Pediatric and Adult Cancer Patients Face Different Issues in Care, Survivorship

By Don Norwood

The challenges faced by children and adults with cancer can differ markedly, even when they have the same type of cancer.

Adults and children often are affected by different types of cancer, which is expected considering that some cancers in adults are linked with long-term exposure to carcinogens. However, in cancers common to both adults and children—which include hematological malignancies, sarcomas, and brain tumors—adults' and children's tolerance of and response to treatment, likelihood of remission, and survival rates and durations can be very different.



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Making Cancer History*

Pediatric and Adult Cancer Patients Face Different Issues

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Same cancer, different disease

"Pediatric malignancies generally are more responsive to chemotherapy than are malignancies in adults because of differences in the biology of the cancer," said Anna Franklin, M.D., an assistant professor in the Division of Pediatrics at The University of Texas MD Anderson Cancer Center. "In addition, children generally tolerate chemotherapy better than adults because children are less likely to have other health issues like heart disease, kidney disease, lung disease, or diabetes."

A vivid example of this difference in treatment response occurs in patients with pre-B-cell acute lymphoblastic leukemia. "Treatment of this disease in children has become quite successful because oncologists have developed intensive, repeated chemotherapy regimens that these patients can tolerate," said Dean Lee, M.D., Ph.D., also an assistant professor in the Division of Pediatrics at MD Anderson. These same regimens have proven to be too toxic for adults, however. According to Dr. Franklin, the 5-year survival rate for children with this cancer is as high as 90%, whereas the 5-year survival rate for adults with the disease is only about 40%.

Some treatment advances, such as those in bone marrow transplantation, benefit both children and adults. Dr. Lee's current research includes the development of adoptive immune therapy within the context of stem cell transplantation. Hematological malignancies are common in children, and the advances made possible by clinical research in bone marrow and stem cell transplantation for adults have also greatly improved the quality of life of children who receive these transplants.

Successful cancer treatment brings challenges of its own. The high longterm survival rate of pediatric cancer patients and their longer life expectancy mean that their treatments—especially chemotherapy and radiation therapy—can cause problems later in life, sometimes decades after therapy has ceased. These problems—which include second cancers, kidney disease, cogni-

"Pediatric malignancies

generally are more responsive to chemotherapy than are malignancies in adults because of differences in the biology of the cancer."

- Dr. Anna Franklin

tive disorders, sterility, and heart and lung dysfunction—may be exacerbated in children because their bodies are still developing.

The development of the brain, in particular, seems to be affected by cancer treatment. Dr. Lee said, "The 'chemo brain' that adults describe when they're getting chemotherapy, which makes them really forgetful and causes problems, isn't always temporary in children." He said people treated with chemotherapy as children have more problems finding jobs and are less likely to get married compared with the general population.

Parent power

"Parents are worried about what will happen to their child 5 or 10 years after cancer treatment," Dr. Lee said. "That's completely reasonable because, to help focus their energy on the positive, parents may assume their child will be a survivor and focus on the child's life after treatment." But occasionally those concerns lead to conflict between parents and physicians about whether to stop therapy prematurely. Unless a patient completes the entire course of treatment as it was done in a clinical trial, physicians cannot accurately predict the chances of the treatment's success.

Dr. Lee said these uncertainties can make it difficult for physicians to guide parents who are worried about treatment-related toxicities. "If there weren't risks of long-term complications from treatment, these decisions would be much easier," he said. Dr. Lee added that conflicts about treatment between parents and physicians, although potentially serious, are rare because parents and physicians share the goal of successfully treating the child's cancer.

Dr. Franklin said the support that pediatric patients receive from their parents is crucial and often can make a major difference in the success of cancer treatment. "Parents of pediatric patients will bring them in when they are not feeling well and ensure they take their medicines as prescribed," she said. Adult patients, on the other hand, sometimes lack dedicated, full-time caregivers who ensure they make it to appointments, and adult patients may skip doses of medicines that have harsh side effects.

"Adherence to prescribed medical therapy plays an ever-increasing role in cancer treatment," said Dr. Franklin. "When chemotherapy is given intravenously at the hospital, we know they received the medicine. But many targeted therapies used today are pills taken at home, so the responsibility to take the pills lies with the patient. Discussing what the medicine is for, how it should be taken, and its potential side effects can help increase adherence for both adult and pediatric patients."

Parents help pediatric patients deal with factors like navigating traffic and paying expensive parking fees for office visits, which seem minor to those who do not have to deal with them but can be barriers to treatment. "The drive of parents to do everything they can to save their child is highly motivating, more so probably than the drive for self-preservation," Dr. Lee said.

Clinical trials

To address the differences in cancer treatment between young adults and children, pediatric and adult oncologists are collaborating more in taking

a fresh look at treatment regimens. For example, Dr. Lee said that in the past, a 17-year-old patient with Hodgkin lymphoma would see a pediatric oncologist, whereas an 18-year-old patient with the disease would see an oncologist for adults, often resulting in different courses of treatment. Now, he said, the treatments two such patients receive are more likely to be similar.

It is also becoming more common for pediatric and adult patients to be included in the same clinical trials, as is currently being done in treatment trials for Ewing sarcoma.

"Ewing sarcoma in a 15-year-old is probably the same disease one sees in a 25-year-old," said Dr. Lee. "There's a lot more emphasis on pooling those patients in whatever clinical trials we do, whether the trial is sponsored by an adult treatment group or a pediatric group. The adult treatment groups are getting a lot better at lowering the age limits on their trials, and the pediatric groups are getting better at increasing the limits on their trials. So there are more patients enrolled and more common treatments pushed forward."

The need for adequate sample sizes in studies of childhood cancers has also led to multi-institutional collaboration. "In pediatrics, cancer is much less common than in adults, so we had to learn early on to pool together across multiple centers to get enough patients to actually move the field forward," Dr. Lee said.

Clinical studies of treatments for some cancers in adults have the opposite problem; for adult patients with commonly occurring cancers that have well-established treatment regimens, physicians may be hesitant to recommend participation in a trial. Individual

Common Childhood and **Adult Cancers**

In the United States, the most common cancers in children are:

- leukemia,
- brain and other central nervous system tumors,
- neuroblastoma.
- Wilms tumor,
- lymphoma,
- rhabdomyosarcoma,
- retinoblastoma, and
- bone cancer (osteosarcoma and Ewing sarcoma).

The most common cancer sites in adults are:

- skin.
- prostate,
- breast,
- lung and bronchus, and
- colon and rectum.

Source: American Cancer Society. http://www.cancer.org.

oncologists or institutions may see enough patients with a particular type of cancer to develop their own standards of what constitutes good therapy, making the need for clinical trials seem less apparent.

Survivorship

Regardless of whether they participate in a clinical trial, pediatric patients make trip after trip to hospitals for treatment and follow-up, which

essentially robs them of significant parts of their childhood. It is therefore not surprising that adult survivors of childhood cancers rarely want to relive their difficult past, and this reluctance can complicate the unique set of survivorship issues they face.

"I think sometimes kids who've spent years in the hospital, where the focus of their life was their cancer, don't want to be constantly reminded of their cancer once they have been cured," Dr. Lee said. "They just want to move on. It's at least one reason that we don't have very good long-term follow-up in survivorship clinics for former pediatric

Another problem facing survivors of pediatric cancers is health insurance coverage. A child's cancer treatment is almost always covered by his or her parents' insurance or by Medicaid. Until recently, many such patients lost their coverage in their late teens or early 20s and did not qualify for new plans because their cancers were considered to be preexisting conditions. Dr. Franklin said this has begun to change as provisions of the Affordable Care Act are taking effect.

Oncologists are well aware of the differences between adult and pediatric cancer patients and are making great strides toward narrowing these differences. One way that MD Anderson has done this is by establishing survivorship clinics (see OncoLog, January 2012). Dr. Franklin said that although cancer survivorship programs for children are quite common in the United States, survivorship programs for adult cancer patients are not. MD Anderson has made such an adult program a goal, creating survivorship clinics to help patients of all ages adjust to life after cancer treatment.

While differences remain in the treatment success rates for children and adults with cancer, clinical research and a focus on survivorship continue to benefit both groups of patients.

"The 'chemo brain' that

adults describe when they're getting chemotherapy, which makes them really forgetful and causes problems, isn't always temporary in children."

- Dr. Dean Lee

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Palliative Care May Offer Survival Benefits

By Bryan Tutt

Recent studies indicate that palliative care, which has been shown to improve quality of life in patients with advanced cancer, may also help patients live longer.

Patients with cancer or any lifethreatening disease face a broad array of physical, spiritual, emotional, and financial problems. "Palliative care has a body of knowledge that can help patients, families, and even the primary care physicians treating those patients cope with problems related to debilitating chronic disease," said Eduardo Bruera, M.D., a professor in and chair of the Department of Palliative Care and Rehabilitation Medicine at The University of Texas MD Anderson Cancer Center.

Benefits of palliative care

For cancer patients, the most noticeable benefit of palliative care (also called supportive care) is the relief of physical symptoms such as pain, fatigue, lack of appetite, nausea and vomiting, or shortness of breath. "We have demonstrated consistently that when people are seen by the supportive care team in addition to their oncologist, they feel better," Dr. Bruera said.

But palliative care is not limited to pain management; it includes counseling and other services that can ease the emotional and spiritual distress of patients and their families.

Palliative care may also offer a financial benefit to patients and their families. Dr. Bruera said that patients who receive palliative care concurrently with cancer treatment and continue to do so after treatment options have been exhausted are less likely than those not receiving palliative care to be given a costly and unnecessary escalation of care in emergency rooms or intensive care units at the end of life.

These benefits, plus a survival benefit, were documented in a 2010 study

reported in the New England Journal of Medicine. In the study, patients with metastatic non-small cell lung cancer who received palliative care had better quality of life, were less likely to receive aggressive care at the end of life, and had a longer median survival duration than those who did not receive palliative care.

Similar studies to determine whether palliative care will lengthen survival for patients with other types of cancer are under way at MD Anderson and other centers, and Dr. Bruera said preliminary data from these studies are promising. He hypothesized that the survival benefits from palliative care likely result from a combination of factors. "If patients feel better emotionally and physically, they are able to continue their

cancer treatment," Dr. Bruera said. "Another point that has been shown very clearly for other diseases is that untreated physical and emotional distress can shorten lives. If a patient has untreated pain, fatigue, depression, and nausea, there is a chance that he or she will die of complications from that continued stress."

For these reasons, Dr. Bruera encourages oncologists to refer patients to a palliative care center at the first sign of physical or emotional distress.

Outpatient care

A referral for palliative care can take place at any point in the disease or treatment process because palliative care can be given in conjunction with chemotherapy or radiation therapy. To ensure that all patients have access to palliative care services, MD Anderson has both inpatient and outpatient palliative care centers.

Outpatient palliative care is important because many cancer patients even those with incurable diseasecontinue living at home and working while undergoing treatment.



Drs. Eduardo Bruera (left) and David Hui of the Department of Palliative Care and Rehabilitation Medicine at MD Anderson discuss a case.

"Ours is a

program in which patients' overall physical and emotional care is integrated with their cancer treatment."

- Dr. Eduardo Bruera

"Our model is based on collaborating closely with the primary oncologist early in the treatment of the disease," Dr. Bruera said. "In fact, more than 80% of the patients seen at our palliative care center are receiving active cancer treatment. Ours is a program in which patients' overall physical and emotional care is integrated with their cancer treatment."

What's in a name?

Dr. Bruera, who served on the committee that drafted the World Health Organization's definition of palliative care in 1986, said that although palliative care has always been intended for any patient with a serious chronic or life-threatening illness, the misconception that palliative care is primarily a transition to end-of-life care persists.

In 2007, MD Anderson conducted a survey of its oncologists and mid-level providers and found that the name 'palliative care" was a deterrent to their referring patients who had early stages of cancer or who were undergoing active treatment. To more accurately reflect its services, the Palliative Care and Rehabilitation Medicine Center changed its name to the Supportive Care Center.

Since the name change, the number of referrals has increased by about 40%, and patients arrive about a month and a half earlier in their treatment process than they did before. "We believe these improvements are because clinicians

What Is Palliative Care?

The field of palliative care has its roots in the hospice movement that began in the United Kingdom in the 1960s. Over the next two decades, palliative care grew into a multidisciplinary field. The following definition was adopted by the World Health Organization in 1986:

"Palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial, and spiritual. Palliative care:

- provides relief from pain and other distressing symptoms;
- affirms life and regards dying as a normal process;
- intends neither to hasten or postpone death;
- integrates the psychological and spiritual aspects of patient care;
- offers a support system to help patients live as actively as possible until death:
- · offers a support system to help the family cope during the patient's illness and in their own bereavement;
- · uses a team approach to address the needs of patients and their families, including bereavement counselling, if indicated;
- will enhance quality of life and may also positively influence the course of illness:
- is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications."

Source: World Health Organization. http://www.who.int/cancer/palliative/definition/en/.

feel more comfortable referring their patients to a place called supportive care, which is not closely associated with the end of life," Dr. Bruera said.

Patient-centered care

Patients being treated at MD Anderson can be referred to the Supportive Care Center by their oncologist. During a patient's first visit to the outpatient clinic at the Supportive Care Center, the patient, usually accompanied by family members, goes directly to a comfortable hotel-style

room; there is no waiting room. Together, the patient, the patient's family, a nurse, and a palliative care physician identify any physical, emotional, spiritual, social, and financial problems and establish a personalized care plan that addresses these issues.

"No one comes to the center with just one problem," Dr. Bruera said. "Patients usually come with seven or eight problems, and during the initial visit we establish a plan to deal with every one of them. Our care is multi-

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Targeted Therapy Causes Chronic Lymphocytic Leukemia Remission

A new, targeted therapy has produced durable remissions in patients with relapsed or treatment-resistant chronic lymphocytic leukemia (CLL), according to the results of a multicenter phase I/II trial.

"PCI-32765, one of a new class of experimental drugs called B cell receptor inhibitors, has shown impressive potential in this clinical trial for its effectiveness and relatively minimal toxicity," said lead investigator Susan O'Brien, M.D., a professor in the Department of Leukemia at The University of Texas MD Anderson Cancer Center.

PCI-32765 is administered orally and inhibits Bruton tyrosine kinase, which is central to B cell receptor signaling. Disrupting this signaling induces apoptosis (cell death) and hinders cell migration and adhesion in malignant B cells.

In the clinical trial, 61 patients received a daily dose of either 420 mg or 840 mg of PCI-32765. Of the 27 patients receiving 420 mg daily, 67% had experienced a complete or partial remission at a median follow-up of 10.2 months.

Of the 34 patients receiving 840 mg daily, 68% achieved a complete or partial remission at a median follow-up of 6.5 months, which was similar to the response rate of the lower-dose cohort at 6.2 months.

The 6-month progression-free survival rates were 92% and 90% for the 420-mg and 840-mg cohorts, respectively. Serious adverse events considered potentially related to PCI-32765 occurred in only 10% of patients. "The main side effect is mild diarrhea that is usually self-limiting," said Dr. O'Brien, who added that unlike the standard combination chemotherapies used to treat CLL, PCI-32765 is not myelosuppressive.

The results of the trial were reported at the 53rd Annual Meeting of the American Society of Hematology in

December. A phase III clinical trial of PCI-32765 is being planned. ■

Study Finds Acupuncture Can Prevent Radiation-**Induced Chronic Drv** Mouth

Acupuncture performed on patients receiving radiation therapy can reduce the severity of xerostomia and other side effects, according to researchers at The University of Texas MD Anderson Cancer Center and Fudan University Shanghai Cancer Center.

The findings from the first randomized controlled trial of acupuncture for the prevention of xerostomia were reported in the journal Cancer.

Xerostomia, or severe dry mouth, is characterized by reduced salivary flow and commonly affects patients receiving radiation therapy for head and neck cancer.

"There have been a number of small studies examining the benefits of acupuncture after xerostomia develops, but no one previously examined if it could prevent xerostomia," said principal investigator Lorenzo Cohen, Ph.D., a professor in the Department of General Oncology and the Department of Behavioral Science and the director of the Integrative Medicine Program at MD Anderson. "We found that incorporating acupuncture alongside radiation therapy diminished the incidence and severity of this side effect."

"The medical implications are quite profound in terms of quality of life."

- Dr. Lorenzo Cohen

In the study, 86 patients receiving radiation therapy for nasopharyngeal carcinoma at Fudan University Shanghai Cancer Center were randomly assigned to receive acupuncture or the standard of care. The 40 patients in the acu-

puncture group received acupuncture therapy three times per week during the 7-week course of radiation therapy. Patients were evaluated before beginning radiation therapy, weekly during therapy, and then again 1 and 6 months after the completion of therapy.

During evaluations, investigators measured saliva flow, and patients completed two questionnaires that assessed symptoms consistent with xerostomia as well as other cancer-related symptoms and their interference with quality of

One month after the end of radiation therapy, 54% of the acupuncture group and 86% of the control group reported clinically significant xerostomia symptoms. Six months after the completion of radiation therapy, 24% of the acupuncture group and 63% of the control group still reported xerostomia symptoms. Saliva flow rates were higher for patients in the acupuncture group than for those in the control group starting at 3 weeks into radiation therapy and persisting through the 6-month follow-up visit.

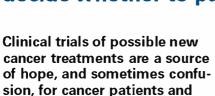
Acupuncture also reduced the severity of cancer-related symptoms other than xerostomia; the differences between the acupuncture and control groups emerged at 3 weeks and continued through the 6-month follow-up

"The medical implications are quite profound in terms of quality of life because while chronic dry mouth may sound benign, it has a significant impact on sleeping, eating, and speaking," Dr. Cohen said. "Without saliva, there also can be an increase in microbial growth, possible bone infection, and irreversible nutritional deficits."

Further research is ongoing, including a large trial being conducted at MD Anderson and Fudan University Shanghai Cancer Center in which patients undergoing radiation therapy for head and neck cancer receive one of two forms of acupuncture or the standard of care. Researchers will examine saliva flow along with other measures to better determine the mechanisms of acupuncture's effect.

Clinical Trials

Understanding the risks, benefits, and purpose of a trial can help cancer patients decide whether to participate



their families. Here are a few facts

to help you decide whether you want to take part in a clinical trial.

Clinical trials are research studies aimed at finding better ways to prevent, diagnose, or treat cancer. Although this article will focus on trials of drugs for cancer treatment, trials for all three purposes are conducted in a similar fashion.

Long before a clinical trial can be considered, researchers must investigate a new drug in a lengthy series of laboratory and animal studies, usually over several years. If the results are promising, physicians proceed to studying the treatment in people.

The federal government sets strict rules that doctors must follow when designing clinical trials and determining the criteria for who may join each trial. Eligibility criteria may include such factors as patients' cancer type and stage, previous cancer treatments, overall health, age, sex, and any medicines being taken for other conditions.

A physician may offer a patient a clinical trial as a treatment option when standard treatments have limited benefit or when a patient's disease has not responded to or becomes resistant to previous therapy. If you are a patient and find a trial you would like to consider, you should talk to your doctor to determine whether you are eligible.

Get the facts

You can learn more during a process called informed consent, when the physician or research nurse explains the clinical trial's purpose, plan, risks, and possible benefits. This is the time to ask as many questions as you need to ask until the answers are clear to you. These are some of the questions you might want to ask:

What are my treatment options? Find out the standard treatment for your type of cancer-or other treatments if you have already had the standard treatment—and what treatment will be given in this clinical trial.

What is my prognosis? Your prognosis is what may happen with your cancer and how your cancer might respond to treatment. How might the clinical trial affect your prognosis? How might other treatment options affect it?

What phase is this clinical trial? Phase I trials test whether a new treatment is safe, the doses at which it can be safely given, the best way to deliver the treatment, and if and how patients' cancers respond to the treatment. Usually only a few patients take part in a phase I trial.

Phase II trials usually involve fewer than 100 patients and study how one type of cancer responds to the new treatment. Phase II trials often compare different doses or treatment schedules to determine which should be used in a phase III trial.

Phase III trials, which can include hundreds or thousands of patients, test whether a new treatment is better than



a standard treatment. Whether each patient gets the new treatment or the standard treatment is determined randomly (as if by the flip of a coin).

Think it over

Each clinical trial has potential benefits and risks. The main advantage of participating is that you will have access to promising new interventions that are often not available to the general public. If the new treatment works, you may be among the first to benefit

Other benefits of a clinical trial are that you will receive regular and careful medical attention from a research team of doctors, nurses, and other health professionals. Finally, the results of the trial Other benefits of a clinical trial are may help future cancer patients.

One of the key risks of participating in a clinical trial is the possibility of unexpected side effects that could be worse than those of the standard treatment. New treatments do not always turn out to be better than, or as good as, standard treatments. It is also possible that the new treatment might not work for you even if it does for other

Take some time to make your decision about whether to participate in a trial. If you wish, you can take home the written informed consent document to review before signing it. This document explains the treatment in detail, the types of medical tests patients receive, who pays for the costs of the clinical trial, and who to call if you have more questions.

- K. Stuyck

FOR MORE INFORMATION

- Talk to your physician
- Visit www.mdanderson.org
- Call askMDAnderson at 877-632-6789
- For a list of clinical trials available at MD Anderson, visit www.clinicaltrials.org

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Palliative Care May Offer Survival Benefits

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Rapid and early

access to supportive and palliative care might be a win-win situation in which patients benefit from reduced emotional, spiritual, symptom, and family distress as well as longer survival."

Dr. Eduardo Bruera

disciplinary. It includes doctors, nurses, counselors, social workers, chaplains, and in many cases physical and occupational therapists." Several of these professionals typically see the patient during the initial visit.

The Supportive Care Center is organized so that the physicians, nurses, and other professionals come to the patient, who remains in the room where he or she can relax. "We try to minimize the number of places the patient has to visit," Dr. Bruera said.

Follow-up visits to the Supportive Care Center are scheduled on days when the patient is coming to MD Anderson for other treatment or tests. The patient is encouraged to call the Supportive Care Center between visits if he or she has questions or needs support. "We get 30-40 phone calls every day from our patients to discuss how they're feeling," Dr. Bruera said.

A win-win situation

In addition to maintaining contact with the patient, the palliative care physician consults with the patient's oncologists to ensure that supportive care services complement the patient's cancer treatment.

"In the past, there was the thought that a referral for palliative care might be some sort of trade-off in which patients would have better quality of life but shorter survival, perhaps because their treatment would be less aggressive," Dr. Bruera said. "But now we've seen that this is not true. Rapid and early access to supportive and palliative care might be a win-win situation in which patients benefit from reduced emotional, spiritual, symptom, and family distress as well as longer survival." ■

FOR MORE INFORMATION

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FURTHER READING

Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small cell lung cancer. N Engl J Med 2010;363(8):733-742.

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