

Mantle Cell Lymphoma and New Treatments on the Horizon

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Learn about:

- Diagnosing mantle cell lymphoma
- Current treatments
- New drugs in development
- Coping with treatment side effects



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Clinical trials on mantle cell lymphoma have improved our understanding and treatment of the disease dramatically.

Mantle cell lymphoma is a relatively rare form of **B-cell lymphoma**, a type of non-Hodgkin lymphoma, which is a blood cancer. Each year in the United States, approximately 1,400 people are diagnosed with mantle cell lymphoma. The incidence of this type of cancer varies in different countries. It appears to be more common in people who are Caucasian or of European descent. It is less common in Asia and among people of Asian descent.

Lymphomas are cancers that begin in **lymphocytes**, a type of white blood cell that is an important part of our infection-



fighting immune system. These lymphocytes are found mainly in lymph nodes (sometimes called "lymph glands"), as well as in other parts of the body that make up the immune system, such as the spleen or the bone marrow. Lymph nodes are a linked system of small bean-shaped structures throughout the body that helps filter out and destroy bacteria and other toxic substances. One of the

first signs of mantle cell lymphoma can be a swelling in the neck, armpit, or groin due to an enlarged lymph node. However, a swollen lymph node is usually due to an infection and not cancer.

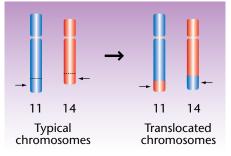
Although there are exceptions, people diagnosed with mantle cell lymphoma are usually older adults. For unknown reasons, it also tends to occur more often in men than in women. Generally, the cancer is not confined to one place in the body—that is, it's not localized. Mantle cell lymphoma occurs in one or more lymph nodes, but at the same time it can also appear in the digestive system, lungs, skin, spleen, bone marrow, or blood. Often, mantle cell lymphoma has spread by the time it is diagnosed by a doctor.

What Is Mantle Cell Lymphoma?

Mantle cell lymphoma gets its name from the mantle zone, which is the outer edge of lymph nodes where changes take place that lead to this cancer. It wasn't until recently that mantle cell lymphoma was recognized as a distinct form of B-cell lymphoma. Once doctors understood how it is different, they were better able to treat it.

Doctors had observed that in some people with B-cell lymphoma, the cancer grew much more quickly. However, it was difficult to figure out why, or how to know which patients would be affected in that way. During the past decade, there were a series of breakthroughs, as researchers figured out that a number of people with B-cell lymphoma shared a particular genetic mutation, or change.

Researchers discovered that most people with mantle cell lymphoma have a mutation in two of their **chromosomes**, the strands of genes that shape all of our characteristics. In mantle cell lymphoma, parts of



chromosomes 11 and 14 exchange places, what doctors call a **translocation**. This translocation leads to the release of too much of a substance called cyclin D1. A buildup of cyclin

D1 leads to the uncontrollable growth of a type of B cell and mantle cell lymphoma. An excess of cyclin D1 is almost always found in the lymph nodes of people with mantle cell lymphoma.

Another important research finding was that mantle cell lymphoma could be identified through either the presence or absence of B-cell **markers** on the surface of mantle cell lymphoma cells. There are several types of markers associated with mantle cell lymphoma: CD5, CD19, and CD20. The absence of other B-cell markers, such as CD23 and CD10, is also used to identify mantle cell lymphoma.

Armed with this information, researchers worldwide have joined to look back at a large number of patients who, in the past, were diagnosed with B-cell non-Hodgkin lymphoma. Based on information in these records, doctors can now

isolate the cases of mantle cell lymphoma to better understand its course and how it differs from other non-Hodgkin lymphomas.

Diagnosing and Staging Mantle Cell Lymphoma

The job of a **pathologist** is to correctly identify the nature, origin, progress, and cause of disease. This is especially important with mantle cell lymphoma in order to treat it properly. If your doctor suspects that you may have lymphoma,



he or she will work with a pathologist to determine exactly what type of lymphoma you have. A number of tests must be conducted:

A series of blood tests to find out whether blood cell counts are normal, and to test the function of the kidneys, liver, and certain proteins in the blood that may point to mantle cell lymphoma. These proteins include lactic acid dehydrogenase (LDH) and beta 2-microglobulin. The test is done on a sample of blood that is drawn from a vein.

- A **biopsy** of the affected tissue, usually an enlarged lymph node, which is examined under a microscope. To obtain the biopsy, tissue from a lymph node may be removed surgically or through a hollow needle inserted through the skin into the node. The pathologist will test the sample for mantle cell lymphoma tumor markers, to find out whether the cells contain too much cyclin D1 or to check whether there is a translocation of chromosomes 11 and 14, which helps pinpoint the type of lymphoma.
- A **bone marrow biopsy** to determine whether cancer has spread to this area. A hollow needle is usually inserted into the hip bone to obtain the sample.
- A CT or PET scan to search for tumors throughout the body.
- A **colonoscopy** or **flexible sigmoidoscopy**. In each of these tests, a thin tube with a tiny video camera and light is inserted into the rectum so the doctor can see

the inside of the colon, where mantle cell lymphoma commonly spreads.

In addition to correctly diagnosing mantle cell lymphoma, these tests also help doctors **stage** the



disease—that is, determine the extent of the cancer and how quickly it is growing or spreading. Your doctor should review the results of these tests with you, discuss your treatment options, and make a plan to monitor your progress.

Treatment of Mantle Cell Lymphoma

As with most lymphomas, the treatment of mantle cell lymphoma depends on the stage of the cancer and the person's age, general health, and treatment goals.

CHEMOTHERAPY

Through clinical trials we have learned that standard chemotherapy combinations developed for other types of lymphomas, such as CHOP (cyclophosphamide [Cytoxan and others], doxorubicin [Adriamycin and others], vincristine [Oncovin and others], and prednisone), have not worked well in mantle cell lymphoma.

But there have been exciting changes in treating mantle cell lymphoma. The first major change was the development of a treatment approach known as **hyperCVAD**. This is a complex, intensive combination of four chemotherapy drugs: cyclophosphamide, vincristine, doxorubicin, and the steroid dexamethasone. Doctors alternate these drugs with high doses of cytarabine (also known as cytosine arabinoside or Cytosar-U) and methotrexate. The "hyper" stands for hyperfractionated,



which means that the drugs are given in frequent small doses to reduce the side effects that this aggressive treatment causes.

More recently, doctors are combining hyperCVAD with rituximab (Rituxan), a **monoclonal antibody** that specifically targets B cells. Most people with mantle cell lymphoma who receive this combination have experienced a **complete remission**.

This successful but aggressive treatment can be difficult to complete, however. The side effects include low levels of

infection-fighting blood cells (requiring transfusions), nausea, diarrhea, and mouth sores. Researchers are now studying ways to make the treatment easier for patients to tolerate. Removing or reducing the dose of methotrexate from the mix of drugs seems to help older patients in particular.

A number of other drug treatments are also being studied and used, all of which appear to be active against mantle cell lymphoma. One of these novel treatments, bortezomib (Velcade), was recently approved by the U.S. Food and Drug Administration for use in treating mantle cell lymphoma that failed to respond to at least one prior treatment. Other drugs being tested in clinical trials include lenalidomide (Revlimid), thalidomide (Thalomid), and gemcitabine (Gemzar). Researchers want to know whether these drugs, perhaps in combination with previously used chemotherapy, could someday become the standard treatment for this disease.

TRANSPLANTATION

High-dose drug treatment combined with **autologous bone marrow transplantation** has helped many mantle cell lymphoma patients achieve remission. In this procedure, a patient's own **stem cells** are collected from his or her bone marrow and frozen. After intense chemotherapy designed to kill as many cancer cells in the body as possible, the stem cells are returned to the patient through a vein. The stem cells then take root and mature into cancer-free B cells. Blood stem cells from another person—a matched donor—may be used in what doctors call an **allogeneic transplant**. Allogeneic bone marrow transplants can cause mouth sores, fatigue, nausea, and vomiting.

RADIATION

Mantle cell lymphoma is sensitive to radiation; however, because this type of cancer is rarely localized, radiation alone cannot be used to treat it. To enhance this form of treatment, a radioactive compound can be attached to a monoclonal

antibody, which guides the radiation to the abnormal B cells, wherever they are in the body, and destroys the cancer. A number of different monoclonal antibodies are being studied. Among the side effects of radiation and monoclonal antibodies that some people experience is fatigue.

Coping With Treatment Side Effects

Most people being treated for mantle cell lymphoma will experience side effects from their medications, although each



person's reaction can be different. You need to work closely with your doctor and report any symptoms you may have.

There are a number of medications available that can prevent side effects such as nausea and vomiting. Talk with your health care team about steps that can be taken before symptoms such as mouth sores or fatigue, for example, become worse. Your doctor will want to make sure that you are receiving enough fluids to stay hydrated and the right medications to keep

you comfortable and on track with your treatment plan.

Choosing a Treatment

Here are some points to discuss with your doctor when considering treatment:

Is my disease slow-growing or aggressive? In a small number of people with mantle cell lymphoma, the disease is slow-growing and they feel well. For these people, doctors may recommend a period of "watchful waiting" during which time the patient is closely monitored before treatment begins. Treatment often starts when the cancer shows signs of progressing, such as enlarged lymph nodes.

Is my general state of health strong enough for a

The Importance of Clinical Trials

The progress in treating mantle cell lymphoma has been made possible because researchers have banded together with patients to test new drugs. They have also worked through the clinical trials system to figure out how mantle cell lymphoma differs from other types of lymphoma so that the best treatments could be applied. Without this research and the active participation and support of patients and their caregivers, doctors would not have the powerful tools they need to help people with mantle cell lymphoma.

This is a very exciting time for the treatment of mantle cell lymphoma. Doctors believe and hope that we are not far from finding even more effective treatments so that all patients can benefit.

Clinical trials are the standard by which we measure the worth of new medications and the quality of life for people with all types of cancers as they go through treatment. For all these reasons, doctors and scientists urge patients to take part.

Your doctor can guide you in making a decision about whether a clinical trial is right for you. Here are a few things you should know:

- Often, patients who take part in clinical trials gain access to and benefit from new treatments not available to the general public.
- Before you participate in a trial, you will be fully informed as to the risks and benefits of the trial.
- Most trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any benefit.
- You can stop taking part in a clinical trial at any time for any reason.

potentially intense treatment? Generally speaking, the hyperCVAD treatment is better tolerated by young and relatively fit patients. However, age alone does not determine

your tolerance. For example, some older patients can be more fit and prepared for intense treatment than younger patients.

How can we meet my treatment goal? Different people have different treatment goals. For example, if your goal is complete remission, discuss with your doctor whether this is possible and which treatment would be necessary. If you are more concerned about avoiding certain side effects, your treatment plan might be different.

Communicating With Your Health Care Team

When you are diagnosed with mantle cell lymphoma, you're faced with a series of choices that will have a major effect on your life, and maybe you're not sure where to turn. Of course, your most important resources are your health care team, family members, and friends. It is very important to develop good communication with them. You can also turn to these resources:

Oncology social workers and nurse practitioners

are specially trained to help you find out more about your treatment options, learn how to navigate the health care system, and get the best care possible, including finding experts in mantle cell lymphoma.



Often, when people are coping with cancer, they need someone to talk with who can help them and their families sort through the complex emotions and issues that arise. For instance, some people with mantle cell lymphoma may need extra help managing intense side effects or finding the best treatment or clinical trial. Oncology social workers and nurse practitioners can provide emotional support, help

you cope with treatment and its side effects, and guide you to resources. Cancer Care® offers free counseling from professional oncology social workers on staff.

Support groups can reduce the feeling that you are going through cancer alone. These groups provide reassurance, suggestions, insight—a safe haven where you can share similar concerns with your peers in a supportive environment. It may be helpful to meet others with mantle cell lymphoma to learn how they are coping with uncertainties, aggressive treatments, and other concerns. At Cancer*Care*, people with cancer and their loved ones and caregivers can take part in support groups in person, online, or on the telephone.

Financial help is offered by a number of organizations, including Cancer*Care*, to help cover cancer-related costs such as transportation to treatment, child care, or help needed around the home. Cancer*Care* can also refer you to other resources in your community that can provide assistance.

Frequently Asked Questions

What role do imaging techniques such as CT scans and PET scans play in treatment for mantle cell lymphoma?

A Neither test is perfect, but used together they appear to be increasing our ability to detect all types of cancer. PET scans allow us to spot cancers by seeing cells with an abnormal metabolism of glucose, or sugar. CT scans give us a view of the body in layers of cross-sections to look for structures that shouldn't be there, such as large lymph nodes or injury to an organ, from cancer, for instance.

I'm in complete remission from mantle cell lymphoma now but am worried that my cancer could come back. What can I do?

As with any cancer that has been successfully treated, there could still be some undetectable cancer cells left in the body, what doctors call "minimal residual disease." That is why follow-up testing and **surveillance** are so important. Your doctor will recommend a schedule of tests to monitor your health.

Are researchers working on a vaccine for mantle cell lymphoma?

A Yes, there are several efforts ongoing. Researchers have been encouraged by the progress on a vaccine for a different type of B-cell lymphoma called follicular lymphoma. They are using a similar strategy for a mantle cell lymphoma vaccine. So certainly there is progress, and we are looking forward to the results of clinical trials.

Glossary

allogeneic transplant In this procedure, a cancer patient receives healthy blood stem cells from another person whose tissue type makes him or her a "matched donor." The donor may be a brother or sister. An unrelated person can also donate blood stem cells if he or she matches the patient's tissue type either completely or closely. Before the donor's stem cells are transplanted, the person with cancer receives chemotherapy or radiation to help destroy tumor cells and prevent the immune system from rejecting the donated cells.

autologous bone marrow or stem cell transplantation

In this procedure, a patient's stem cells are collected from his or her bone marrow or blood and frozen. After intense chemotherapy designed to kill as many cancer cells in the body as possible, the stem cells are returned to the patient through a vein. The stem cells then take root and mature into cancer-free B cells.

B-cell lymphoma A type of non-Hodgkin lymphoma (a blood cancer).

biopsy Obtaining tissue from the body for examination under a microscope. A biopsy is often performed surgically, or by using a hollow needle that is inserted through the skin into the affected area so tissue can be withdrawn.

bone marrow The soft tissue found in the hollow interior of bones. Marrow in large bones produces new blood cells.

bone marrow biopsy A test to determine whether cancer has spread to the bone marrow. A hollow needle is usually inserted into the hip bone to obtain the sample.

chromosomes The strands of genes that shape all of our characteristics.

colonoscopy A test in which a thin tube with a tiny video camera and light is inserted into the rectum so the doctor can see the inside of the colon, where mantle cell lymphoma commonly spreads.

complete remission Currently available tests cannot detect any cancer. Surveillance is important for people in complete remission, as there may be undetectable cancer cells left in the body, and the earlier any developing tumors are detected, the more treatable they are.

CT scan A special type of x-ray to search for tumors throughout the body.

flexible sigmoidoscopy A test in which a thin tube with a tiny video camera and light is inserted into the rectum so the doctor can see the inside of the colon, where mantle cell lymphoma commonly spreads.

hyperCVAD A complex, intensive combination of four chemotherapy drugs: cyclophosphamide, vincristine, doxorubicin, and the steroid dexamethasone. Doctors alternate these drugs with high doses of cytarabine and methotrexate. This treatment plan is often combined with rituximab, leading to a complete remission for many people with mantle cell lymphoma.

lymph node(s) Part of a network of small filtering stations that removes waste and fluids from our organs and tissues and transports lymphocytes, helping us to fight infections. In mantle cell lymphoma, the nodes are the main site where this cancer begins.

lymphocytes A type of white blood cell that is an important part of our infection-fighting immune system.

markers Substances that can be found in abnormal amounts or distribution in the blood, urine, or tissues of some patients with cancer. In some cases, the absence of a marker is important for diagnosis as well.

monoclonal antibody Often compared to a guided missile, these substances home in on cancer cells to deliver treatment such as radiation that destroys the tumor.

pathologist A medical specialist who is trained to correctly identify the nature, origin, progress, and cause of disease.

PET scan A test that allows doctors to spot cancers by seeing cells with an abnormal metabolism of glucose, or sugar.

spleen An organ that filters blood, removing waste, and produces infection-fighting lymphocytes for the immune system. The spleen is located on the left side of the body in the upper abdomen.

stage A measure of the tumor's size; whether it has spread; how fast-growing it is; and what, if any, additional treatment is needed.

stem cells Cells produced by healthy bone marrow. They are capable of maturing into red blood cells, white blood cells, and other essential cells.

surveillance Continued monitoring of the body for signs of cancer.

translocation An exchange of genetic material between two chromosomes—the strands of genes that shape all of our characteristics. In the case of mantle cell lymphoma, a translocation that occurs between chromosomes 11 and 14 leads to the uncontrollable growth of B lymphocytes.

Resources

Cancer Care

1-800-813-HOPE (4673) www.cancercare.org

American Cancer Society

1-800-227-2345 www.cancer.org

Cancer.Net

(Patient information from the American Society of Clinical Oncology) www.cancer.net

Lymphoma Research Foundation

1-800-500-9976 www.lymphoma.org

National Bone Marrow Transplant Link

1-800-546-5268 www.nbmtlink.org

The National Coalition for Cancer Survivorship

1-877-622-7937 www.canceradvocacy.org

National Marrow Donor Program

1-800-627-7692 www.marrow.org

The Wellness Community

1-888-793-9355 www.thewellnesscommunity.org

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