

MANTLE CELL LYMPHOMA

What is lymphoma?

Lymphomas are cancers that originate in a lymphocyte, which is a cell found principally in lymph nodes and other lymphatic tissue sites, such as the skin, spleen and the wall of the intestines. The transformation of a lymphocyte to a malignant cell gives it a growth and survival advantage over normal cells. The malignant cell multiplies and enlarges the lymph node so that it may be felt or observed if it is in a location near the surface of the body. The malignant lymphocytes may travel to other lymph nodes and those nodes may enlarge from uncontrolled malignant cell multiplication.



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What is the derivation of the word lymphoma?

Lymph is the fluid that is present in the small tubular channels, called lymphatics, that connect lymph nodes one to another, permitting lymphocytes to circulate through the lymph nodes. Thus, the lymphatics contain lymphocytes suspended in a watery fluid, the lymph, that circulates throughout the body from one lymph node to another. The lymphatic channels collect into larger lymphatic vessels that ultimately enter into the blood and this connection permits a small proportion of lymphocytes to be present in the blood, also.

The term lymph comes from the Greek for colorless fluid or sap, highlighting its difference from the red or bluish-red color of blood in arteries or veins. The lymph nodes are collections of lymphocytes the size of beans in which new lymphocytes are made. Lymphoma is a shortened version of lymphocytoma. The latter term is composed from the name of the cell type involved, the lymphocyte, which has undergone a malignant transformation and the Greek for tumorous affliction - oma. Hence, the shortened term lymphoma for a malignant tumor of lymphocytes.

Lymphomas are divided into two major categories: Hodgkin's disease and all other lymphomas (referred to as non-Hodgkin's lymphomas). In Hodgkin's disease, specific types of cells are present that are not found in the non-Hodgkin's lymphomas. Further information on the lymphocytes and lymphoma can be obtained in The Leukemia & Lymphoma Society booklet "The Lymphomas."



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What is mantle cell lymphoma?

Mantle cell lymphoma (MCL) is a type of lymphoma that arises from malignant B lymphocytes in the portion of lymph nodes called the “mantle zone.” As the disease progresses, the “mantle zone” areas are obliterated by the growing cells and the lymph node loses these boundaries. This change results in lymphocytes spreading diffusely through the node. This is seen as “diffuse” lymphoma under the microscope.

The disease was first described by a German pathologist, Karl Lennert in 1973, and it was called by various terms until 1992, when the name mantle cell lymphoma was proposed. Its existence as a special type of lymphoma was formalized in 1994 by the International Lymphoma Study Group.

Mantle Cell Lymphoma forms from small to medium-sized lymphocytes. When viewed under a microscope, very few large cells are present. These lymphoma cells produce characteristic antigens (proteins on the outer surface of the cell that can cause an antibody response) which are referred to as CD5 and CD 20. CD followed by a number is the medical designation for specific cell antigens that can be used to identify cells. These antigens on tumor cells can help determine the normal cells from which the tumor developed since they each, normal and tumor cell, may share these identifying features.

Many patients with mantle cell lymphoma have an acquired genetic alteration that exchanges pieces of



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chromosome 11 and chromosome 14. This is called an 11:14 translocation. Thus, part of one chromosome is transferred to another chromosome and vice versa. The 11:14 translocation causes overexpression of a protein called cyclin D1, resulting in excessive production of B lymphocytes. The cyclin proteins can influence the rate that cells divide and grow.

Mantle cell lymphoma cells tend to grow more quickly than those of other lymphomas. They frequently expand in the bone marrow, and are not as responsive to chemotherapy as other lymphomas.

How is mantle cell lymphoma diagnosed?

Symptoms include loss of appetite, weight loss, nausea, vomiting, indigestion, abdominal pain or bloating, or a feeling of fullness or discomfort due to enlarged liver or spleen.

The disease usually causes enlargement of the lymph nodes, especially those that are in the back of the throat, including the tonsils and adenoids. This area of lymph nodes is called Waldeyer's ring. The liver and spleen may become enlarged, and involvement of the gastrointestinal tract is common. The lymphoma cells may also invade the brain and spinal cord. Rarely, patients may develop multiple polyps in their small or large intestine which contain lymphoma cells. The enlarged lymph nodes, liver, and spleen often are detected during medical examination.



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If cells have accumulated in the bone marrow, the formation of normal red blood cells may be suppressed, causing anemia. A bone marrow biopsy may reveal the presence of lymphoma cells.

A biopsy may be taken from an enlarged lymph node, liver, or other sites, for microscopic examination. Tests for the 11:14 translocation in the lymphoma cells may be performed on biopsy samples by cytogenetic or molecular methods. Staining of the cell for cyclin D1 may be helpful in making a specific diagnosis.

At the time of diagnosis, efforts are made to determine whether the disease is progressing rapidly. Rapid lymph node enlargement, severe weight loss and weakness, liver enlargement, and elevations in the blood level of an enzyme, lactic dehydrogenase , referred to as LDH, are signs of rapid progression.

How common is mantle cell lymphoma?

The disease occurs more often in males than females (2:1 ratio) with a median age of 58 years at diagnosis. It is an uncommon disease, comprising about 3 percent of lymphomas in the US (about 1500 new cases per year) and about 8 percent of lymphomas in Europe.

How did I get mantle cell lymphoma?

The cause of mantle cell lymphoma and most other lymphomas is not known. It is known, however, that most of these diseases result from an acquired injury to



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the DNA in the genes of a single cell, which becomes malignant. The possible causes of some lymphoma are mentioned in The Leukemia & Lymphoma Society booklet “The Lymphomas.”

How will I be treated for mantle cell lymphoma?

Standard chemotherapy combinations usually do not cure this type of lymphoma. Therefore, patients are encouraged to consider participating in clinical trials (controlled studies of newer treatment approaches) or innovative treatment protocols, and, if eligible, may be advised to have early marrow or blood stem cell transplantation. Some of the major treatments being used are mentioned here. Your physician is the best resource for specific treatment procedures (protocols) and management techniques. In addition, improved treatment programs may be introduced in the future.

Treatment planning is individualized and takes into account whether the lymphoma is likely to grow more slowly or quickly. Patients with slowly progressive disease might be managed with chlorambucil, cyclophosphamide, or three drugs simultaneously, for example cyclophosphamide, vincristine, and prednisone, referred to as CVP. Patients who have severe symptoms or rapidly progressive disease may be treated with four drugs simultaneously, (cyclophosphamide, doxorubicin, vincristine, and prednisone) referred to as CHOP.

If the disease has spread to the central nervous system, drugs may be administered directly into fluid bathing the spinal canal. This is referred to as intrathecal therapy.



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What are the newest treatments for mantle cell lymphoma?

Genetic engineering techniques have enabled pharmaceutical companies to produce drugs made from monoclonal antibodies that specifically target the CD 20 antigen that is present on the surface of mantle cell lymphoma cells. Once attached to the lymphoma cell, the cells are severely damaged by a radioactive compound attached to the monoclonal antibody (iodine I 131 tositumomab or Bexxar) or by the effect of the antibody alone on the cell (rituximab or Rituxan). These drugs are now being tested in clinical trials for their effects in mantle cell lymphoma patients.

Several researchers have started investigating the use of bone marrow transplantation as a treatment in this disease. For transplantation of the patient's own marrow (autologous transplantation) the marrow cells may be first treated with monoclonal antibody directed against the lymphoma cells. This procedure minimizes the chance of returning lymphoma cells in the marrow to the patient. Results so far have been disappointing, but it is possible that transplantation performed at an earlier stage of the disease may be more beneficial than performing the procedure later in the disease after relapse.

Preliminary results indicate that treatments that include high-dose therapy with cytarabine as part of a multi-drug combination, followed by autologous stem cell transplantation, can increase the response rate.



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How successful is treatment for mantle cell lymphoma?

With standard chemotherapy approaches, most patients have a poor prognosis and often a survival time less than 3 years. The reason for resistance to therapy is not clear, and patients vary widely in their responses. Treatment does not usually change the natural history of the disease. For this reason, patients are encouraged to consider participation in clinical trials and innovative treatment protocols that may extend survival times and prolong periods of remission from the disease. Since mantle cell lymphoma tends to become resistant to therapy early in the course of the disease, patients should consider participation in these clinical trials at the time of diagnosis or soon thereafter.



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1. Press OW, Grogan TM, Fisher RI. Evaluation and management of mantle cell lymphoma. *Advances in Leukemia and Lymphoma* 1996;6(1):3-11.
2. Barela M. Mantle cell lymphoma. *Lymphoma Resource Pages* (Internet) 1998.
3. Foon KA, Fisher RI. Lymphomas. In: Williams (ed). *Hematology*. New York: McGraw Hill, 1995, p. 1976.

Other Resources:

The Leukemia & Lymphoma Society publication:

- The Lymphomas

More information on mantle cell lymphoma:

To get more information, talk to your physician or call The Leukemia & Lymphoma Society, 1-800-955-4572. Web sites that discuss mantle cell lymphoma include:

- <http://eyesite.ucsd.edu/~mcl>
- The Leukemia & Lymphoma Society at www.leukemia-lymphoma.org

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