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OncoLog MD Anderson's Report to Physicians

2004

OncoLog Volume 49, Number 11, November 2004

Rachel Williams

Steve C. Stuyck MPH

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REPORT TO PHYSICIANS

NOVEMBER 2004 Vol. 49, No. 11

OncoLog

Infants and older children often get the same types of cancer, but the prognosis, behavior, and treatment of these cancers can be very different in infants.

The Youngest Cancer Patients

by Rachel Williams

New parents lose a lot of sleep worrying about their newborn's adjustments to this world, but some parents have more serious concerns—like coping with the dismay of finding out that their baby has cancer.

In fact, about 10% of all cancers to strike children under the age of 15 are diagnosed in infants one year old or younger. Infants get the same types of cancer that tend to develop in older children and adolescents—acute leukemias and tumors of the brain, nervous system, lymphatic system, kidneys, bones, and muscles—but the prognosis, behavior, and treatment of these cancers in infants can be very different.

While infants with cancer have a much lower five-year survival rate than older

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Dr. Joann Ater, a professor in the Division of Pediatrics, visits with 3-month-old patient

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The Youngest Cancer Patients

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children (33% vs. 75% respectively), pediatric specialists at The University of Texas M. D. Anderson Cancer Center point out that some types of cancer actually have a better prognosis in infants than in older children. And in every case, treatment options improve with specialized care.

“For example, children under one year who have neuroblastoma have a better prognosis than older children and are therefore treated a little differently,” said Joann Ater, M.D., a professor in the Division of Pediatrics who has worked at M. D. Anderson for 15 years treating this most common form of infant cancer. “Stage 4, or metastatic, disease has a much more serious prognosis in a patient who is 18 months or older than it does in an infant. Usually, older children get bone marrow transplants, but the really young ones have a good chance of being cured with surgery and chemotherapy. For some of them, if the tumor is local and not metastatic, it is curable with just surgery.”

Surprisingly, though, some neuroblastomas are curable in infants without any treatment at all. Over time, stage 4S neuroblastoma (a special stage, distinct from stage 4) can actually regress or even entirely disappear on its own.

Genes may be key

A tumor’s unique behavior in infants may have an underlying genetic cause. “Tumors in babies are genetically different in many cases from tumors that occur in older people, even in the same types of cancer,” explained Dr. Ater.

Cynthia E. Herzog, M.D., an associate professor in the Division of Pediatrics, explained that there is no specific biomarker that allows researchers to distinguish the type of neuroblastoma that can regress on its own from others, so it is a matter of watchful waiting and careful balancing of treatment decisions.

“It is different, but we cannot say exactly how it is different. It can’t be defined biologically or histologically, and we can’t predict which kids have this type of tumor and which do not,” said Dr. Herzog. “The trick is that you



_____ (r), traveled to M. D. Anderson from _____ to seek treatment for his neuroblastoma. _____ is receiving chemotherapy, which will be followed by surgery to remove the tumor.

don’t want to overtreat kids who have tumors that will regress on their own; on the other hand, you don’t want to undertreat the ones that don’t have the kind that will go away.”

Leukemia, the second most common cancer in infants, also behaves differently in infants than in older children. According to Michael Rytting, M.D., an assistant professor in the Division of Pediatrics and a specialist in treating pediatric leukemia, infants with leukemia generally have a worse prognosis than older children, and the poorer prognosis has a genetic link.

“Infants with leukemia frequently have a rearrangement of the MLL gene in the leukemia cell,” said Dr. Rytting. “This rearrangement is the principal difference between babies and older children with the disease, and it is known to be a poor prognostic factor.”

Dr. Rytting explained that accurately diagnosing leukemia in infants can be difficult. “Some infants with trisomy 21 have a transient myeloproliferative disorder that looks very similar to leukemia,” he explained. “This illness frequently resolves on its own, though these children remain at high risk for leukemia later in life.

“When the MLL rearrangement is involved, it takes a little longer to achieve remission than you might see with older children, and resistant disease probably is more common,” said Dr. Rytting. “These patients tend to be negative for CD10, the common acute

lymphocytic leukemia antigen, and those patients are known to not do very well. However, the small group of infants who are positive for CD10 and do not have the MLL rearrangement do almost as well as other older children, so it is important to make that distinction.”

Specialized care is best

Regardless of the type of cancer, experts agree that treatment of infants is best handled in a highly specialized environment. “Babies present a challenge and really should be treated in a center that can meet their distinctive needs,” Dr. Rytting said.

For parents, having access to non-medical support staff who specialize in pediatric cancer can ease the strain during a very difficult time. “For young and sometimes inexperienced parents, having an infant with cancer can be a very shocking emotional experience, so we have a lot of support staff to help,” said Dr. Ater.

For instance, M. D. Anderson psychologists developed a program called “Maternal Problem Solving” to help mothers learn to cope with catastrophic illness. “We’re very geared toward helping young parents through problematic times when their baby is diagnosed with cancer,” Dr. Ater concluded. “It just makes things a little easier.” ●

FOR MORE INFORMATION, contact Dr. Ater at (713) 792-6665, Dr. Herzog at (713) 745-0157, or Dr. Rytting at (713) 792-4855.

Meeting the Rising Demand for Outpatient Care

M. D. Anderson is meeting the growing need for outpatient services with a new facility designed with patient comfort and convenience in mind.

It wasn't long ago that hospitalization was routine for most cancer treatments. Two decades ago, a mastectomy meant at least a week's hospital stay, and even chemotherapy was considered an inpatient treatment.

But lengthy hospital stays are largely a thing of the past. Today, cancer patients receive much of their care as outpatients—a trend that many see as benefitting both patients and payers. In recent years, treatment advances and the creation of multidisciplinary outpatient care centers have enabled increasing numbers of M. D. Anderson patients to receive their treatments in a safe, comfortable, and convenient outpatient setting. Now, a new outpatient treatment building scheduled for completion in March 2005 will even further expand the center's ability to provide high-quality outpatient care designed with patient convenience in mind.

The trend toward outpatient care

"Much of the move toward outpatient care in this country has been driven by third-party payers in an effort to control expenses," said Michael S. Ewer, M.D., special assistant to the vice president and chief medical officer at M. D. Anderson. "But this change has been perhaps one of the benefits of managed care, in that it has challenged healthcare providers to find safe and effective ways to deliver care on an outpatient basis, which is clearly to the benefit of our patients."

In fact, when given a choice, the overwhelming majority of patients with cancer would prefer not to be hospitalized. "If I ask people whether they want to come in to the center for five days in a row to get chemotherapy on an outpatient basis or be admitted for the whole five days, probably 90% of them



would prefer to come in daily," said Carmen P. Escalante, M.D., an associate professor in the Department of General Internal Medicine, Ambulatory Treatment, and Emergency Care.

In addition to the benefits it affords patients, outpatient care is becoming more and more necessary for logistical
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(Above) **Dr. Michael Ewer** surveys the main reception area of the new Ambulatory Clinical Building in its final stages of completion. The eight-floor building (inset) will house care centers for breast, genitourinary and gynecologic cancers along with a host of support programs.

Meeting the Rising Demand for Outpatient Care

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Patients and caregivers helped architects plan a building that will provide advanced care in a relaxed environment that doesn't feel like a hospital.

reasons—a chronic shortage of inpatient hospital beds. “It’s a significant problem in hospitals throughout the country,” said Dr. Escalante. “One way to deal with the overload is to treat as many patients as possible in the outpatient venue and save our inpatient beds for the very sick patients with complicated cases.”

Treatment advances

Another reason for the increase in outpatient care has been the development of equipment and treatment advances that are as effective but less invasive and debilitating than previous treatments.

“At M. D. Anderson, we have found ways to treat patients on an outpatient basis that would have been considered absolutely unfeasible years ago,” said Dr. Ewer. One example is the 23-hour mastectomy. According to Raphael E. Pollock, M.D., Ph.D., division head and a professor in the Department of Surgical Oncology, “Twenty years ago, if you were having a mastectomy, you were an inpatient for eight days, and now it’s routinely done as outpatient surgery.” Studies show that outpatient surgery can be performed safely, effectively, and to the patient’s satisfaction, by careful coordination of inpatient and outpatient services. In fact, last year over a third of the surgeries performed at M. D. Anderson were done on an outpatient basis.

Significant advances in chemotherapy administration have also made it possible to offer outpatient treatment to more patients. Previously, extremely sedating drugs used to control common chemotherapy side effects such as nausea and vomiting made hospitalization a necessity. Now, newer nonsedating antiemetic

drugs such as Zofran (ondansetron) are very effective in controlling these side effects. Low-risk patients with febrile neutropenia or deep venous thrombosis can also be treated successfully as outpatients. With these advances, almost all chemotherapy administration is now done in an outpatient setting. M. D. Anderson’s quickly growing Ambulatory Treatment Center (ATC) is now the largest outpatient infusion center in the world, with over 50,000 patient visits a year.

One-stop shopping

M. D. Anderson’s outpatient services have expanded exponentially in recent years to meet the growing demand. Multidisciplinary care centers were implemented throughout the institution in the 1990s to provide patients with a convenient and comfortable setting in which to receive outpatient care. These specialized clinics, organized around specific types of cancer, provide coordinated care from many different specialties, including diagnostic imaging, medical oncology, phlebotomy, radiation oncology, surgical oncology, and supportive care specialties, allowing patients to receive all their treatments at one facility. The care centers have become the hub of patient care at M. D. Anderson and continue to grow, with

over 600,000 patient visits during the past year alone.

To continue to meet the growing need for high-quality outpatient care, M. D. Anderson will open a new Ambulatory Clinical Building (ACB) in March. The eight-floor, 781,000-square-foot facility will house expanded multidisciplinary care centers for breast, genitourinary, and gynecologic cancers, as well as a host of support programs. Patients in these centers will have access to most services they need under one roof.

“The idea was to take a ‘one-stop shopping’ approach so patients wouldn’t have to shuttle all around our growing campus for different services,” said Janet Sisolak, facilities project director. Toward that end, the ACB features a





75-bed Ambulatory Treatment Center for chemotherapy and transfusion services, outpatient surgery, laboratory and pathology services, fine-needle aspiration, a pharmacy, and a number of other treatment support services. Diagnostic Imaging and Radiation Oncology will greatly expand in the ACB while continuing to provide services on the main campus as well. The service will be equipped with 80 pieces of diagnostic equipment, six linear accelerators (with the capacity for two more), four magnetic resonance imaging machines, six computed tomography machines, two positron emission tomography cameras, and 11 nuclear medicine machines.

Filled with natural light, cheerful colors, and décor meant to soothe, the

Ambulatory Clinical Building was designed with patient comfort and convenience in mind. Extensive focus groups with patients and caregivers helped architects plan a building that will provide advanced care in a relaxed environment that doesn't feel like a hospital. The facility features a two-story water wall, bubble columns, outdoor gardens, and glass etched with nature scenes. It will also provide social services support, case managers, a chaplain, patient advocates, an international center, a patient library, a children's play area, the Place...of wellness program, and a 200-seat food court. A climate-controlled, quarter-mile pedestrian bridge will connect the ACB to the existing outpatient clinic building, the new Cancer Prevention Building, and other

Spacious lounge areas (l), outdoor gardens (top), and a 200-seat foot court (above) are just a few of the new facility's features.

campus buildings, and motorized carts will be available to speed the journey.

And speeding the journey is what the Ambulatory Clinical Building is all about. The goal is to provide easy access to services in a cheerful, uplifting atmosphere in the hope of making cancer treatment less stressful so patients can focus all their energies on the most important journey: the road to recovery. ●

The ACB is scheduled for completion in early 2005. To refer a patient to any M. D. Anderson clinic, physicians should call Physician Relations at (713) 792-2202 (in Houston) and (800) 252-0502 (outside of Houston).

Herceptin Boosts Response Rates in Breast Cancer

Adding trastuzumab (Herceptin) to pre-surgery chemotherapy treatment dramatically shrinks breast tumors in women with early-stage, HER-2-positive breast cancer, according to recent research at M. D. Anderson Cancer Center. Studies showed that the addition of Herceptin to the treatment regimen completely eradicated tumors in twice as many women as with chemotherapy alone (65% versus 26%).

About 25 to 30% of all breast cancer patients have tumors that are HER-2 positive, a marker that can signal a poorer prognosis due to increased risk of recurrence and decreased sensitivity to chemotherapy, said Aman Buzdar, M.D., professor in the Department of Breast Medical Oncology. "This is a significant stride in treating women with confined breast tumors who have tested positive for the HER-2 gene," said Buzdar.

According to Buzdar, even though most of the breast tumors either virtually disappeared or shrank dramatically with the presurgery chemotherapy and Herceptin treatment, the breast still had to be treated surgically. Buzdar said the research team will look more closely at the effect the treatment may have on the type of surgery necessary after chemotherapy.

New Blood Test Predicts Breast Cancer Prognosis

Women with advanced breast cancer who have more than five circulating tumor cells in the blood may have a more dangerous form of the disease, according to a recent M. D. Anderson-led study published in the *New England Journal of Medicine*.

The findings could lead to more tailored treatments that would spare some women from the most potent chemotherapy or, conversely, recognize

which patients need more aggressive therapy at the start of treatment, said the study's lead author, Massimo Cristofanilli, M.D., associate professor in the Department of Breast Medical Oncology.

"This is the first time that we can actually stratify metastatic breast cancer patients based on their risk," said Cristofanilli. New technology makes it possible to reliably isolate circulating tumor cells in the bloodstream with a blood test. This study found that the presence of cancer cells in the blood predicted prognosis more accurately than the site of metastatic disease or the presence of estrogen receptor on the tumor cells.

"If we can discover in a newly diagnosed patient that tumor cells are already in the blood, both patient and physician would be aware that we are dealing with a more aggressive cancer that requires more aggressive treatment early on," Cristofanilli said.

Biologic Drug Effective In Rare Leukemia

A biologic agent, Lipo-ATRA, appears to be as effective as chemotherapy in some patients with a rare form of leukemia, but without the risks and negative side effects of traditional chemotherapy.

Researchers showed that approximately one third of patients with acute promyelocytic leukemia (APL) can achieve long-term, disease-free remission with the drug, a finding that opens the door to the development of biologic agents for more common forms of leukemia.

"This is the first time we have seen patients with an acute leukemia potentially cured without use of chemotherapy," said the study's principal investigator, Elihu Estey, M.D., a professor in the Department of Leukemia at M. D. Anderson.

Traditional treatment of APL combines the chemotherapy drug

idarubicin with orally administered ATRA (all-trans retinoic acid), a form of vitamin A. Realizing that little of the vitamin A is absorbed when swallowed, M. D. Anderson researchers worked to find a more effective way to deliver ATRA.

The solution involved encasing ATRA in liposomes and injecting it so that it is not metabolized and stays longer in tissues. The approach was effective—of the 34 patients who received Lipo-ATRA, 10 remain in remission for an average of five years, despite never receiving chemotherapy.

Novel Agent Combination Shrinks Lung Tumors

A combination of two new agents shows promise in treating lung cancer, according to studies at M. D. Anderson. The agents have shown little benefit in treating lung cancer but they had a substantial impact when used individually in low doses.

In a study published in the October 20 issue of the *Journal of the National Cancer Institute*, researchers tested an experimental targeted therapy, the farnesyltransferase inhibitor lonafarnib (also known as SCH66336) and the insulin-like growth factor binding protein-3 (IGFBP-3), in mice implanted with human lung tumors. The combined treatment shrank tumors to 45% the size of those in untreated mice. The treatment worked even in low doses and did not cause measurable side effects in the mice.

"Together these agents work on the pathway that is critical for the survival of a cancer cell," said Ho-Young Lee, Ph.D., assistant professor in the Department of Thoracic/Head & Neck Medical Oncology Research and lead author of the study. Scientists from the U.S. Food and Drug Administration and Emory University also participated. Clinical trials are under development.





Going Beyond the Headlines

Tips to help you evaluate cancer stories in the news media

Every day, we are bombarded by news reports stating that this food may prevent cancer or that newly discovered gene may contribute to a certain kind of cancer. It is hard to know where all these stories come from and whether they are trustworthy, especially when several reports seem to contradict each other.

In fact, most cancer-related news stories in the mainstream media are triggered by studies reported in scientific journals. Journalists who report on cancer frequently check these journals. Here are some tips for getting the most out of cancer studies reported in the news.

1 The basics

First, look for the basics. Most cancer news stories—even the very briefest ones—answer the following three questions:

- **What was the study's major finding?** For example, an article might say, "Researchers have found that among women with a high risk of breast cancer, MRI is more effective than standard mammography in the detection of breast tumors." However, a careful reading of this article will show that the findings apply only to women with a specific genetic mutation rather than to all women at high risk.
- **Who conducted the study, and at what institution(s) do these people work?**
- **When and where was the study report published?**

2 Additional study details

Next, look for details about the study design:

- **Did the study involve people? Or was it a laboratory study—for example, a study conducted with tumor cells or mice?** A study showing that a drug cures cancer in mice doesn't mean that the drug will cure cancer in people—it just means that the drug may eventually be studied in humans. In contrast, studies involving people

may lead to changes in the way cancer is treated.

- **If the study involved people, how many people were included?** In

general, the more people included, the stronger a study's findings. If a study was small, further studies with more patients will probably be needed to confirm the findings.

- **If the study involved people, what kinds of people were included?**

Often, study findings apply to only a small subgroup. For example, a major study published in 2001 showed that the drug trastuzumab (Herceptin) was effective against metastatic breast cancer—but only in women who had a modification in a specific gene, the *HER-2* gene.

3 Context and commentary

Many cancer news stories use interviews with cancer experts to answer the question: "What do these findings mean?" Journalists may interview the study authors as well as cancer specialists not directly involved with the study. Among the issues experts may address are:

- **Should clinical practice be changed as a result of the findings?** In December 2003, a major study reported in the *New England Journal of Medicine* showed that "virtual colonoscopy," which uses x-rays, was just as effective as standard colonoscopy for colon cancer screening. However, experts noted that even though the study was large and well designed, further research was needed before virtual colonoscopy could be considered a standard screening option.
- **What questions remain to be answered?** Experts interviewed about the virtual colonoscopy study noted that physicians were still not sure which patients with polyps

discovered on virtual colonoscopy should have them surgically removed.

- **For studies about new prevention, diagnosis, or treatment strategies, does the new strategy have any drawbacks?** Experts interviewed

about virtual colonoscopy drew attention to the fact that about a third of patients in the study thought virtual colonoscopy was more uncomfortable than standard colonoscopy.



Sometimes experts will disagree about what findings mean, and further studies may be needed to resolve questions.

4 Going beyond the story

Major new findings about cancer are usually reported by multiple media outlets. To get the most complete picture of what new findings mean, read, watch, and listen to as many different news reports as possible. Another excellent resource for help with interpreting cancer news is the Cancer Information Service (1-800-4-CANCER). This National Cancer Institute-sponsored service connects callers with knowledgeable staff who explain cancer-related information in easy-to-understand terms.

Most important of all, talk with your doctor. He or she can explain new findings in context and help you determine whether they are relevant to you. ●

For more information, contact your physician or contact the M. D. Anderson Information Line:

 (800) 392-1611, Option 3, within the United States, or

 (713) 792-3245 in Houston and outside the United States.

November 2004

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DiaLog

Cancer Information in the Media

Stephen C. Stuyck, M.P.H.
Vice President for Public Affairs

Knowledgeable patients with provocative questions are nothing new for oncologists. Nearly every physician has encountered patients who pull out a newspaper or magazine article reporting research findings and ask, "What about this for me?" If the question doesn't come from the patient, it is likely to be posed by a caregiver. Many patients now also research health information on the Internet.



Of course, not every patient comes to a doctor's appointment armed with the latest information from the news media, but the number is bound to grow. The American Cancer Society estimates that 76% of all cancers are diagnosed at age 55 or older. As the first wave of baby boomers reaches 55, this new generation of patients can be expected to take part in decisions about their health care in ways prior generations never considered.

What is the state of cancer information in the mainstream news media? Generally, quite good, within the limits of the print space, air time, and reporting talent available. Journalists sometimes misunderstand scientific information or try too hard to make cancer stories "sexy." Their sources sometimes use too much jargon, misstate the facts, or even regret their accurately reported words once they hear or read them.

But, by and large, the increase in both the quality and quantity of media coverage of cancer has been impressive in the past 20 years.

Consider this: A recent Gallup poll reported that 63% of Americans surveyed are either "very" or "somewhat" worried about cancer, while another university-sponsored poll found that 71% of respondents believe that the cancer mortality rate will drop by 50% in the next 15 years. What do these polls tell us? Cancer is a subject of serious concern to the public, but there is optimism about it as well. News media coverage of cancer tends to reflect both the worry and the hope of Americans.

Today, the Internet is providing people with unparalleled access to health information. For example, a Google search for "prostate cancer treatment" yielded 69,500 entries in less than a half second. Even the esoteric term "anti-angiogenesis" generated 11,600 references just as quickly. A recent Harris Poll survey found that 111 million U.S. adults have sought health information online. In other words, there is a lot of health information available, and there are a lot of people seeking that information.

My sense is that many doctors appreciate the give-and-take with patients who are well informed about their illnesses and interested in their care. I suspect that such patients sometimes can be challenging and demanding. But these patients are often the fighters, and I've been told they also tend to be the ones who work hardest to comply with treatment plans.

As for the future: Doctor, prepare yourself for more.

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Published by the Department of Scientific Publications-234,
The University of Texas M. D. Anderson Cancer Center,
1515 Holcombe Boulevard, Houston, Texas 77030,
713-792-3305.

Made possible in part by a gift from the late Mrs. Harry
C. Wiess.

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