic anemia and demyelinating peripheral neuropathy. These are rare.

More information can be found on the WMFC website: www.wmfc.ca and the IWMF website: www.iwmf.com

WM is a rare, currently incurable, but treatable blood cancer.



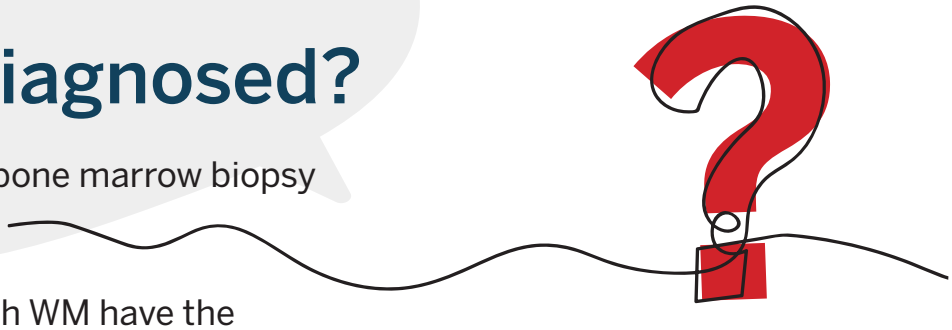
- WM is usually an indolent, slow-growing cancer, and many patients do not require treatment but only periodic blood tests. Most people with WM requiring treatment have time to consider their treatment options.



How rare is WM? What is the incidence of WM?

- There are about 1,500-3,000 new cases of WM per year in the US and about 1,500-3,000 per year in Europe. Overall, WM comprises only 1-2% of all blood cancers.[1]
- This rarity means most community oncologists see few, if any, WM cases in their career.

How is WM diagnosed?



- In addition to blood tests, a bone marrow biopsy is essential for diagnosis.
- About 90-95% of people with WM have the same genetic mutation in the gene that encodes a protein called MYD88, while 30-40% have a genetic mutation in the *CXCR4* gene. Some *CXCR4* mutations affect the effectiveness of different treatments.

Why did I get WM? Will my kids get it?

- The cause of WM is unknown. However, the genetic mutations associated with WM (*MYD88* and *CXCR4*) are acquired during your lifetime and are not passed down from your parents to you, or from you to your children.
- Up to 25% of people with WM do have a first-degree (parent, sibling or child) or second-degree relative (grandparent, aunt, uncle, cousin) with WM or another B-cell lymphoma.
- A small number of families with WM exist where both parents and children (as well as siblings) have WM.
- In cases of "familial" WM, a reasonable step would be to perform blood tests to check blood cell numbers and test for an abnormal protein by doing serum protein electrophoresis. Your primary care physician can consider ordering these blood tests for offspring who are 40 years of age or older, given the late onset of WM.

WM usually occurs in stages. Will I go through all the stages?

- It often starts with a diagnosis of MGUS (monoclonal gammopathy of undetermined significance), which, most commonly, is a precursor to WM. From there, some people progress to asymptomatic (or smoldering) WM. It is only when someone progresses to symptomatic WM that treatment is needed.
- Not everyone progresses through these stages. In fact, most patients with MGUS do not progress to symptomatic WM. One could remain in the MGUS or the asymptomatic stage forever.

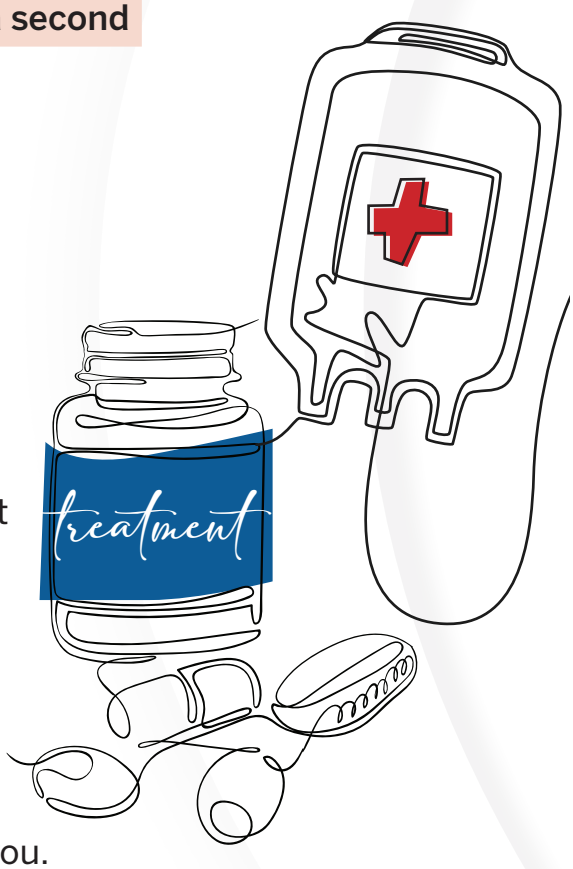
When do I need treatment?

- Usually, treatment is needed when a person has symptoms related to either low blood counts and high tumour load – like fatigue or bleeding – or when elevated IgM levels cause symptomatic hyperviscosity, or damage cells or organs.
- The course of WM can vary significantly from person to person. For example, some people are symptomatic with a low level of IgM, while others do fine with a high IgM level. Therefore, physicians generally treat people based on their symptoms. Only when IgM levels are becoming very high, your physician might decide to start treatment to reduce the risk of developing hyperviscosity.

Should I get a second opinion?

Since WM is a rare disease, it's recommended that you try to get a second opinion from a physician listed in the IWMF International Physician's Directory. Discuss getting a second opinion with your medical team.[2]

What are my treatment options?



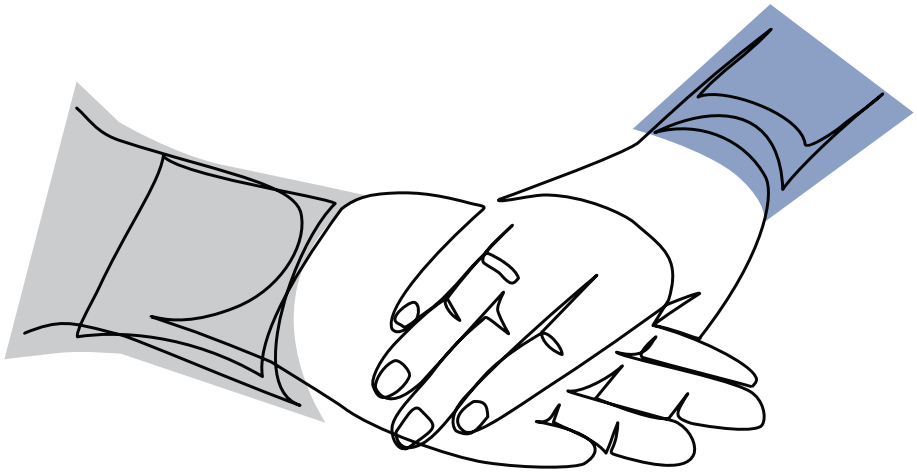
- The good news is these days there are many treatment options. In the past, there were only a few, often with significant side effects.
- Treatment roughly falls into two categories: oral medication(s) that you may take indefinitely, or an infusion treatment you take for a limited time. Your medical team will help you decide the best option for you.
- Rituximab is a medication used to treat many blood cancers, including WM. Unfortunately, it sometimes causes a short-term rise in IgM levels – called an IgM flare – that could be dangerous. Some people require a medical procedure called plasmapheresis to reduce their IgM level on a short-term basis before starting therapy with rituximab. Alternatively, rituximab may be started later in the treatment regimen.
- Make sure you tell your medical team about any side effects you experience following treatment. There are often strategies that can be employed to reduce their impact.

What if my WM comes back?

- WM may come back or progress after an initial treatment, despite a long period of remission after chemotherapy treatment or being on continuous therapy. If the initial treatment was successful for several years, your doctor may repeat it or recommend a new treatment. In many patients, direct treatment is not needed immediately because the relapse is asymptomatic, and the patient can be followed with regular controls. Discuss options with your medical team.

How long am I going to live?

- The life span of people with WM has increased dramatically in recent years. In the past, many patients were told they had 3-5 years to live after diagnosis.
- It is now much longer, with some WM thought leaders saying 15-20 years on average from the date of diagnosis. In fact, many patients' cause of death is unrelated to their WM. What's most important is that the time frame has increased dramatically and is continuing to increase with newer, safer and more effective drugs.



APPENDIX: CANADIAN UPDATES

1. There are about 150-200 cases per year in Canada.
2. See the WMFC's discussion of second opinions at **https://www.wmfc.ca/about-wm/common-canadian-questions-answered**, under the headings "Can I request an Oncologist / Hematologist Second Opinion?" and "Examples of US Medical Institutions Offering Second Opinions".

WMFC

Waldenstrom's Macroglobulinemia Foundation of Canada

CONTACT US:
info@wmfc.ca | www.wmfc.ca
www.youtube.com/@WMFC

The WMFC is an all-volunteer organization, and is the only Canadian charity dedicated solely to the support and education of WM patients and their families, and to fund research for a cure for WM.

Our Mission

The mission of the WMFC is to support Canadians with WM, and their families, by offering a range of services that can enhance the quality of life of those with WM through education and Support Groups across Canada.

The WMFC is committed to creating a world without WM by finding a cure. Since 2002, the WMFC has invested over $1.3 million in WM research projects. Doing our part in a worldwide research initiative, WM patients are living longer and have better treatment options that can lead to longer-lasting remissions, with fewer side effects.

Visit our website www.wmfc.ca and join the WMFC to:

- Find and join a local WMFC Support Group
- Read our articles and view our recorded presentations to keep up to date on WM
- Join the WMFC Facebook group
- Get alerted to our national Zoom educational seminars
- Attend our annual WMFC Education Forum and our online webinars
- Receive our periodic emails and newsletters
- Keep current on changes in treatments and research

WM is a rare disease, but with the WMFC

you are never alone.

PATIENT RESOURCES

The IWMF, the only international organization dedicated solely to WM, is a patient-founded and patient-directed nonprofit with a simple but compelling vision and mission.

OUR VISION

A world without WM

OUR MISSION

Support and educate everyone affected by WM while advancing the search for a cure.

The IWMF is committed to creating a world without WM by finding a cure. Since 1999, the IWMF has invested over $21 million in WM research projects throughout the world. Thanks to this research, WM patients are living longer and have better treatment options that can lead to longer-lasting remissions, with fewer side effects.

www.iwmf.com

Lymphoma Canada (LC) is a national Canadian registered charity whose mission is to empower patients and the lymphoma community through education, support, advocacy and research. Based out of Mississauga, ON, we collaborate with patients, caregivers, healthcare professionals and other organizations and stakeholders, to promote early detection, find new and better treatments for lymphoma patients, help patients access those treatments, learn about the causes of lymphoma and work together to find a cure. Resources are provided in both English and French.

www.lymphoma.ca

The Leukemia and Lymphoma Society of Canada

Our mission

We won't stop until there is a cure for leukemia, lymphoma, myeloma, myelodysplastic syndromes and myeloproliferative neoplasms, and are able to improve the quality of life of people affected by blood cancers and their families by funding life-enhancing research and providing educational resources, services and support.

What we do

In Canada, there are currently over 155,000 people living with or in remission from one of the 137 types of blood cancers. Today, we are the largest registered charitable health agency dedicated to supporting the blood cancer community in Canada. Our focus includes:

- Funding research from bench to bedside
- Rethinking how a person navigates their blood cancer experience and provide 1:1 personalized support
- Providing easy to understand and vetted blood cancer information
- Offering tools for psychological and emotional support
- Empowering Canadians to take charge of their blood cancer experience through practical support and advocacy

www.bloodcancers.ca | Toll-free 1-833-222-4884

Lymphoma Coalition is a worldwide network of patient organizations that support those affected by lymphoma. Lymphoma Coalition acts as a central hub for reliable and current information, as well as advocating for equitable care globally. Its mission is to enable global impact by fostering a lymphoma ecosystem that ensures local change and evidence-based action. Today, there are more than 80 member organizations from over 50 countries.

www.lymphomacoalition.org

WMFC

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Published by the Waldenstrom's Macroglobulinemia Foundation of Canada.

Please consider supporting our mission to educate everyone affected by WM and fund innovative research by joining and/or contributing. You can do so by visiting our website at www.wmfc.ca, or by mailing a cheque to:

WMFC, 55 Albert Street Unit 100, Markham, ON L3P 2T4

The WMFC has Canadian Charitable Registration #86755 2713 RR0001.