What Are the Risk Factors for Waldenstrom Macroglobulinemia?

- Monoclonal gammopathy of undetermined significance (MGUS)
- Age
- Race
- Sex
- Heredity
- Hepatitis C
- Certain autoimmune diseases

A risk factor is anything that affects your chance of getting a disease such as cancer. Different cancers have different risk factors. Some cancer risk factors, like smoking, can be changed. Others, like a person's age or family history, can't be changed.

Researchers have found a few risk factors that make a person more likely to develop Waldenstrom macroglobulinemia (WM). But most people with these risk factors never develop WM.

## Monoclonal gammopathy of undetermined significance (MGUS) Sex

WM is more common among White people than among African Americans. In contrast, multiple myeloma is about twice as common among African Americans as White Americans. The reasons for these differences are not known.

# Sex

Men are more likely than women to develop this disease. The reason for this is not known.

# Heredity

Inherited genes seem to play a role in at least some people who get WM. About 1 in 5 people with WM has a close relative with WM or with a related B-cell disease, such as MGUS or certain types of lymphoma or <u>leukemia</u><sup>3</sup>.

# Hepatitis C

Hepatitis C is caused by infection with a virus (known as the hepatitis C virus, or HCV). Some studies have found that people with chronic hepatitis C infection might be more likely to develop WM than people without the virus. But not all studies have found such a link.

### Certain autoimmune diseases

Some research has suggested that people with certain types of autoimmune disease, such as Sjögren (Sjogren) syndrome, might be at higher risk for WM.

## **Hyperlinks**

- 1. <u>www.cancer.org/cancer/types/multiple-myeloma.html</u>
- 2. www.cancer.org/cancer/types/non-hodgkin-lymphoma.html
- 3. <u>www.cancer.org/cancer/types/leukemia.html</u>
- 4. <u>www.cancer.org/cancer/types/waldenstrom-macroglobulinemia/references.html</u>

#### References

Castillo JJ. Plasma cell disorders. Prim Care. 2016; 43:667-691. doi:

10.1016/j.pop.2016.07.002. Epub 2016 Oct 14.

Giordano TP, Henderson L, Landgren O, et al. Risk of non-Hodgkin lymphoma and lymphoproliferative precursor diseases in US veterans with hepatitis C virus. *JAMA*. 2007;297:2010–2017.

Kristinsson SY, Koshiol J, Björkholm M, et al. Immune-Related and Inflammatory Conditions and Risk of Lymphoplasmacytic Lymphoma or Waldenström Macroglobulinemia. *JNCI Journal of the National Cancer Institute*. 2010;102(8):557-567. doi:10.1093/jnci/djq043.

Rajkumar SV, Dispenzieri A. Chapter 104: Multiple myeloma and related disorders. In: Niederhuber JE, Armitage JO, Dorshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa. Elsevier: 2014.

# Do We Know What Causes Waldenstrom Macroglobulinemia?

DNA affects more than how we look.

- Some genes control when cells grow, divide to make new cells, and die at the right time. They are called **oncogenes**.
- Other genes slow down cell division or make cells die at the right time. They are called **tumor suppressor genes**.

Cancers can be caused by DNA changes that turn on oncogenes or turn off tumor suppressor genes.

Some people inherit DNA changes from a parent that increase their risk for certain types of cancer. Researchers are studying families that have many cases of WM to try to find the genes that might cause this disorder in some people.

The DNA changes found in WM cells are usually acquired after birth (not passed on from a parent). Some of these acquired changes may have outside causes, but often they occur for no apparent reason. They seem to happen more often as we age, which might help explain why WM usually occurs in older people.

Recent research has found that about 9 times out of 10, WM cells have a mutation (change) in a gene known as *MYD88*, which normally helps immune system cells signal each other and helps keep them alive. The DNA change in this gene might make it stay turned on all the time, which might help the WM cells survive longer than they should.

Sometimes, WM cells have other kinds of DNA changes. In each human cell, the DNA is packaged in 23 pairs of chromosomes. In some WM cells, a piece of a chromosome is missing. This is called a **deletion**. The most common chromosome defect seen in WM is a deletion of part of chromosome 6. It's not clear exactly which genes this might affect.

Another type of chromosome defect in WM is called a **translocation**. In a translocation, a piece of one chromosome becomes attached to a different chromosome. Chromosome changes like these can cause oncogenes to be turned on or tumor suppressor genes turned off.

Researchers have found that some patients with WM have important changes or defects in other bone marrow cells. These changes might also help cancer cells grow. Certain cells in the bone marrow called dendritic cellsrelease a hormone called interleukin-6 (IL-6) that helps normal plasma cells and plasmacytoid lymphocytes grow. Excess IL-6 production by these cells appears to be an important factor in the development of WM.

Scientists are learning about the exact gene changes that cause WM. But even though they have found some of these gene changes, they still do not know why these changes occur.

# Hyperlinks

- 1. <u>www.cancer.org/cancer/types/waldenstrom-macroglobulinemia/detection-</u> <u>diagnosis-staging/signs-symptoms.html</u>
- 2. <u>www.cancer.org/cancer/types/non-hodgkin-lymphoma.html</u>
- 3. www.cancer.org/cancer/types/multiple-myeloma.html
- 4. <u>www.cancer.org/cancer/types/waldenstrom-macroglobulinemia/detection-</u> <u>diagnosis-staging/signs-symptoms.html</u>
- 5. www.cancer.org/cancer/types/waldenstrom-macroglobulinemia/references.html

### References

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology: Waldenstrom's macroglobulinemia/Lymphoplasmacytic lymphoma. V.1.2018. Accessed at www.nccn.org/professionals/physician\_gls/pdf/waldenstroms.pdf on June 21, 2018.

Rajkumar SV, Dispenzieri A. Chapter 104: Multiple myeloma and related disorders. In: Niederhuber JE, Armitage JO, Dorshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa. Elsevier: 2014.

Treon SP. XIII. Waldenström's macroglobulinaemia: An indolent B-cell lymphoma with distinct molecular and clinical features. *Hematol Oncol.* 2013;31 Suppl 1:76–80.

Treon SP, Hunter ZR, Aggarwal A, et al. Characterization of familial Waldenstrom's macroglobulinemia. *Ann Oncol.* 2006;17:488–494.

Treon SP, Xu L, Yang G, et al. MYD88 L265P somatic mutation in Waldenström's macroglobulinemia. *N Engl J Med*. 2012;367:826–833.

See all references for Waldenstrom Macroglobulinemia

Last Revised: July 19, 2018

# Can Waldenstrom Macroglobulinemia Be Prevented?

Most of the risk factors for Waldenstrom macroglobulinemia (WM), such as older age or monoclonal gammopathy of undetermined significance (MGUS), can't be changed or controlled, so there is no way to prevent cancers that might be related to these risk factors.

Some research suggests that people with hepatitis C might be more likely to develop WM. There is currently no vaccine to prevent <u>hepatitis C</u><sup>1</sup>, but there are ways to lower your risk of getting it, such as avoiding known risk factors like injection drug use or unprotected sex with many partners. Hepatitis C can also be treated effectively in many cases, although it's not known how this might affect a person's risk of WM.

# **Hyperlinks**

www.cancer.org/cancer/risk-prevention/infections/infections-that-can-lead-to-hepatitis 0rev /virn

Last Revised: July 19, 2018

### Written by

The American Cancer Society medical and editorial content team (<u>https://www.cancer.org/cancer/acs-medical-content-and-news-staff.html</u>)

Our team is made up of doctors and oncology certified nurses with deep knowledge of cancer care as well as journalists, editors, and translators with extensive experience in medical writing.

American Cancer Society medical information is copyrighted material. For reprint requests, please see our Content Usage Policy (www.cancer.org/aboutus/policies/content-usage.html).

cancer.org | 1.800.227.2345