

<b>Title</b>	Lymphoma
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## Purpose

The purpose of this course is to provide the reader with a basic understanding of lymphomas with an emphasis on rare T-cell cutaneous lymphoma. It is also to assist health care providers in identifying T-cell skin lesions, providing appropriate nursing care, and understanding the various treatment modalities available.

## Objectives

1. Define lymphoma
  2. Recognize signs and symptoms of each stage of T-cell lymphoma
  3. Identify one therapy for each stage of T-cell lymphoma
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Lymphoma is a type of cancer of the lymphatic system, lymph nodes or the lymphocytes. Lymphocytes compose about 20 percent of the white blood cells in the blood. The lymphatic system is part of the human body's immune system. It consists of vessels that begin as tiny, blind-ended tubes that connect to larger lymphatic ducts and branches throughout the body. These vessels carry a clear fluid called lymph that flows through the lymph nodes and other lymphatic tissue including the spleen, the tonsils, the bone marrow and the thymus glands. The lymph fluid's primary role is to carry the white blood cells or the lymphocytes to locations around the body where they are needed to respond to bacteria, virus or other foreign bodies.

Lymphoma cancer is a malignancy, which occurs when the normal lymphocytes undergo a transformation or change whereby they grow and multiply uncontrollably. It is after this structural alteration that the lymphoma cells form lymphoma cell masses, which gather in the lymph nodes or other parts of the lymphatic system. In the cancer, lymphoma, abnormal cells travel from one lymph node to another one and sometimes into the visceral or organs of the body. Any lymphoma development outside of the lymph nodes is called extranodal disease.

The primary role of lymphocytes in the immune system is to recognize pathogens (infections and abnormal cells) and destroy them. The two major types of lymphocytes within the lymphatic system are B-lymphocytes and T-lymphocytes or more commonly know as B-cells and T-cells.

The primary role of B-cells is to produce antibodies that circulate throughout the lymphatic system and fasten to infectious organisms and abnormal cells in an attempt to rid the body of these abnormal cells. Once the body is rid of this foreign organism, the B-cells typically "remember" the infectious organism or abnormal cells and will fight it off again should it reenter into the body at a later time. The B-cells work in conjunction with the T-cells to make antibodies that assist the neutrophils and monocytes to fight against infections or foreign organisms.

According to Parker and Bradley, (2006) the role of the T-cells is to survey and protect the body from infectious agents, environmental stressors and malignancies. T-cells are often called "the attackers". They attack directly and kill. T-cells are programmed to protect different parts of the body. Some are programmed to protect the skin, while others are programmed to provide protection to other parts of the body such as the gastrointestinal tract.

The process of the T-cells attacking and killing directly can be demonstrated with what occurs when a person is exposed to poison ivy or other antigens. Immediately upon a sensitive person's contact with this allergen, the T-cells are activated to attack and kill. The T-cells gather at the site of exposure and attempt to rid the person of this allergen that can be identified in the form of a rash and redness to the skin. Once the T-cells have completed their attack upon this environmental stressor, they exit the skin and re-enter into the lymphatic system and re-circulate or undergo the process of natural death. A problem occurs within the body if at this point the T-cell undergoes a change and begins to multiply uncontrollably. In Cutaneous T-cell lymphoma (CTCL), the malignant T-cells cycle and divide without dying off. They remain in the skin and reproduce, thus the disease process has begun.

The two main types of lymphoma are Hodgkin and Non-Hodgkin lymphoma. Lymphomas are further broken down into approximately 35 different subtypes. About 12% of people with lymphoma have Hodgkin lymphomas with the remaining having Non- Hodgkin lymphoma.

Lymphoma cancer can occur at any age. Hodgkin lymphoma is most common in young adults age 16-34 and in older adults age 55 and older. Non-Hodgkin lymphoma is most likely to occur in older people. Cutaneous T-cell lymphoma (CTCL) is an example of a Non -Hodgkin lymphoma.

Dr. Wendy Hu and Kathryn Hale, states that the exact causes of lymphoma are not known. Certain risk factors contribute to the development of lymphoma. The following are risk factors:

- Age: The risk of NHL increases as one gets older.
- Infections. Individuals who have experienced an infection with HIV, human t-lymphocytic virus type 1, Epstein-Barr virus, Helicobacter pylori and hepatitis B or hepatitis C.
- Illness which compromises the immune system such as HIV, autoimmune disease, and inherited immunodeficiency diseases. Individuals who are on immune suppressive therapy are also at risk.
- Exposure to toxic chemicals. Individuals who are exposed to pesticides, herbicides or benzene. For more than 20 years it has been demonstrated that individuals who use black hair dye have been linked to higher rates of NHL.
- Genetics

Lymphomas may be either T-cell or B-cell. B-cell lymphomas, tend to be nodal based, are more common and rarely have cutaneous symptoms. CTCL (Cutaneous T-cell lymphoma) is commonly manifested in the skin with secondary affects elsewhere in the body.

In CTCL, the T-cells do not exit the site nor undergo natural cell death, but rather multiply or undergo cellular change. The T-cells accumulate and take on the appearance of a rash. The nature and appearance of the rash on the patient's skin so closely resembles psoriasis or eczema thus delaying appropriate treatment for years, which increases the patient's risk of severe morbidity and mortality.

CTCL is the most common type of cutaneous lymphoma representing 65 % of skin lymphoma cases. One might also hear CTCL called mycosis fungoides, Sezary syndrome and reticulum cell sarcoma of the skin. These are really different forms of the same disease.

CTCL is a rare disease, with an annual incidence of about .29 cases per 100,000 persons in the United States. It is about half as common in Eastern Europe. CTCL is found in twice as many men as women and the average age of diagnosis is 55 to 60 years. It is twice as common in black persons as in white persons, but it may affect persons in any age or ethnic group. The average life expectancy at diagnosis is 7-10 years even without treatment.

The three general phases of the development of CTCL is patches, infiltrated plaques and tumors. Early skin lesions may mimic eczema, secondary syphilis, psoriasis or contact dermatitis. Often the lesions may diminish when treated with topical corticosteroid or exposed to sunlight similar to psoriasis thus often causing a significant delay in appropriately diagnosing CTCL.

In most patients, CTCL begins as an itchy, dry-surfaced or scaly, non-raised patch on the skin. Itching is a universal symptom of lymphoma. It is this profound itching which usually causes a patient to seek health care. The itching can be so severe that a patient is not able to sleep at night.

The lesions or patches are often red and resemble a rash. In darker individuals they may appear darker or lighter than the natural skin color. The most classic presentation of the lesions is found in the areas of the body covered by under garments as well as the outer most layers of clothes. The flank and peri-axillary regions are the most common sites of involvement, but CTCL can be present on any part of the body.

The disease progresses to palpable plaques that are deeper red, thicker with a more defined edge. As the cancer advances, the appearance changes to that of mushroom shaped tumors. This is known as mycosis fungoides. These raised bumps or tumors may or may not ulcerate. The name mycosis fungoides leads one to believe that the rash is related to a fungus, however, this is not true. It is possible for each lesion on a patient's body to be different stages of CTCL. For instance one may have one lesion that is at the patch stage while another one is at the mycosis fungoides phase.

With the advancement of the disease, the cancer may progress to involve the lymph nodes or internal organs. Symptoms at this time may include enlarged lymph nodes, generally at the site where the skin involvement exist, disorders of the lung, upper digestive tract, central nervous system or liver.

The probability of the spread to internal organs within the body is directly related to the amount or percentage of skin involvement. Visceral (internal organs) involvement is almost never seen with minimal skin involvement. Approximately 15 to 20 percent of all patients diagnosed with CTCL will have internal organ involvement.

As earlier stated, diagnosis of CTCL is often difficult in the early stages due to the slow growth of the lesions and the ability to mimic other less threatening skin conditions. It is most likely discovered or diagnosed when a doctor suspects the possibility of this disease based on clinical assessment of the patient and confirmation of the diagnosis by performing a skin biopsy of the lesions.

The team that provides care for a patient with CTCL, consist of primary care provider, dermatologist, medical oncologist, nursing personnel and if radiation therapy is utilized a radiation oncologist. Generally the initial assessment of the patient will be addressed by the primary care provider who identifies the presence of the skin lesions and refers the patient to a dermatologist.

Once the dermatologist has obtained the patient's general history, assessed the lesion's

characteristics, performed an overall physical exam of the patient, it is necessary for a physician to perform specific laboratory tests, skin biopsies of the lesion and other radiological tests.

Specific laboratory blood tests that assist in the diagnosis of CTCL assesses the cellular proteins on the surface of abnormal cells. Other blood tests are ordered which measure certain chemicals or enzymes. For example, one test measures an enzyme, called lactate dehydrogenase (LDH). High levels of LDH may indicate an aggressive form of non-Hodgkin lymphoma. A physician may also order a blood test called the southern blot analysis which identifies genetic changes for a gene which encodes the T-cell receptors.

Skin biopsies will demonstrate abnormal cells in the epidermal tissue. A biopsy is the removal and microscopic examination of the tissue to check for abnormal T-cells. Due to the nature and slow growth of lesions repeated skin biopsies may be necessary to make a definite diagnosis.

Since in the later stages, CTCL can affect the lymph nodes or other organs in the body it is necessary to perform radiological tests such as CT, MRI and PET scans. PET scans are one of the most useful tools to assess or detect areas of the body affected by lymphomas. A PET scan consists of injecting a tiny amount of radioactive substance into the body and it is observed as it travels throughout the body. Sites of radioactivity or hot spots on the scan indicate areas of increased metabolic activity which demonstrates the presence of a tumor.

Based on the information obtained from the clinical assessment, lab values and biopsy, the physician will perform staging of the disease. The purpose of staging is to define the relations between the symptoms and the prognosis of the disease. Another way to say this is that staging is classifying the cancer and determines whether and how much it has spread around the body. Three components of the disease are utilized in the assignment of the grade or stage of the disease. These are based on the skin involvement, lymph node involvement and any presence of the disease in any of the internal organs.

Stage I A consists of plaques covering less than 10 percent of the body, no internal organ or lymph node involvement. Prognosis of this disease at this stage is very good. The average survival rate for an individual diagnosed with CTCL, Stage IA is 20 or more years with death being from something other than CTCL.

Stage IIB is characterized by greater than 10 percent of the body being covered by plaques as well as enlarged lymph nodes. Average survival rate for an individual with stage II B is about 12 years.

Stage III is characterized by most of the skin being dry, red, and scaly. The lymph nodes are normal or larger than normal but are not cancerous. Skin involvement is greater than 70 percent. Patients diagnosed in this stage have a mean life expectancy of about five years.

Stage IVA and Stage IVB are the final two stages of the disease. This stage is characterized by dry, red, scaly skin, cancer cells are present in the lymph nodes and cancer has spread to other organs of the body. Over 50 % of the deaths from CTCL occur during this stage due to Staphylococcus aureus or Pseudomonas aeruginosa sepsis which patient's are unable to fight off due to their weakened immune system. (Parker & Bradley, 2006) Once a patient is in Stage IVB, the mean life expectancy is one year. Treatment of CTCL depends on the patient's age, overall health status, medical history, the type and stage of the disease, and the patient's preference, other patient issues such as cost of care, accessibility of health care, and physician preferences. Treatment choices include topical therapy, phototherapy, radiation, chemotherapy or a combination of chemotherapy with other therapies.

The treatment for stage IA is generally topical skin treatments. The lotions or gels used for this stage of the disease should be applied to the lesions only and not to the unaffected skin. Corticosteroids are often used initially. Anytime one applies corticosteroids to the skin, one should assure that it is rubbed in thoroughly and the patient should wait one hour before bathing to avoid removing the medication. Little or no risk relates to short-term use of corticosteroids on the skin. The risk of long-term use of corticosteroids includes thinning of the skin and adrenal corticoid hormone suppression.

Topical nitrogen mustard in ointment, aqueous solution or gel is a chemotherapy agent used to treat CTCL. Even though it is not officially FDA approved for treatment of CTCL, it has been used to treat CTCL for over four decades. Individuals in the early stages of the disease respond best to this form of therapy, but relapses are common once the application stops. Systemic side effects are rare.

Phototherapy involving the use of ultraviolet light is another therapy which may be utilized in the early stages of the disease. It is most effective when the skin lesions consist of non-raised or barely-raised lesions. Many dermatologists have phototherapy units in their office. The physician determines the specific wavelength and ultraviolet energy to be administered, decreasing or increasing the energy based upon the patient's specific response to the therapy. The patient generally will receive treatment three times per week with the exposure time and energy dose to be increased with each treatment until the physician has determined that the optimal response has been achieved. Once the expected response has been achieved, the exposure time is maintained and the frequency of treatment is decreased to once a week or every other week.

During the administration of the ultraviolet light, male genitalia should be shielded as well as other parts of the body at risk such as the hands and face to reduce the likelihood of developing other forms of skin cancer. The most common side effects of phototherapy are skin burning, pigmentation, and photo aging.

Photochemotherapy is a process whereby the patient receives a drug that is combined with the use of skin exposure to an ultraviolet light. Psoralen is a medication given by mouth to the patient prior to his/her exposure to ultraviolet light. This medication serves to enhance the effects of the phototherapy thus assisting in ridding the body of the cancer.

Nurses should also inform all patients who have been given Psoralen to use ultraviolet light protective glasses during the treatment and for the remainder of the day after the treatment in order to avoid ocular toxicity.

The initial photochemotherapy treatment occurs several times per week for one or two months and less frequently thereafter. Maintenance therapy is usually continued for a year or more. This intervention is most successful for individuals in the early stages of CTCL.

Nurses play an important role in the care of patients with CTCL by providing the patient with valuable information relating to specific care measures in regard to their disease process. These can be implemented to improve the patient's quality of life and provide emotional support to the patient and family.

One of the most significant side effects of photochemotherapy is severe itching of the skin. A nurse can teach a patient to implement certain interventions which will decrease the amount of itching thus improving their day to day life. The following interventions will serve as a way to decrease the amount of itching:

- Shower or bath in warm water

- Use mild soaps when bathing
- Oatmeal bath soaks
- Apply moisturizers to the skin immediately after bathing
- Oral antihistamines
- Use moisturizers on skin
- Keep environment moist through the use of a humidifier
- Apply a brewed solution of chickweed to the skin using cloth compresses.
- Application of evening primrose oil topically

Another form of therapy for CTCL is the use of electron beam therapy whereby radiation is delivered to the skin surface. This therapy is also known as total skin electron beam (TSEB). This therapy is safe as the electron beams up to 1 cm deep in the body.

The standard therapy is to deliver radiation in small fractions three times a week for approximately 10 weeks. Patients are required to stand on a slowly rotating platform while the radiation is delivered over a course of 10 to 15 minutes. This form of therapy is generally effective in the treatment of skin lymphoma. Other maintenance therapies may be required upon the completion of this therapy.

Toxicity may result in erythema, tenderness, swelling, loss of hair, shedding of nails and loss of the ability to sweat. Patients may not perspire as they did prior to the therapy. Nurses should educate patients to avoid strenuous activity in hot humid weather, drink plenty of fluids, and wear layers of clothing to keep warm if they feel chilled.

Fatigue is the most common complaint after electron beam therapy. The patient develops fatigue during treatment with radiation therapy because of the biological effect of the radiation, inadequate sleep and nutrition, pain and anxiety associated with the disease and treatments. Nurses should encourage patients to take naps, curtail work schedules, and improve nutrition by eating foods high in proteins and calories.

Chemotherapy is usually only administered when CTCL is advanced. It is given to control the symptoms and make a patient more comfortable. Effective chemotherapies include methotrexate, gemcitabine, and liposomal anthracyclines. Other agents such as etoposide, cyclophosphamide and pentostatin may also be used. The most common drug combinations include cyclophosphamide, doxorubicin, vincristine and prednisone. This drug combination is utilized only in patients with organ or visceral involvement.

Patients have a responsibility in assuring that their treatment of T-cell lymphoma is optimal by becoming educated regarding the disease and its treatment. The patient should ask the medical team questions, read literature, report any new symptoms and keep scheduled appointments. Regular check ups with the physician is important as this provides an opportunity for the patient and the physician to develop a more personal collaborative relationship, provide the physician with valuable information regarding the patient's present status and allow any concern of the patient to be addressed.

It is very important that if the patient notices even minute changes, he/she should discuss them with his/her physician regardless of how minute they may appear. For example, during the course of the illness, lymphoma symptoms may closely resemble flu or viral infections. If it is a flu or virus, it may not be significant. However, should the symptoms be related to a change in the lymphoma and the physician is not aware of these symptoms, the disease may progress or become aggressive and the necessary treatment delayed.

The diagnosis and treatment of CTCL is challenging for both the patient and the care team. This disease is extremely manageable if diagnosed early. The earlier the diagnosis is made the more

likely the patient can live many years productively. It is the responsibility of the medical team to be knowledgeable regarding the signs and symptoms, assuring appropriate diagnosis, and providing optimal care of the patient and family experiencing this disease.

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## Course Exam

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1. The primary role of the T-cells is to survey, protect and attack infectious agents, environmental stressors and malignancies.  
 True  False
2. The following are considered risk factors of lymphoma: age, infections with HIV, Epstein Barr, and exposure to toxic chemicals.  
 True  False
3. The extensive use of red hair dye has been noted to cause an increase in Non-Hodgkin Lymphoma.  
 True  False
4. T-cell cutaneous lymphoma is often confused and treated as psoriasis, eczema, secondary syphilis, or contact dermatitis.  
 True  False
5. There is absolutely no correlation between the spread of T-cell cutaneous lymphoma skin involvement and the probability of spread to internal organs.  
 True  False
6. T-cell cutaneous lymphoma is also called mycosis fungoides.

True    False

7. Research has demonstrated that in addition to T-cell overproduction, mycosis fungoides is also known to be fungal in origin.

True    False

8. 50 percent of all deaths from CTCL occur in Stage IVB due to infections from Staphylococcus aureus or Pseudomonas aeruginosa.

True    False

9. Any patient taking Psoralen during photochemotherapy should be instructed to wear ultraviolet light protective glasses during the treatment and for the remainder of the day after the treatment to avoid ocular toxicity.

True    False

10. The primary role of the lymphatic system is to carry red blood cells and lymphocytes around the body to locations where they are needed in response to bacteria, viruses or other foreign bodies.

True    False