

# UNDERSTANDING

## Extranodal Marginal Zone Lymphoma of Mucosa-Associated Lymphoid Tissue (MALT)



### Overview

Lymphoma is the most common form of blood cancer. Lymphoma occurs when cells of the immune system called lymphocytes, a type of white blood cell, grow and multiply uncontrollably.

#### WHAT ARE LYMPHOCYTES?

Lymphocytes are a type of white blood cell and are a major part of the lymphatic system. Together with other cells of the immune system, they work to fight infection and prevent disease. Lymphocytes can be found in the blood and bone marrow; however, most of them are normally circulating in the lymphatic system.

There are two main types of lymphocytes that can develop into lymphomas: B lymphocytes and T lymphocytes. The types of cells that become cancerous in extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT) are B lymphocytes (B cells). B lymphocytes make antibodies to fight infections. They are called B cells because they mature in the bone marrow.

**There are over 80 different subtypes of lymphoma. They fall into two main categories:**

- Hodgkin lymphoma (HL)
- Non-Hodgkin lymphoma (NHL)

MALT lymphoma is a type of NHL. NHL is approximately eight times more common than HL – 85% of all lymphomas are NHL. One of the main differences between HL and NHL is the presence of Reed-Sternberg cells which are large abnormal cells that can be detected under a microscope. Reed-Sternberg cells are typically present in Hodgkin lymphoma and are absent in Non-Hodgkin lymphoma.

**NHL is further sub-categorized by 'grade':**

- Low-grade: indolent (or slow-growing) NHLs
- Intermediate or high-grade: aggressive (or fast-growing) NHLs

MALT lymphoma is an indolent lymphoma. Indolent lymphomas develop more slowly than aggressive lymphomas. Patients with indolent lymphoma usually do not show symptoms until later, often as the disease progresses, and may therefore not require immediate treatment. Aggressive lymphomas on the other hand develop much more rapidly. Patients will usually experience symptoms from the onset of the disease and may require immediate and more intensive treatment. MALT lymphoma, though indolent, is usually localized at presentation and is often treated right away; it is rarely managed with watchful waiting.

MALT lymphoma is one of three subtypes of marginal zone lymphoma (MZL); the other two types are nodal marginal zone lymphoma (NMZL) and splenic marginal zone lymphoma (SMZL). MALT lymphoma originates in lymphoid tissues of the mucosa (a protective layer of tissue that surrounds organs and cavities), whereas NMZL and SMZL originate in the lymph nodes and spleen, respectively. They are called “marginal zone lymphomas” as they develop at the edge of normal lymphoid tissues called the marginal zone. The marginal zone is frequently exposed to external antigens (substances that trigger an immune response), which over time can harm the tissue causing lymphoma to develop in this region.

## Who gets MALT lymphoma?

MALT lymphoma is the most common marginal zone lymphoma, accounting for approximately two thirds of all MZL cases and approximately 5% of all NHL cases. It is most frequently diagnosed in patients aged between 50 and 60 years. It occurs equally in both men and women. It also is more commonly diagnosed in those who have been infected by the Hepatitis C virus. Specific bacteria and autoimmune diseases can also be linked to the development of MALT in certain organs.

## Types of MALT lymphoma

**There are two types of MALT lymphoma depending on the area of the body that the disease affects. They include:**

### 1. GASTRIC MALT LYMPHOMA

Gastric MALT lymphoma develops in the lining of the stomach. The stomach is the most common place in the body where MALT lymphoma can develop. It is strongly linked to infection with a type of bacteria called *Helicobacter pylori* (*H. pylori*), which is more commonly known to cause stomach ulcers. Approximately 90% of people with this type of lymphoma are infected with this type of bacteria. Various genetic and environmental factors can also increase the risk for developing this type of lymphoma.

### 2. NON-GASTRIC MALT LYMPHOMA

Non-gastric MALT lymphoma develops in regions other than the stomach including the salivary glands, thyroid, lungs, skin, bladder, breast, bowels or tissues around the eye. This lymphoma can be associated with bacterial and/or viral infections, however, is not linked with *H. pylori* infection. People with non-gastric MALT lymphoma often have a history of autoimmune disorders such as Hashimoto’s thyroiditis or Sjogren’s syndrome.

# Symptoms

Symptoms of MALT lymphoma depend on where in the body the disease develops. Unlike many lymphomas, MALT lymphoma develops outside of the lymph nodes and does not cause typical symptoms associated with lymphoma, such as swollen lymph nodes and B symptoms (unexplained weight loss, fever, night sweats).

People with gastric MALT lymphoma usually experience symptoms such as persistent indigestion, stomach pain, nausea, and weight loss. They may also experience symptoms of anemia caused by bleeding in the stomach, which can include fatigue, weakness and shortness of breath. There may also be patients that do not experience any symptoms due to their gastric MALT lymphoma.

## Symptoms of non-gastric MALT lymphoma can vary widely depending on which part of the body is affected:

- **MALT lymphoma affecting the bowels** may cause diarrhea, bloating, abdominal pain and weight loss.
- **MALT lymphoma affecting the lungs** often does not cause symptoms, but if it does it can cause coughing, shortness of breath, coughing up blood and chest pain.
- **MALT lymphoma affecting the salivary glands** may cause a lump to form in your mouth, jaw or at the front of your ear.
- **MALT lymphoma affecting the tear ducts/tissues around the eyes** may cause redness of the eye, dark bumps inside the eyelid, a droopy eyelid or double vision. Usually, these symptoms develop in only one eye, and less commonly can develop in both eyes.
- **MALT lymphoma affecting the thyroid gland** may cause a lump to form at the front of the neck, a hoarse voice or difficulty swallowing.
- **MALT lymphoma affecting the skin** may cause patches or lumps of a red or purple colour to develop on the skin. These can appear in several areas on the body.

Often, people with MALT lymphoma have more than one area of the body that is affected. This may cause a combination of the above symptoms.

# Diagnosis

A diagnosis of MALT lymphoma is typically confirmed by a tissue biopsy. This type of biopsy involves removing a sample of tissue (cells) from an area of the body that has been affected by the lymphoma. The removed tissue is then sent to a lab where it is examined under a microscope by a hematopathologist (a doctor who specializes in diagnosing diseases of the blood and bone marrow). This type of biopsy procedure can usually be performed under local anesthetic.

If the lymphoma is located in your stomach or bowels, a biopsy may be taken while performing an endoscopy. An endoscopy is a procedure where a thin tube with a small camera at the end is passed through your mouth down your esophagus to your stomach (gastroscopy) or through your rear end into your bowels (colonoscopy). If the lymphoma is in your lungs, a biopsy may be taken while performing a bronchoscopy, which is a type of endoscopy where a tube is passed through your nose or mouth and into your lungs. Other tests may also be performed to confirm your diagnosis. Because MALT lymphoma is a blood cancer, it is important to look at the entire body to find all of the lymphoma. This is usually done with blood tests and imaging scans which can include a whole-body computed tomography (CT) scan, positron emission tomography (PET) scan, and/or a magnetic resonance imaging (MRI) scan.

## Staging

Staging describes a cancer based on how much cancer is in the body and where it is located when first diagnosed. MALT lymphoma is staged based on the findings from your clinical examinations. Knowing the stage of your lymphoma helps your doctor determine the extent of your disease and monitor its progression over time.

Your MALT lymphoma can be staged using the classic Ann Arbor Staging System or the Ann Arbor Classification of Gastric Lymphoma. The stage is determined by the number and location of lymph nodes or extranodal sites affected, whether the affected lymph nodes are above, below or on both sides of the diaphragm (the large, dome-shaped muscle under the ribcage that separates the chest from the abdomen), and whether the disease has spread to the bone marrow or to other organs such as the liver.

### FOR EXTRANODAL MALT LYMPHOMA, THERE ARE THREE MAIN STAGES:

- **Stage I** The lymphoma is in one extranodal site/organ
- **Stage II** The lymphoma is in one extranodal organ and in the local/regional lymph nodes
- **Stage IV** The lymphoma is in the extranodal organ and is widespread to other organs and lymph nodes throughout the body

Stages I and II are considered early stages. Stage IV is considered advanced.

### FOR GASTRIC MALT LYMPHOMA, THERE ARE FOUR MAIN STAGES:

- **Stage IE** The lymphoma is restricted to the stomach (no lymph node involvement)
  - IE1** The lymphoma limited to the mucosa and submucosa of the stomach
  - IE2** The lymphoma extends beyond the submucosa of the stomach
- **Stage IIE** The lymphoma extends into the lymph nodes
  - IIE1** The lymphoma extends to the perigastric lymph nodes
  - IIE2** The lymphoma involves the stomach and extends to the sub-diaphragmatic lymph nodes
- **Stage IIIE** The lymphoma involves the gastrointestinal tract and/or extends to the lymph nodes on both sides of the diaphragm
- **Stage IVE** The lymphoma extends to the extra-gastrointestinal tissues and/or organs

## **YOUR DOCTOR MAY ALSO ADD A SINGLE LETTER TO THE STAGE:**

- **A** generally means the patient has not experienced any troublesome symptoms
- **B** means the patient has experienced B symptoms (fever, night sweats, weight loss)
- **X** means the patient has bulky disease (large tumours)
- **E** means the patient has extranodal disease (disease outside of the lymph nodes)

# Prognosis

## **WHAT IS PROGNOSIS?**

Prognosis is the medical term used to describe how the disease will progress, how well the patient will respond to treatment, and the likelihood of recovery. It is usually based on information gathered from thousands of other patients who have had the same disease which provides a general idea of what to expect when a patient is diagnosed with MALT lymphoma. However, it is important to remember that no two patients are alike and that it is not possible to accurately predict what will happen to a specific patient.

## **MARGINAL ZONE LYMPHOMA INTERNATIONAL PROGNOSTIC INDEX (MALT-IPI)**

Your doctor may give you a prognostic score using the Marginal Zone Lymphoma International Prognostic Index (MALT-IPI). The MALT-IPI is a clinical tool developed by oncologists to aid in predicting the prognosis (outcome and survival) of patients with MALT lymphoma.

### **One point is assigned for each of the following IPI risk factors:**

- Age 70 years and over;
- Ann Arbor stage III/IV;
- Serum lactate dehydrogenase (LDH) level above normal;

### **These risk factors help identify if the patient is:**

- Low-risk (0-1 factors);
- Low/intermediate-risk (2 factors);
- Intermediate/high-risk (3 factors);
- High-risk (4-5 factors).

# Treatment Options

Treatment for MALT lymphoma depends on whether you experience any symptoms and the stage of your disease.

Asymptomatic patients (patients that do not experience any symptoms) may undergo a 'watch & wait' approach where they are closely monitored for symptoms that may indicate disease progression, rather than receive immediate treatment which may not improve outcome and survival. Certain symptoms such as B symptoms and high tumor burden, will suggest moving from watch and wait to treatment. However, the development of these symptoms is relatively uncommon.

For gastric MALT lymphoma patients infected by the bacteria *H. pylori*, antibiotics are often used as an initial treatment. Antibiotics are combined with proton pump inhibitors (PPIs) which reduce the production of stomach acid to help prevent or heal ulcers. Clearing the bacteria will often clear the lymphoma, and patients usually will not require further treatment. Likewise, MALT lymphoma patients with the Hepatitis C virus will typically be given antivirals as an initial treatment, and this may clear the lymphoma completely. If the antibiotic or antiviral drugs are unsuccessful, or your MALT lymphoma is not associated with any infection, then you may be treated with other therapies.

If your lymphoma is causing symptoms and is not linked to an infection, or the antibiotics/antivirals do not clear it, you will likely be treated with radiation therapy. Radiation therapy uses x-rays to target specific regions of the body where the MALT lymphoma is present. Radiotherapy may be very effective if your lymphoma is isolated in specific regions of the body. If you have widespread MALT lymphoma, chemotherapy is typically used.

**Chemotherapy can be used alone or in combination with radiation therapy. Some commonly used treatments include:**

- **Single-agent chemotherapy:**
  - Chlorambucil (Leukeran)
  - Bendamustine (Treanda)
  - Fludarabine (Fludara)
- **Combination chemotherapy:**
  - **CVP** (cyclophosphamide, vincristine [Oncovin], prednisone)
  - **CHOP** (cyclophosphamide, doxorubicin [Hydroxydaunorubicin], vincristine [Oncovin], prednisone)
  - **Rituximab (Rituxan)**, a monoclonal antibody, can be used either alone or in combination with chemotherapy.

These drugs are typically administered intravenously (into a vein) which is performed in the hospital. A central-line, which is a catheter placed in a large vein, may be used to administer chemotherapy drugs and draw blood for testing. The chemotherapy is usually given in cycles of 2 to 4 weeks. A cycle includes treatment days followed by a period of rest and healing. The number of cycles you receive (called the 'course' or 'regimen') depends on the recommendation of your medical team based on your test results. Many patients will be able to receive their treatment as an out-patient, which means you will not have to stay in the hospital overnight.

A patient may require multiple lines of therapy if their lymphoma relapses or is refractory to their previous treatment(s). Patients with relapsed or refractory MALT lymphoma are often encouraged to participate in clinical trials so that they can receive newer treatments that are not yet on the market. Clinical trials are crucial for establishing more effective, less toxic treatments for patients. You should consult your medical team for more information on whether a clinical trial is an appropriate treatment option for you.

## Treatment Side Effects

**Many people may be frightened to learn that there can be side effects associated with the therapies they may take to treat their lymphoma. However, it is important to understand that:**

- Not all patients who receive therapy experience side effects;
- Side effects are not always severe, they can be mild;
- Different therapies have different side effects;
- There are many effective treatments that can reduce side effects or prevent them from happening altogether.

Some of the most common side effects of chemotherapy include decreased blood cell production (myelosuppression), fatigue, vomiting, diarrhea, loss of appetite, change in taste, hair loss, “chemo-brain” (cognitive impairment(s) that cause difficulties with concentrating and remembering) and peripheral neuropathy (affects nerve endings causing tingling and numbness).

Most side effects are short-lived, but some can last for a few weeks or months after treatment has finished. Occasionally, side effects can be permanent. Some side effects can start long after treatment has finished. These are called late side effects. Your doctor will talk to you about any potential side effects before you start treatment.

Depending on the side effects you experience and how strongly you feel them, you might not be able to maintain your usual level of activity during and following treatment. You may need to set aside more time for rest and healing. Additionally, depending on the severity of your side effects related to a therapy, your doctor may suggest to stop your treatment and can change your treatment to one that may not cause as many, or any, side effects.

## Transformation

Less than 10% of patients with MALT lymphoma will have their lymphoma change into a more aggressive lymphoma, often referred to as histologic transformation. A transformed lymphoma is one that was initially diagnosed as indolent (slow-growing), such as MALT lymphoma, but then later develops into an aggressive (fast-growing) disease. Transformation typically occurs within 2-5 years after the lymphoma was initially diagnosed, however it can occur at any time. As transformed lymphomas are more aggressive in their behavior, they can require different treatments than what you may have received previously for your MALT lymphoma.

## Follow-Up Care

Once you have completed treatment, you will likely be given a follow-up care plan to monitor your response to treatment and recovery, as well as to watch for late effects (side effects that develop months or years after treatment) or a potential recurrence. Follow-up care for your MALT lymphoma is often shared between your cancer specialists and your family doctor. Your medical team will work with you to decide on the correct follow-up care plan to meet your needs. Follow-up care after treatment is an important part of your cancer care. It is very important to go to all of your follow-up appointments. Your schedule of visits and the tests and procedures that you will undergo during your follow-up are tailored to your individual lymphoma.

Your doctor will also tell you to watch for specific signs or symptoms that may indicate a relapse or recurrence (i.e. your MALT lymphoma comes back). Relapse becomes less likely as time goes on and if it does occur, symptoms usually present within the first year after you have finished treatment. It is important to watch for symptoms throughout your body, as relapse can occur at the site of your original diagnosis, or it may appear in a new region throughout your body. Doctors may perform additional testing including blood tests and imaging scans to confirm if your lymphoma has relapsed or transformed.

Use the time during your follow-up appointments to talk to your medical team about any changes or problems you notice and any questions or concerns you may have about your health after treatment. If you notice any change in your signs and symptoms between follow-up appointments, be sure to contact your medical team right away.

## YOU DON'T HAVE TO FACE LYMPHOMA ALONE.

Lymphoma Canada connects patients, their family and friends, medical professionals, researchers, volunteers and donors, to build a strong lymphoma community.

For more information please visit [lymphoma.ca](http://lymphoma.ca) or call 1-866-659-5556, or email us at [info@lymphoma.ca](mailto:info@lymphoma.ca).



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