OncoLog
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Overcoming Challenges in Cutaneous T Cell Lymphomas

By Joe Munch

Cutaneous T cell lymphomas (CTCLs) not only are largely incurable but also make patients miserable with itching, burning skin and unsightly lesions. Because CTCL can resemble various benign skin conditions, many patients are diagnosed at an advanced and difficult-to-treat stage. But ongoing clinical trials may offer patients with CTCL improved treatments and better quality of life.

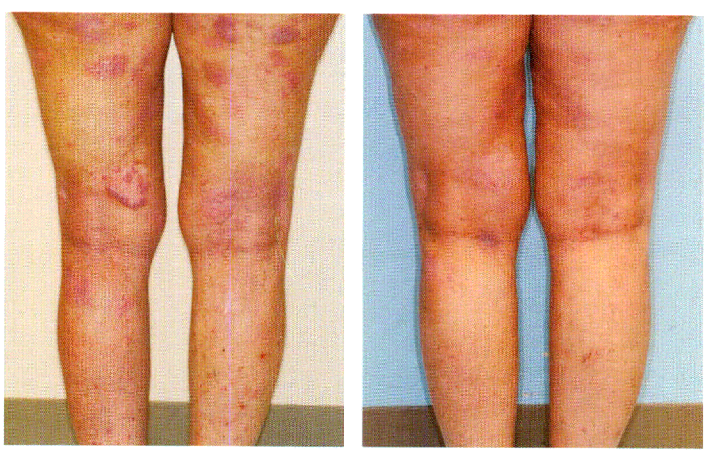
"Most cancer patients have disease on the inside, but CTCL is a disease that patients wear every day," said Madeleine Duvic, M.D., a professor in the Department of Dermatology at The University of Texas MD Anderson Cancer Center. "It's also a disease with many clinical facets, and its diagnosis and treatment require collaboration among dermatologists, medical oncologists, and radiation oncologists."

A difficult diagnosis

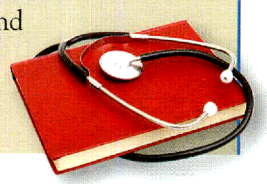
CTCL comprises a heterogeneous group of non-Hodgkin lymphomas categorized by clinical findings and T cell markers. The most common forms of CTCL are mycosis fungoides and its leukemic variant, Sézary syndrome; other forms include anaplastic large T cell lymphoma and subcutaneous panniculitis-like T cell lymphoma.

With early diagnosis and treatment, these diseases can be put into long-term remission and prevented from becoming incurable or uncontrollable. "Patients whose disease is caught and treated early can be in complete remission for years and never get worse," Dr. Duvic said. "Unfortunately, just diagnosing CTCL is difficult, and it requires expertise in immunopathology and understanding of T cell markers."

One of the main challenges in diagnosing CTCL is the cancer's resemblance to other skin diseases. In many cases, lesions that appear to be benign may in fact be malignant. Mycosis fungoides, which usually starts as patches and plaques on unexposed areas, is often initially misdiagnosed as psoriasis or eczema, and patients often undergo multiple biopsies before the disease is correctly identified. Sézary syndrome,



A patient with refractory mycosis fungoides is shown before (left) and after (right) 15 cycles over 52 weeks of combination therapy with the retinoid bexarotene given orally and the chemotherapeutic drug pralatrexate given intravenously.



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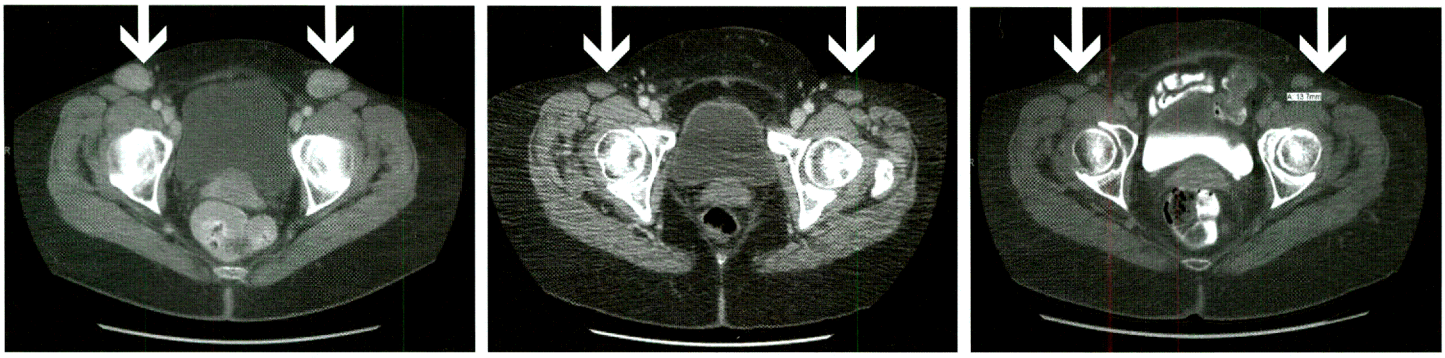

In the patient with refractory mycosis fungoides shown on page 1, reductions in involved lymph nodes (arrows) can be seen in computed tomography scans taken before (left), after 6 cycles (center), and after 15 cycles (right) of combination therapy with the oral retinoid bexarotene and the intravenous chemotherapeutic drug pralatrexate.

too, can be erythrodermic and often mistaken for psoriasis or eczema. This is problematic because many of the antipsoriatic agents used to treat psoriasis or eczema are very immunosuppressive and can exacerbate Sézary syndrome or promote opportunistic infections.

Therefore, Dr. Duvic said, CTCL should be suspected in patients whose lesions resemble psoriasis or eczema but do not respond to treatment or occur in sun-shielded regions of the skin. When CTCL is suspected, a biopsy of the involved sites—if 1 month has passed since treatment with topical steroids, which rid the skin of lymphocytes—should be performed to make the correct diagnosis. In addition, full skin examinations are essential to detecting mycosis fungoides when the disease is suspected, as it tends to develop on unexposed areas. Finally, flow cytometry of a blood sample can detect atypical T cells indicative of CTCL.

In other cases, lesions that appear to be malignant may in fact be benign. For example, the benign form of CD30-positive anaplastic large T cell lymphoma, lymphomatoid papulosis, appears as a solitary papule that usually resolves without intervention in 3–4 months. But the malignant form of the disease can be associated with Hodgkin disease, mycosis fungoides, or cutaneous anaplastic large T cell lymphoma. A solitary lesion resembling lymphomatoid papulosis typically is removed surgically for biopsy; however, the benign and malignant forms appear identical on biopsy. Therefore, the differential diagnosis is a clinical one, and aggressive cancer treatment is withheld unless further lesions appear to confirm malignancy.

Treatment

The correct diagnosis of CTCL is essential to effectively treating the disease, as treatments vary according to the type and extent of the disease. For patients with mycosis fungoides or Sézary syndrome, treatment depends on the disease stage and consists of skin-directed therapy, including radiation therapy, with or without systemic therapy.

Treatment by disease characteristics

For patients with early-stage mycosis fungoides involving 10% or less of the body, the primary treatment is topical steroids, which have response rates of around 70%, with or without phototherapy. For patients with more than 10% skin involvement, topical steroids may be combined with more intensive phototherapy in the form of narrow-band ultraviolet B radiation or with psoralen plus ultraviolet A radiation. Retinoids such as the vitamin A derivative bexarotene, which may be administered topically or orally, and/or topical chemotherapy with nitrogen mustard may also be used in these patients.

"Most cancer patients have disease on the inside, but CTCL is a disease that patients wear every day."

– Dr. Madeleine Duvic

Patients with refractory mycosis fungoides involving more than 10% of the skin may require additional systemic therapy. Such patients may receive oral retinoids such as bexarotene or acitretin with or without interferon-alpha or interferon-gamma. Histone deacetylase (HDAC) inhibitors, such as oral vorinostat or intravenous romidepsin, may also be used to help manage refractory mycosis fungoides or anaplastic large T cell lymphoma. Although only about 30% of CTCL patients have even a partial response to HDAC inhibitors, these agents do reduce itching, a major issue in these patients.

First-line systemic therapy for Sézary syndrome, a disease characterized by Sézary T lymphocytes in the blood, includes photopheresis plus interferon or bexarotene. In photopheresis, T lymphocytes collected from the patient's peripheral blood are exposed to a photosensitizing agent and then ultraviolet light to damage their DNA. Once reintroduced into the patient, the photochemically damaged abnormal cells are taken up by macrophages, which then trigger an immune response against the disease. Sézary syndrome patients may also receive sequential single-agent chemotherapy.

Combination chemotherapy, which is generally not used in patients with mycosis fungoides, may be used in those with Sézary syndrome or anaplastic large T cell lymphoma. "We usually don't use combination chemotherapy for any type of CTCL unless patients have visceral or bulky nodal disease or single-agent therapy has failed," Dr. Duvic said. "When CTCL patients get multiple chemotherapy agents, they get further and further along the pathway of immunosuppression, and they may die of opportunistic infections."

Stem cell transplant is also an option for patients with Sézary syndrome. "We've found that if Sézary syndrome is diagnosed early enough, before patients' immune systems are totally gone, you can treat them with electron-beam radiation to get rid of the lymphoma cells in the skin and then replace their bone marrow with allogeneic stem cells," said Dr. Duvic, who estimates that about 50% of Sézary syndrome patients who undergo the procedure are cured.

The role of radiation therapy

Radiation therapy, a mainstay of CTCL treatment, can be used alone or in conjunction with other skin-directed therapies and/or systemic treatments. Electron-beam radiation is typically used. Unlike photons, which release their maximum energy several centimeters deep in the body and thus may expose internal organs to the radiation dose, electrons release most of their energy near the surface to treat the skin while avoiding damage to internal organs.

Whether radiation is given locally or bodywide in the form of total skin electron-beam therapy (TSEBT) depends on the extent of the disease. If the disease involves less than 40% of the skin, local radiation therapy typically is used; if 40% or more of the skin is involved, TSEBT may be used. Thus, TSEBT is often used for palliative therapy in Sézary syndrome patients whose disease extent precludes local radiation therapy.

"In general, patients with Sézary syndrome have very extensive disease, and a higher dose of TSEBT—usually 32 Gy—has to be used to give them relief," said Bouthaina Dabaja, M.D., an associate professor in the Department of Radiation Oncology.

Likewise, a sizeable dose of radiation, 24–32 Gy in the form of TSEBT, is given to CTCL patients who will undergo stem cell transplantation. "When a patient is undergoing stem cell transplantation, we give radiation to reduce the burden of skin disease to as little as possible prior to the transplant," Dr. Dabaja said. "This makes the donor stem cells' job easier. Their major role is not necessarily to kill actual cancer cells as much as it is to prevent new cancer cells from forming."

Although highly effective against CTCL, radiation therapy must be used judiciously because of its adverse effects. "Your skin never forgets the radiation that you get," Dr. Dabaja said. "The more radiation a person receives, the more side effects he or she will experience. Eventually, the fat under the skin is depleted, and the skin becomes leathery and cannot heal after wounds, infections, or additional tumors."

Therefore, Dr. Dabaja and others are working to increase the effectiveness of radiation therapy while reducing its side effects in CTCL patients. In a recent International Lymphoma Radiation Oncology Group study, the researchers showed that a high proportion of CD30-positive anaplastic large T cell lymphoma patients achieved complete remission regardless of the radiation dose. As a result of this and other studies, radiation doses for treating many types of CTCL have dropped dramatically. For example, at MD Anderson, 12 Gy is now the most common dose given to patients with mycosis fungoides, whereas patients with the disease once received 32–36 Gy. Similarly, Dr. Dabaja said, doses as low as 6 Gy can achieve complete remission in patients with cutaneous CD30-positive

CLINICAL TRIALS: Cutaneous T Cell Lymphoma

A randomized phase II study to evaluate three treatment regimens of SHAPE, a histone deacetylase inhibitor, in patients with stage IA, IB, or IIA cutaneous T cell lymphoma (2014-0678). Principal investigator (PI): Dr. Madeleine Duvic. The goal of this study is to learn if suberohydroxamic acid phenyl ester (SHAPE) gel can help to control skin lesions of patients with early-stage CTCL when used once or twice daily. The safety of the drug will also be studied.

Phase II trial of brentuximab vedotin (SGN-35) at a dose of 1.8 mg/kg IV every 3 weeks in patients with CD30-positive lymphoproliferative disorders (cutaneous anaplastic large T cell lymphoma [ALCL], mycosis fungoides, and extensive lymphomatoid papulosis [LyP]) (2010-0914). PI: Dr. Duvic. The goal of this study is to learn if brentuximab vedotin can help to control ALCL, LyP, or mycosis fungoides. The safety of the drug will also be studied.

A clinical study to demonstrate the safety and efficacy of E7777 (denileukin diftitox) in persistent or recurrent cutaneous T cell lymphoma (2012-1056). PI: Dr. Duvic. The goal of the first part of the study was to find the highest tolerable dose of an investigational form of E7777 that can be given to patients with mycosis fungoides or Sézary syndrome. Now that this lead-in portion of the study is complete, the goal of the second part of this study is to learn if E7777 can control mycosis fungoides or Sézary syndrome. The safety of the drug will also be studied. ■

FOR MORE INFORMATION

Visit www.clinicaltrials.org.

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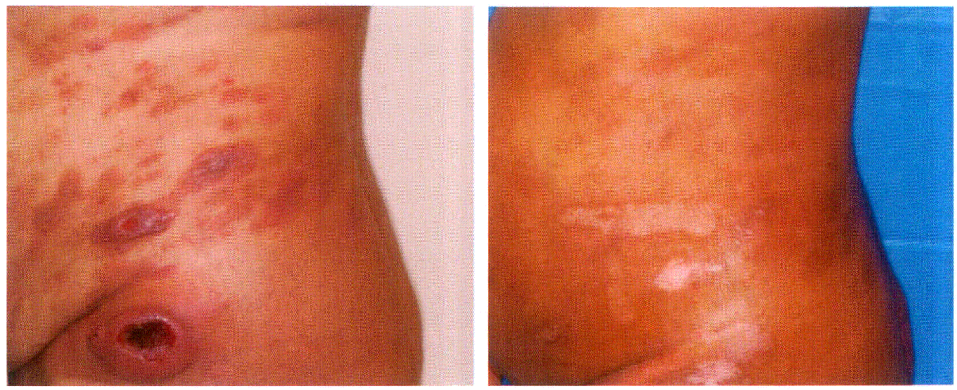
anaplastic large T cell lymphoma, a disease once commonly treated with 45 Gy.

The main takeaway from the recent studies, Dr. Dabaja said, is to always use the smallest radiation dose possible in CTCL patients. "If their disease responds to that dose, they're done. Their disease is extremely sensitive to radiation; giving them a higher dose would only result in more toxicity with no benefit," she said. "If their disease doesn't respond to the lower dose, we can always give more."

However, Dr. Dabaja also cautioned against giving additional radiation in the absence of an immediate response. "We can't panic if we don't see an immediate response," she said. "And we can't be afraid to ease the patient into the therapy by giving a lower dose at 4 Gy or 8 Gy and then watching and waiting. In 4–6 weeks, those lesions are likely going to heal."



A patient with folliculotropic mycosis fungoides that had transformed to large T cell lymphoma is shown before (left) and after (right) total skin electron-beam therapy.

Ongoing research

Just as research has led to changes in radiation therapy, several new systemic agents for the treatment of CTCL are already in or moving toward clinical trials, Dr. Duvic said.

Among these new agents, targeted antibodies represent one of the most exciting areas of development. For example, the humanized monoclonal antibody mogamulizumab, which targets the chemokine receptor CCR4 (a molecule that recruits T cells to the skin), has shown great promise for the treatment of Sézary syndrome. In a phase I/II trial, the agent elicited a response rate of 47% in Sézary syndrome patients, with some having a response that lasted years.

Brentuximab vedotin, a chimeric monoclonal antibody–drug conjugate that targets CD30, has also shown promise against CTCL. Dr. Duvic and her colleagues are investigating the agent, which is already approved for relapsed Hodgkin disease and relapsed anaplastic large T cell lymphoma, in patients with mycosis fungoides, lymphomatoid papulosis, and cutaneous anaplastic large T cell lymphoma.

Among patients with high levels of CD30 on their T cells, Dr. Duvic said, the response rates have been in the range of 75%–80%. She and her colleagues recently published their experience with the agent in 48 patients with CD30-positive lymphoproliferative disorders or mycosis fungoides in the *Journal of Clinical Oncology*.

"We're seeing some amazing responses with brentuximab vedotin—it melts away tumors, which is pretty impressive," Dr. Duvic said. "And we're finding that mogamulizumab gets rid of Sézary cells in the blood in just one or two doses. So we are definitely making progress with these types of agents."

Another agent, E7777, has also shown promise against CTCL. A reformulation of denileukin diftitox (DAB389IL2) with improved purity, E7777 consists of a diphtheria toxin and an interleukin-2 receptor and targets interleukin-2–expressing cells. In its initial formulation, the agent elicited an overall response rate of 30% and complete response rate of 10% in CTCL patients. More recently, Dr. Duvic and her colleagues conducted a phase I dose-finding study that showed that E7777 had activity against persistent or recurrent CTCL at different dose levels and an acceptable toxicity profile. Dr. Duvic said that clinical trials of E7777 are on hold but are expected to resume once a lyophilized formulation of the agent becomes available.

"I think E7777 is one of the best drugs for patients with advanced disease characterized by tumors. It works very quickly for tumors—you can start to see them shrinking in a couple of days. And it's much better tolerated than cytotoxic chemotherapy," Dr. Duvic said.

New topical therapies are also gaining a foothold in the treatment of CTCL. The HDAC inhibitor vorinostat is now being tested as a cream. The oral formulation of vorinostat has multiple side effects, but these are greatly reduced with topical vorinostat. Another topical drug, resiquimod, is a dual toll-like receptor 7/8 agonist that has been found to induce a local immune response that may become systemic: in a phase I dosing study of the drug, researchers found that applying the agent to one lesion can clear lesions at other places on the skin. A larger trial of topical resiquimod is in the planning stages.

Other agents that are entering or already in clinical trials for CTCL patients include phosphoinositide 3–ki-

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"[CTCL] is extremely sensitive to radiation; giving [patients] a higher dose would only result in more toxicity with no benefit."

– Dr. Bouthaina Dabaja

Swallowing Therapy Improves Function and Quality of Life for Patients with Head and Neck Cancer

By Bryan Tutt

In patients with head and neck cancer, loss of swallowing function may result from radiation therapy, surgery, or the cancer itself and lead to poor health and reduced quality of life. At The University of Texas MD Anderson Cancer Center, individualized swallowing therapy programs directed by speech pathologists are helping patients maintain or recover their swallowing function during and after treatment.

Recent studies support the use of thorough evaluation of swallowing function and tailored exercise regimens to maintain or recover swallowing function in patients with dysphagia related to head and neck cancer treatments. Some of these studies assessed the effects of radiation therapy. "A common misconception about radiation-associated dysphagia is that it is primarily an issue of stricture of the esophagus," said Kate Hutcheson, Ph.D., an associate professor in the Department of Head and Neck Surgery and the associate director of research for the Section of Speech Pathology and Audiology. "But meta-analyses with thousands of patients have shown that stricture occurs in less than 10% of patients treated with radiation therapy for head and neck cancer. So esophageal dilation is not always the answer, and nine patients out of 10 need a more complete workup to establish the source of their swallowing difficulty."

Another study of swallowing function in head and neck cancer patients raised questions about the widespread application of electrical stimulation therapy. In fact, recently published results from a multisite randomized clinical trial showed no benefit from adding neuromuscular electrical stimulation therapy to swallowing exercises in head and neck cancer patients with post-treatment dysphagia.

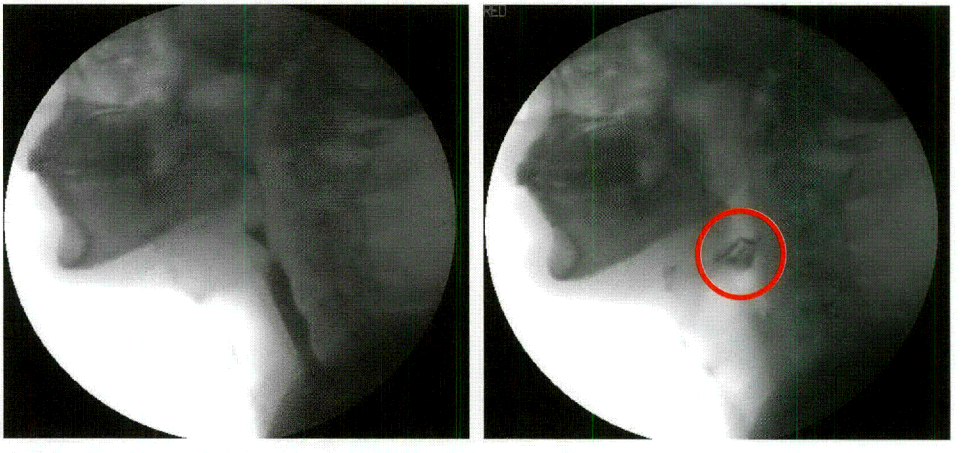
At MD Anderson, individualized swallowing therapy programs are rapidly evolving to improve swallowing function and quality of life for patients with head and neck cancer. These programs typically begin soon after treatment for patients whose tumors are treated with surgery or before treatment, as a preventive measure, for patients who undergo radiation therapy.

Preventive therapy

"A large body of evidence suggests that preventive swallowing therapy is the best practice for patients who are going to receive radiation therapy to the head and neck," Dr. Hutcheson said. "After their multidisciplinary workup here at MD Anderson, patients who are scheduled to receive radiation therapy to the head or neck are enrolled in a proactive, preventive swallowing therapy program even if they have no problem swallowing at the time they are diagnosed."

The preventive swallowing therapy program begins with a pretreatment evaluation that typically includes videofluoroscopy (also called a modified barium swallow study). "Videofluoroscopy gives us the physical and functional parameters of the swallow: how safely and efficiently the patient can move food and liquid through the mouth and throat," Dr. Hutcheson said. "Baseline evaluations uncover subclinical swallowing difficulties fairly often. Knowing this helps us provide patients with specific instructions on how and what they should eat during radiation therapy to avoid swallowing things that will be aspirated—drawn into the lungs—and cause pneumonia."

Patients in the preventive swallowing therapy program also attend an exercise training session before the beginning of radiation therapy. The



Still images from videofluoroscopy performed during the baseline assessment of a patient with newly diagnosed locally advanced cancer at the base of the tongue show adequate airway protection with complete laryngeal closure at peak swallow (left) but tumor-associated swallow inefficiency with post-swallow pharyngeal residue (right, circle).

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training sessions are conducted by speech pathologists, many of whom have specialty certifications in swallowing disorders from the American Speech-Language-Hearing Association.

Each patient is given a specific set of exercises for the pharynx and larynx to maintain activity of the muscles that receive a bystander dose of radiation. The daily regimen includes six to eight exercises and takes less than 15 minutes to perform. Dr. Hutcheson said that proactive swallowing therapy is especially important for patients who will undergo radiation therapy to both sides of the neck, as this group has a high risk of radiation-associated dysphagia.

The exercise regimen is one of two tasks given to patients during radiation therapy; the other task is eating regularly. "The vast majority of patients stop eating solid food during the course of head and neck radiation therapy because it tastes bad or hurts to swallow. But we encourage patients to push through and keep eating to maintain as much normal muscle function as possible," Dr. Hutcheson said.

During radiation therapy to the head and neck, 50%–60% of patients require feeding tubes; the resulting disuse of the musculature can contribute to further deterioration of swallowing function. However, feeding tubes can be avoided in many patients through individualized supportive care.

"We know that patients who keep their swallowing system engaged during the course of their radiation therapy have a better chance of recovering meaningful swallowing ability after their therapy," Dr. Hutcheson said. "We have a philosophy of 'use it or lose it.'"

Patients in the preventive swallowing therapy program return for sessions with their speech pathologist at the midpoint and at the completion of their radiation therapy, with additional therapy sessions if necessary. Patients are advised to continue their home exercise regimen for at least 6 months after the completion of radiation therapy. "We do not have great evidence to show how long or how often the exercises should continue after treatment," Dr. Hutcheson said. "But I tell patients that if it were me, based on what I've seen, I would keep up lifelong maintenance therapy of probably one or two sessions per week."

> **"[W]e've had success in treating patients with very severe or long-standing dysphagia."**
>
> **– Dr. Kate Hutcheson**

Intensive therapy for persistent dysphagia

After surgery or radiation therapy for head and neck cancer, most patients who practice a home exercise regimen recover a reasonable level of swallowing ability. However, 15%–20% develop persistent swallowing difficulties. Persistent dysphagia is a challenging clinical problem that is typically not responsive to a home exercise regimen.

For patients with persistent dysphagia—whether their cancer treatment was done at MD Anderson or elsewhere—Dr. Hutcheson and her colleagues developed a program they call boot camp swallowing therapy. This is an intensive program in which the patient works with a speech pathologist daily for about 3 weeks.

During the daily sessions, speech pathologists use progressive resistance training coupled with functional swallowing tasks to help patients increase the intensity of their swallowing training. Patients' progress can be monitored by various methods of biofeedback, including surface electromyography and manometry. Bolus-driven exercises help patients remove "crutches," such as flushing food down with water, from their eating habits while eating increasingly difficult foods.

Dr. Hutcheson said that because many different swallowing therapies are available, it can be challenging for speech pathologists to find the best ones for a particular patient. "We have an algorithm to work through the therapeutic options and then select the therapies we think will target the individual patient's issue," she said.

The boot camp swallowing therapy program has shown impressive results: about 70% of patients see gains in their functional status. "This intensive program is unique to MD Anderson," Dr. Hutcheson said. "And we've had success in treating patients with very severe or long-standing dysphagia."

Improving quality of life

Not satisfied with the success rate of the current swallowing therapy programs, researchers at MD Anderson continue to address swallowing issues for which treatments are lacking. "We still need therapies that will address chronic aspiration," Dr. Hutcheson said. "There is no proven treatment to reverse chronic aspiration in head and neck cancer survivors." She added that the Section of Speech Pathology and Audiology has a grant-funded program to study expiratory muscle strength training in head and neck cancer patients. Such training has shown promise in reducing aspiration in patients with neurodegenerative dysphagia such as that seen in patients with Parkinson disease, and Dr. Hutcheson is hopeful that it will help her patients as well.

"Swallowing is a huge quality of life issue. The key to improving swallowing function is early and individualized therapy," Dr. Hutcheson said. "A dysphagia-specialized speech pathologist—whether seen at MD Anderson or elsewhere—can help maximize a patient's outcome." ■

FOR MORE INFORMATION

Dr. Kate Hutcheson.....713-792-6513

To learn more about swallowing therapy, visit MD Anderson's Head and Neck Survivorship Clinic at http://bit.ly/1MRmpnY or the American Speech-Language-Hearing Association's Board on Swallowing and Swallowing Disorders at www.swallowingdisorders.org.

Common Cancer Terms

Clearly understanding medical terms helps patients, caregivers

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Many cancer terms are used casually in the media or by doctors and nurses, but patients don't always know exactly what the words mean. And some words have different meanings when used to describe cancer than they do in everyday use. You've probably heard most of the cancer-related terms below, but the precise meanings of some may surprise you.

Abnormal growths

Benign means not cancerous. Benign tumors have abnormal cells that cause the tumors to grow locally without spreading to other parts of the body. However, benign tumors are not always harmless; some can grow quickly and damage nearby tissue.

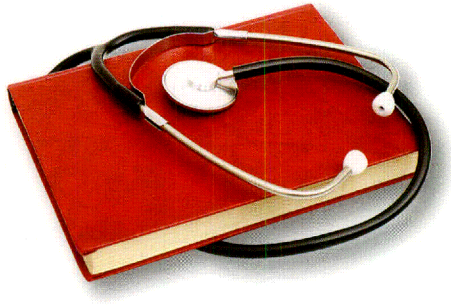
Malignant means cancerous. Malignant cells (cancer cells) are abnormal cells that can invade nearby tissue and spread throughout the body.

Neoplasm is another word for tumor. It refers to any new, abnormal tissue with uncontrolled growth. Neoplasms can be benign or malignant.

Major types of cancer

Carcinoma is any cancer that begins in the epithelial cells, which make up the outer layer of skin and the lining of organs and blood vessels. Carcinomas are the most common types of cancer, accounting for most breast, lung, kidney, thyroid, colon, prostate, stomach, and skin cancers. The risk of carcinoma increases with age, so these cancers mostly affect people 50 years and older.

Sarcoma is any cancer of the bone, cartilage, fat, muscle, blood vessels, or other connective or supportive tissue. The two main types are soft tissue sarcomas and bone sarcomas. According to the Sarcoma Foundation of America, sarcomas represent only 1% of cancers in adults but 15% of cancers in children. Sarcomas can originate anywhere in the body, and they often grow deep within the tissues of the arms, legs, or torso.



Melanoma is a cancer that develops in melanocytes, which are pigment-producing cells in the skin and other organs. Although melanoma can occur in the eyes or mouth, most melanomas develop on the skin as a result of overexposure to sunlight. Melanoma is the most common type of cancer in people 25–29 years old.

Lymphoma is a group of blood cancers that begin in the lymphatic system, which is the network of vessels, organs, and tissues that filter the blood and produce many of the white blood cells (lymphocytes) that fight infection. Lymphomas may be described as B cell or T cell lymphomas, according to the type of blood cell that is affected; or as Hodgkin or non-Hodgkin lymphomas, according to the genetic mutation found in the lymphoma cells. Lymphomas can occur at any age and account for about 8% of childhood cancers.

Leukemia is a group of cancers that begin in the bone marrow tissues that produce blood; these cancers cause the production of abnormal blood cells that crowd out healthy blood cells. Leukemias are classified as acute or chronic and lymphoblastic or myelogenous. In acute leukemias, a large number of immature blood cells (blasts) are produced quickly; these leukemias progress rapidly. In chronic leukemias, most of the abnormal cells are more mature and are not produced as quickly. Lymphoblastic (also called lymphocytic) leukemias affect white blood cells (usually B cells), whereas myelogenous (also called myeloid) leukemias mainly affect red blood cells. Leukemias can occur at any age and account for about 30% of childhood cancers. In fact, acute lymphoblastic leukemia is the most common type of cancer in children.

Myeloma (also called multiple myeloma) is a rare cancer of the plasma cells in the bone marrow that impairs the plasma cells' ability to produce antibodies, which fight infection. Myeloma weakens the immune system, can damage the bone structure itself, and can interfere with the production of normal blood cells. Myeloma usually affects people 60 years or older.

Terms related to cancer stage

Stage refers to the extent of a patient's cancer. Different staging systems are used for different cancer types, but generally cancer stage depends on the tumor's size and whether the cancer has spread to nearby lymph nodes or to distant parts of the body. A small cancer caught before it has spread is often classified as stage I; a cancer that has spread from its initial site to other parts of the body is usually stage IV.

In situ describes early-stage cancer that has not spread to adjacent tissues.

Invasive refers to cancer that has spread from its original location to adjacent tissues.

Metastasis is the spread of cancer cells from the original tumor to other parts of the body, where the cancer cells form new tumors (metastases).

Knowing these and other cancer-related terms can give cancer patients—and their family members and friends—a better understanding of the disease. Definitions of other words related to cancer and its treatment are provided by the National Cancer Institute at www.cancer.gov/publications/dictionaries/cancer-terms. ■

– *C. Graber*

FOR MORE INFORMATION

- *Ask your doctor*
- *Call* askMD Anderson *at 877-632-6789*
- *Visit www.mdanderson.org*

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Cutaneous T Cell Lymphomas

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"Unfortunately, just diagnosing CTCL is difficult, and it requires expertise in immunopathology and understanding of T cell markers."

– Dr. Madeleine Duvic

nase inhibitors, microRNA (e.g., miR155) inhibitors, and ONC201, a compound that induces the tumor necrosis factor–related apoptosis-inducing ligand pathway. ONC201, which has been shown to have activity against several cancers, is given as a pill weekly or once every 3 weeks.

Moving forward

A major hurdle in developing new treatments for CTCL is an incomplete understanding of the genetic features that lead to the various types of the disease. In an effort to overcome this hurdle, Dr. Duvic and her colleagues conducted a multiplatform genomic analysis (genomic exon sequencing in parallel with RNA sequencing and single nucleotide polymorphism analysis) of 37 Sézary syndrome patients to identify new therapeutic targets in the disease. The study, which was reported in *Nature Genetics* in December 2015, yielded valuable insight into the genomic basis of Sézary syndrome.

"We found many driver mutations for Sézary syndrome. Most of them are in the T cell signaling pathway, which is what you might expect," Dr. Duvic said. "In particular, we found that *IL32*, which had been known to be expressed in mycosis fungoides cells, was highly expressed in peripheral blood samples from patients with Sézary syndrome and was associated with a poor prognosis."

The study has opened new avenues toward effective therapy for CTCL. Dr. Duvic said, "The ability to match the correct therapy to the correct patient is where we'd like to be with this disease." ■

FOR MORE INFORMATION

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FURTHER READING

Duvic M, Tetzlaff MT, Gangar P, et al. Results of a phase II trial of brentuximab vedotin for CD30+ cutaneous T cell lymphoma and lymphomatoid papulosis. *J Clin Oncol.* 2015;33:3759–3765.

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