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REPORT TO
PHYSICIANS

JULY/AUGUST 2000
VOL. 45, NO. 7/8

UNIVERSITY OF TEXAS
MD ANDERSON
CANCER CENTER
Making Cancer History™

2

Clinical Trials

Included are studies of nonablative allogeneic transplants and treatment of graft-versus-host disease.

5

Caregiver's To-Do List

Taking care of someone with cancer? *House Call* offers suggestions for meeting your own needs.

6

Umbilical Cord Blood Transplants

An alternative source of stem cells may allow more patients to undergo transplants.

8

Protecting Young Donors

Who decides if a child is capable of donating blood or bone marrow?

MD Anderson Oncology

Advances Allow Expanded Use of Allogeneic Stem Cell Transplantation

by Kerry L. Wright

The tendency of transplanted stem cells to attack their recipient's cancer makes allogeneic transplants more likely than autologous transplants to cure disease, but when this cell-on-cell activity is directed toward normal cells, it can also lead to graft-versus-host disease (GVHD).

In the past, the threat of GVHD limited the number of patients who were able to undergo allogeneic transplantation, but

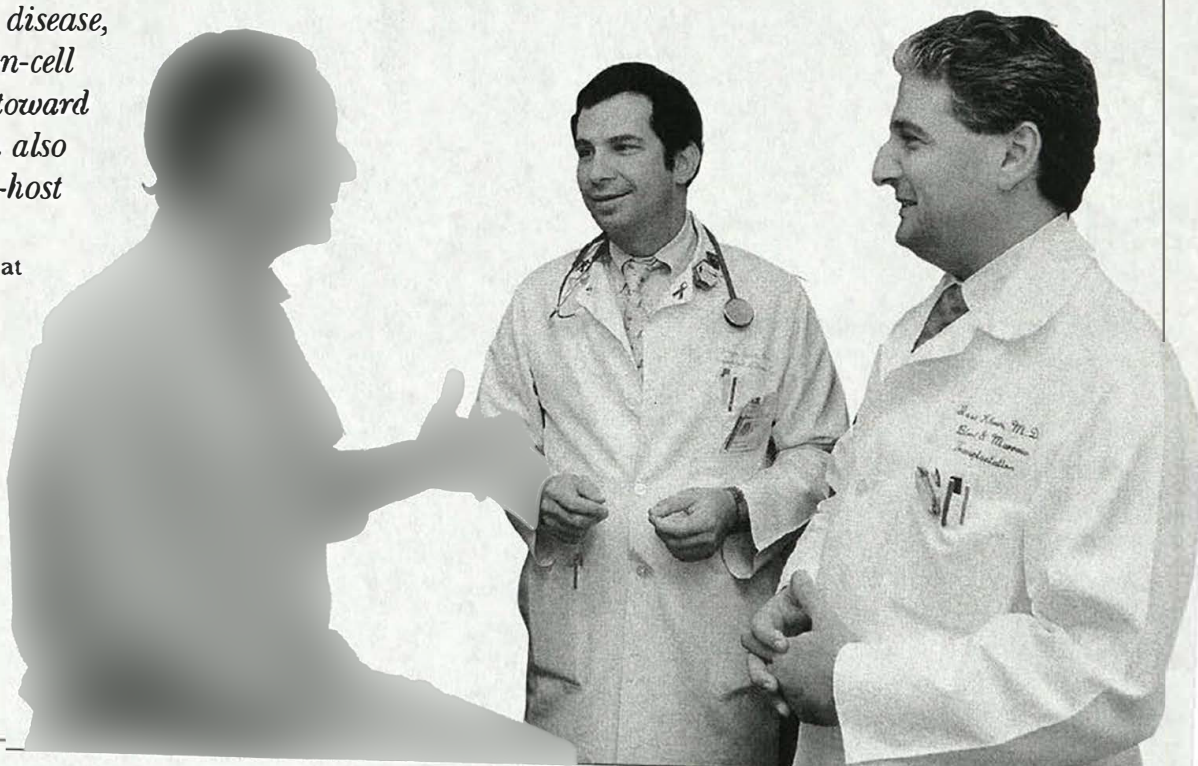
Dr. Sergio Giralto (center) and **Dr. Issa Khouri** (right), associate professors in the Department of Blood and Marrow Transplantation, talk with

thanks to advances in immunosuppressive therapies and cell manipulation techniques, that number has been steadily increasing.

"In the beginning, bone marrow transplants were viewed as a way to give very high doses of chemotherapy and radiation, and the transplant itself was considered supportive care

to help people recover from what would otherwise be permanent destruction of their bone marrow," said Richard E. Champlin, M.D., chairman of the Department of Blood and Marrow Transplantation at The University of Texas M. D. Anderson Cancer Center. The

(Continued on next page)



Advances Expand Use of Allogeneic Transplantation

(Continued from page 1)

chemotherapy was thought to be curative, as it is today in autologous transplantation, but physicians soon discovered that allogeneic transplantation harbored unexpected benefits—immunoreactivity against the cancer. In some cases, this graft-versus-malignancy effect itself can be curative; infusion of additional donor lymphocytes can induce complete remissions in many patients whose diseases have recurred after an allogeneic transplant.

Once the curative potential of allogeneic transplants was identified, physicians began looking for ways to lessen the treatment's toxic effects and make it available to more patients.

"The two major obstacles in transplantation today are to be able to perform transplants in people who don't have related donors and in people who are poor candidates for traditional transplant," said Sergio A. Giralt, M.D., an associate professor in the Department of Blood and Marrow Transplantation.

For patients who do not have a related donor, the National Marrow Donor Program (a registry of more than three million volunteers) and umbilical cord blood banks (traditionally for children) can provide alternative sources of transplantable progenitor cells. In addition, T cell depletion and stem cell purification can be performed to increase trans-

plant success rates for mismatched donors.

The second major problem—performing transplants in patients who are older or in poor medical condition—has been a main focus of M. D. Anderson's Department of Blood and Marrow Transplantation.

"In order to expand this treatment to a larger patient population, we thought to initiate a strategy that relies not so much on high-dose chemotherapy but on the immune modulation generated by the donor cells," said Issa F. Khouri, M.D., an associate professor in the Department of Blood and Marrow Transplantation. Drs. Khouri, Giralt, and Champlin have collaborated since

PROTOCOLS

Clinical Trials of Allogeneic Stem Cell Transplants

Clinical trials in progress at The University of Texas M. D. Anderson Cancer Center include the following for patients receiving allogeneic peripheral blood or marrow stem cell transplants that use nonablative or graft-enhancement preparatory regimens and for transplant recipients who require treatment for graft-versus-host disease (GVHD). For a complete list of blood and marrow transplantation clinical trials, visit the M. D. Anderson Cancer Center clinical trials Web site at <http://www.clinicaltrials.org>.

- Pilot study of mini-allogeneic peripheral blood progenitor cell transplantation for metastatic renal cell carcinoma (DMP99-007). *Physician: Naoto T. Ueno, M.D., Ph.D.*

Study participants must be 65 years old or younger and have pathologically proven metastatic renal cell carcinoma with no brain metastases. Patients must have a human leukocyte antigen (HLA)-compatible related donor and cannot have symptomatic cardiac or pulmonary

disease or any other comorbidity that might compromise their tolerance of the regimen.

- Phase II study of nonablative allogeneic blood stem cell transplantation for patients with indolent lymphoid malignancies (ID99-035). *Physician: Issa Khouri, M.D.*

Patients up to 75 years old who have B-cell chronic lymphocytic leukemia or follicular or small lymphocytic lymphoma that has recurred after at least one remission are eligible. Patients with disease that expresses CD20 will receive rituximab if their disease has not been refractory to prior therapy with that agent. Donors must be HLA-compatible or, if a sibling, have a single antigen mismatch.

- Infliximab plus methylprednisolone (MP) versus MP alone for the treatment of liver graft-versus-host disease (ID99-394). *Physician: Daniel Couriel, M.D.*

Patients who have had successful engraftment of an allogeneic bone marrow or peripheral blood stem cell transplant within the last 100 days may participate. Participants must also be at least 18 years old and have grade 2-4 acute GVHD of the gastrointestinal tract

or liver. Those who have chronic GVHD or are unable to give informed consent are excluded.

- Pilot study of allogeneic peripheral blood stem cell transplantation for patients with AIDS-related lymphomas (DM97-094). *Physician: Issa Khouri, M.D.*

This study is designed for patients, ages 15 to 70 years old, with AIDS-related non-Hodgkin's lymphoma who have not received treatment or whose disease has not responded to frontline conventional chemotherapy. Participants must have an HLA-identical sibling donor who is HIV negative. Patients with previously diagnosed Kaposi's sarcoma, active central nervous system lymphoma, symptomatic cardiac or pulmonary disease, or active infections are not eligible.

- Mini-allogeneic peripheral blood progenitor cell transplantation for recurrent or metastatic breast cancer (DM97-268). *Physician: Naoto T. Ueno, M.D., Ph.D.*

Patients with pathologically proven metastatic or recurrent breast cancer who are 18 to 60 years old are eligible. A partial or complete response to pre-transplanta-

92 to develop a nonablative preparative regimen, also known as a "minitransplant," which allows for a graft-versus-malignancy effect without the toxic effects of traditional myeloablative regimens. More recently, Paolo Anderlini, M.D., an assistant professor in the Department of Blood and Marrow Transplantation, has extended this approach to Hodgkin's disease, and Assistant Professor Naoto T. Ueno, M.D., Ph.D., of the same department, has studied this strategy in breast cancer and renal cell carcinoma.

The preparative regimen had to meet three criteria: it had to be immunosuppressive to prevent rejection, it had to be able to control

the patient's cancer, and it had to be minimally toxic. Radiation therapy was not included in the regimen, and the chemotherapy chosen was based on fludarabine, a purine analogue that meets all three criteria.

The fludarabine-based regimens can be given at low doses in the outpatient setting and are immunosuppressive enough that the transplants will engraft and demonstrate graft-versus-malignancy effects. GVHD has generally been milder and more easily controlled with the fludarabine-based regimens than with traditional high-dose ablative therapy, according to Dr. Champlin. Minitransplants are typically performed between human leukocyte

antigen-identical siblings because as genetic disparity increases between a donor and a recipient, so must the intensity of the preparative regimen. With the new regimens, allogeneic transplantation can now be performed in patients who are up to 75 years old and who have such comorbid conditions as hepatitis and cardiac or lung abnormalities.

"Indolent lymphoma is an area where this treatment has been showing very promising results," said Dr. Khouri. Thirteen patients with low-grade lymphoma have been treated at M. D. Anderson with combination therapy that includes nonablative stem cell transplantation.

(Continued on page 4)

PROTOCOLS

tion standard-dose chemotherapy or, for bone disease, stable disease with clinical improvement is required. Donors must be HLA-compatible relatives; patients whose disease relapsed after autologous transplantation may use an unrelated, HLA-matched donor.

- A pilot study to assess the safety and efficacy of nonmyeloablative chemotherapy and allogeneic stem cell transplantation in patients with severe and refractory autoimmune disease (DMP00-085). *Physician: Samer Bibawi, M.D.*

This study is designed for patients 65 years old or younger with histologically confirmed autoimmune disease. Participants must not have symptomatic cardiac or pulmonary disease, active infectious hepatitis, or HIV. Peripheral blood stem cell donors must have no clinical evidence of autoimmune disease. Follow-up visits will range from daily to once weekly up to 100 days after transplantation, monthly for the following six months, and every six to 12 months thereafter.

- A phase II/III, multicenter, open-label, randomized clinical trial evaluating ABX-CBL when compared to ATG as second-

line therapy in patients with steroid-resistant acute graft-versus-host disease (DM00-029). *Physician: Daniel Couriel, M.D.*

To be eligible, recipients of a single allogeneic stem cell transplant who have acute GVHD must not have received a subsequent infusion of donor cells or any immunosuppressant therapy besides steroids. Participants must exhibit at least one of the following symptoms: skin rash involving at least 25% of the body; total bilirubin count > 3.5 mg/dL; diarrhea > 500 mL/day; nausea and vomiting; epigastric pain; or upper gastrointestinal disease.

- Megadose T cell-depleted HLA-nonidentical blood progenitor cell transplantation for patients with hematological malignancies or bone marrow failure (DM96-122). *Physician: James L. Gajewski, M.D.*

This study is for patients with high-risk hematological malignancies, stage IV low-grade lymphoma, chronic lymphocytic leukemia that has not responded to two treatment regimens, or severe aplastic anemia that has not responded to prior immunomodulatory therapy. Participants must have a related

donor and be recovered from any toxic effects of prior therapy.

- Phase I/II evaluation of safety, pharmacokinetics, and activity of basiliximab (Simulect) plus corticosteroids as initial treatment of cutaneous acute graft-versus-host disease in patients undergoing allogeneic bone marrow or peripheral blood stem cell transplantation (ID99-399). *Physician: Thomas Martin, M.D.*

Patients who have received an allogeneic stem cell transplant and who have cutaneous grade 2 or 3 acute GVHD are eligible to participate. Treatment with Simulect, daclizumab (Zenapax), ATG, OKT3, photopheresis, any experimental anti-T cell-directed monoclonal antibody therapy, or any investigational agent within 30 days of study entry is a basis for exclusion. Other exclusion criteria include a history of steroid-refractory acute GVHD and an inability to tolerate steroids. •

FOR MORE INFORMATION about these clinical trials, physicians or patients may call the M. D. Anderson Information Line. Those within the United States should call (800) 392-1611.

Advances Expand Use of Allogeneic Transplantation

(Continued from page 3)

All 13 patients are alive and in remission. "We have seen similar promising results in chronic lymphocytic leukemia, Richter's transformation, and mantle cell lymphoma, and we are also exploring this therapy for patients with AIDS-related lymphoma," Dr. Khouri added.

For many myeloid malignancies in which traditional allogeneic transplants have a proven benefit, physicians at M. D. Anderson continue to recommend myeloablative regimens for younger patients and nonablative regimens for older ones, who are most at risk for experiencing the toxic effects of high-dose therapy. The treatment-related mortality rate is approximately 20% for all allogeneic transplants, and patients must stay in the hospital for approximately four months while their immune systems recover and signs of infection are monitored.

For large-cell lymphomas, multiple myelomas, and Hodgkin's disease, allogeneic transplants are recommended for those at high risk for recurrence, but autologous transplants are still preferred for most patients. Autologous transplants require a hospital stay of about a month and have a treatment-related mortality rate of less than 5%. Autologous and allogeneic transplants are also being studied in the treatment and support of autoimmune diseases and such solid tumors as ovarian, breast, lung, and renal cell cancers.

For both types of transplant, the use of peripheral blood stem cells has steadily increased over the past five years. Today, almost all autologous transplants and approximately 70% of allogeneic transplants employ peripheral blood stem cells rather than bone marrow, according to Martin Korbling, M.D., a professor in the Department of Blood and Marrow Transplantation. Dr. Korbling led the development of the blood stem cell collection program by apheresis at M. D. Anderson, which now performs approximately 1200 stem cell collections each year.

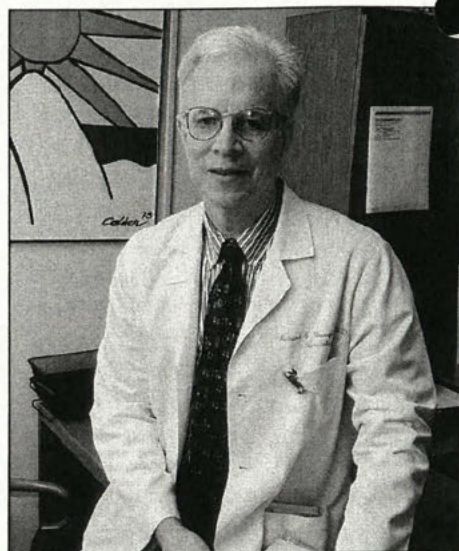
Donors are given granulocyte colony-stimulating factor (G-CSF) to mobilize stem cells from the bone marrow into the peripheral bloodstream, where the cells are harvested via a procedure similar to simple platelet collection.

According to Dr. Korbling, peripheral blood stem cells have several advantages over bone marrow: approximately four times more cells can be collected, they allow faster recovery of blood counts in recipients, and they contain more T cells and thus may produce a stronger immune reaction against the recipients' tumor cells. The disadvantage? Recipients are more likely to experience chronic GVHD.

Several avenues are being investigated to treat and prevent GVHD. Photopheresis, which was originally developed to treat cutaneous T cell lymphoma, is now being studied as a treatment for both acute and chronic GVHD in a clinical trial led by Dr. Anderlini and Michele Donato, M.D., an assistant professor in the Department of Blood and Marrow Transplantation. In addition, Dr. Korbling and colleagues are investigating the use of cytokines in donors and recipients to mobilize or suppress certain cells. These in vivo manipulations could lead to faster engraftment, less GVHD, and a stronger graft-versus-malignancy response.

"The big picture is, technologically, we are able now to in vivo manipulate the donor to collect the graft, ex vivo manipulate the graft, physically eliminating certain subsets of cells, and then, whenever those cells are transplanted, we can again in vivo manipulate the patient by giving certain cytokines," Dr. Korbling said. "So, we have different strategies available."

To reduce the risk of GVHD after blood stem cell transplantation, Dr. Donato is also studying the effects of giving G-CSF to bone marrow donors as an alternative to blood stem cell transplantation. The hope is that G-CSF-primed bone marrow cells will grow just as quickly as the blood stem



Dr. Richard E. Champlin, chairman of the Department of Blood and Marrow Transplantation, has been collaborating with Drs. Issa Khouri and Sergio Giralt in the development of nonablative preparatory regimens, which are allowing more patients to receive allogeneic transplants.

cells but not produce as much GVHD.

Other methods of enhancing engraftment include generation of cytotoxic T cells by ex vivo exposure of donor cells to a patient's tumor and gene therapy both to enable recipients to better withstand preparative chemotherapeutic regimens and to introduce so-called "suicide genes" that induce apoptosis in transplanted cells that are not providing benefit to a patient, a strategy under development by Associate Professor Steven Kornblau, M.D., and Assistant Professor Frank Marini, Ph.D., of the Department of Blood and Marrow Transplantation.

"The important message is that the whole field of blood and marrow transplantation is probably the most dynamic area in all of medicine, where advances in chemotherapy, immunosuppressive agents, genetic therapy, and cellular therapy are all coming together," said Dr. Champlin. "So it's an exciting place to work."

FOR MORE INFORMATION, contact Dr. Champlin at (713) 792-3618, Dr. Khouri at (713) 792-3611, Dr. Giralt at (713) 794-1034, or Dr. Korbling at (713) 792-2808.



Meeting Your Own Needs While Caring For Someone Else

Are you taking care of a loved one who has cancer? If so, who is taking care of you? Caring for someone who has cancer is a heroic undertaking, one that requires physical, emotional, and psychological strength, but some caregivers find it difficult to admit that they need help and many feel guilty about taking time out of their caregiver duties to take care of themselves.

A recent study of 148 patients with colorectal cancer published in the journal *Cancer* examined the mental health and quality of life of spouses or partners caring for patients with cancer at home. The researchers found that caring for someone with cancer can take an emotional toll on the caregiver, which can lead to depression. This is especially true if the patient and caregiver have a strained relationship, a low income, or are isolated.

Even if you don't become depressed, being a caregiver can add a lot of stress to your life. Here are a few suggestions for reducing that stress:

✓ *Tell someone you trust how you're feeling.*

It is normal to sometimes feel angry at the patient in your care or to resent your responsibilities. Instead of feeling guilty about these emotions and holding them inside, talk about them—with a friend, relative, or clergy. Also, many patients with cancer go through periods of withdrawal or irritability, so don't take such negative emotions personally. The University of Texas M. D. Anderson Cancer Center offers a Caregiver Telephone Support Line. To use it, call the Anderson Network at **1-800-345-6324**, and a staff member will make arrangements for another caregiver to phone you within 24 to 36 hours.

✓ *Request help.*

Don't expect others to ask you if you need help. Make a list of tasks that others can do for you—running an errand, preparing a meal, or looking after your children while you go to a doctor's appointment. Enlist the help of family, friends, and neighbors.

✓ *Use available community resources.*

Home care agencies can often provide medical equipment and visits from nurses, physical therapists, and social workers. Services include meal preparation, medication delivery, and helping the patient bathe, eat, or dress. Your

state or local health department and the American Cancer Society can help you locate available services. Government-sponsored programs such as Medicaid, Medicare, and the Veterans Administration may also cover home care costs. The Red Cross and various church or social service organizations often provide free or low-cost transportation.

✓ *Give yourself a break.*

Everyone needs some time off. Taking care of yourself will make you feel better, which will make you a better caregiver. Perhaps the patient might participate in an adult daycare program. Or maybe someone can come to your house regularly to stay with the patient for a few hours while you go out.

✓ *Take care of your health.*

Exercise regularly, eat balanced meals, and see that you get enough sleep.

✓ *Make time to relax.*

Read, pursue a hobby, or keep a journal. Go to a movie or out to dinner with friends. Practice relaxation techniques such as meditation, progressive muscle relaxation, or deep breathing.

Remember, taking care of yourself is as important as taking care of your loved one. ●

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

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

☎ (713) 792-6161 in Houston and outside the United States.

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✓ *Join a support group.*

Talking to others who are experiencing the same kinds of problems is a way to vent frustrations, share solutions, and gain some much-needed help and support.

✓ *Get more information.*

Libraries have books, articles, and films on caregiving. Some hospitals, adult education centers, and the Southern Regional Resource Center offer courses and additional resources that can help.

✓ *Set realistic goals.*

Recognize your limits—what you can and cannot do—then define your priorities. Do only the things you need to do. Ask others to help you with some of the tasks.

Use of Umbilical Cord Blood Expands Option of Transplantation to More Children

New Protocol for Adults Combines

Umbilical Cord Blood from Multiple Donors

by Dawn Chalaire

Every year at The University of Texas M. D. Anderson Cancer Center, about 30 children—most with leukemia or lymphoma—will need a stem cell transplant to treat their diseases. Of these, fully half will never receive that transplant—either because an appropriate donor is never found or because the child is no longer a candidate for transplant by the time a donor is located.

According to Ka Wah Chan, M.D., a professor in the Department of Clinical Pediatrics at M. D. Anderson, a possible solution to the problem of making stem cell transplantation available to more of these patients has come from an unlikely source—what was once considered medical waste.

Umbilical cord blood was first reported to be a source of cells for transplant about 10 years ago, Dr. Chan said. “This approach was then extended in the past five years to include umbilical cord blood from unrelated donors. Currently, there are about 20,000 units of umbilical cord blood stored worldwide in various banks,” he said.

Since 1996, 25 umbilical cord blood transplants, all from mismatched donors, have been performed in pediatric patients at M. D. Anderson in a clinical trial led by Dr. Chan. All but three of the patients have had advanced acute leukemia. After a median follow-up of 22

months, 14 patients are alive, and 12 are in remission.

The major advantage of umbilical cord blood transplantation is that unlike unrelated bone marrow transplants, which require that the donor and recipient be a perfect human leukocyte antigen (HLA) match, umbilical cord blood transplant recipients can tolerate some mismatches in HLA type (as many as 2 of 6 antigens). This has opened the door for umbilical cord blood transplants because finding a perfect bone marrow match can be difficult. The uneven representation of ethnic groups in bone marrow registries (more than 75% of donors registered worldwide are white) makes it especially difficult for minority patients to find an unrelated bone marrow donor.

At M. D. Anderson, the approach to finding unrelated bone marrow donors and umbilical cord blood donors for pediatric patients is the same. A search for both types of donors is conducted through a computerized registry, and the choice is based on the patient’s condition and the availability of matched donors. On average, the search for an umbilical cord blood donor is shorter than that for a bone marrow donor, so patients who are very sick and cannot wait two to three months to find a perfectly matched bone marrow donor may now receive umbilical cord blood transplants.

“That doesn’t mean that we’ve reduced the number of unrelated bone marrow transplants,” said Dr. Chan. “In fact, the total number of unrelated donor transplants is probably higher because many of the patients who are now receiving umbilical cord blood transplants might not have had a transplant if they had been required to wait for

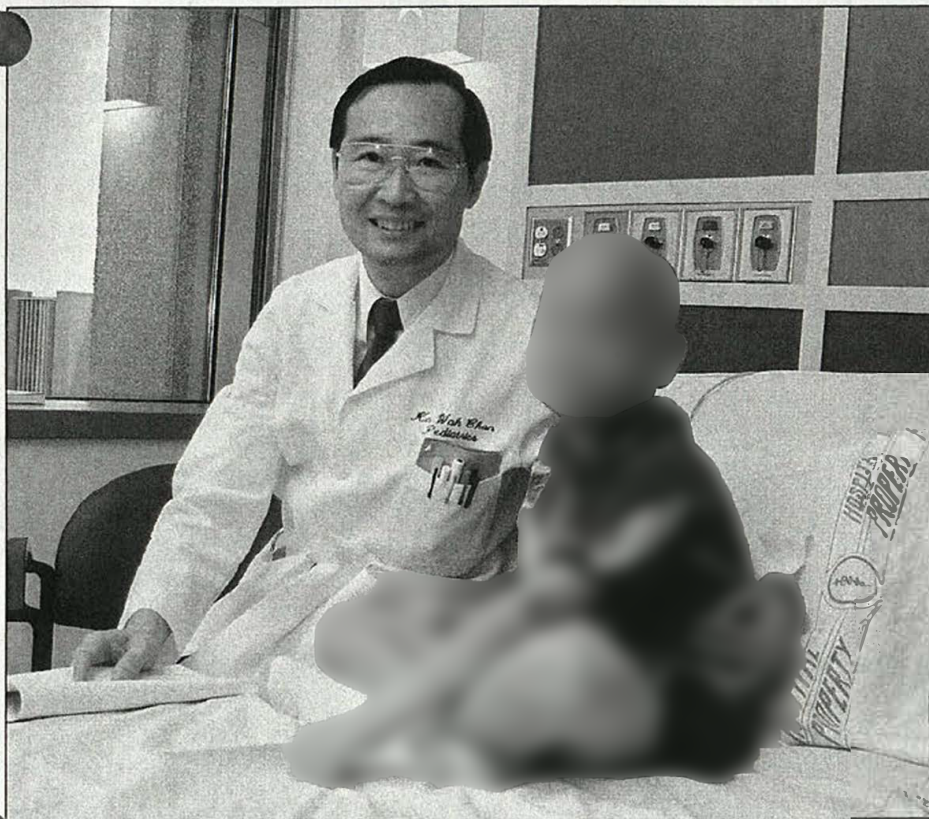
an unrelated bone marrow donor.”

Using umbilical cord blood as a source of stem cells in transplantation has other advantages as well. For instance, umbilical cord blood is a widely available, otherwise discarded resource that poses no risk or discomfort to the donor.

“There’s really no loss, no attrition, of donors,” Dr. Chan said. “Whereas the bone marrow donor might not come back to donate or might have a medical reason for not donating, cord blood, once stored, is available.”

Perhaps because lymphocytes collected from umbilical cord blood are more naive (less differentiated) than lymphocytes found in bone marrow, umbilical cord blood transplantation has been shown to cause less graft-versus-host disease, a common complication in unrelated donor transplants. However, the naivete of umbilical cord blood cells has led some to question if the cells have the ability to attack tumor cells. In the current study, Dr. Chan said, when immunosuppressive therapy was suspended in two patients with leukemia who had relapses after umbilical cord blood transplantation, both patients (one of whom was also given granulocyte-macrophage colony-stimulating factor) went into “spontaneous” remission, suggesting that umbilical cord blood cells do have a graft-versus-leukemia effect.

Despite these positive indications, several problems with umbilical cord blood transplantation have been reported in other studies. The small number of cells that are available from each donor unit (10 times fewer than in bone marrow transplants) means that it takes longer for the transplant to engraft. During this period of pancytopenia after the transplant, infection poses



During a recent follow-up visit, **Ka Wah Chan, M.D.**, a professor in the Department of Clinical Pediatrics, poses with [REDACTED], an umbilical cord blood transplant recipient. Since 1996, umbilical cord blood transplantation has been an option at M. D. Anderson for patients who do not have a related stem cell donor.

The major advantage of umbilical cord blood transplantation is that transplant recipients can tolerate some mismatches in HLA type.

While no results are yet available from Dr. de Lima's study, the overall survival rate reported worldwide in the literature for both pediatric and adult single-donor umbilical cord blood transplant recipients is only about 40%.

With an overall success rate of 56%, Dr. Chan and his colleagues have so far had better results, due, in part, to a modification in approach. In most centers where pediatric umbilical cord blood transplants are performed, patients are given antithymocyte globulin (ATG), an immunosuppressive drug, to prevent rejection. At M. D. Anderson, melphalan and fludarabine are used instead, and tacrolimus is used in place of cyclosporin to prevent graft-versus-host disease. Also, the protocol at M. D. Anderson calls for about 50% less radiation than most protocols at other institutions, said Dr. Chan.

Because the experiences of other centers with umbilical cord blood transplants have not been as favorable, Dr. Chan said, most prefer to use unrelated bone marrow transplants or other methods. "Our success rate is such that we encourage umbilical cord blood transplants to be done," he said. "Our approach is different." ●

FOR MORE INFORMATION, contact Dr. Chan at (713) 792-7751 or Dr. de Lima at (713) 792-8750.

the greatest threat to patients.

"The reported incidence of fatal complications in umbilical cord blood transplants exceeds 30% in the first 100 days," said Dr. Chan.

The small number of stem cells contained in umbilical cord blood has also limited transplant recipients to children and low-weight adults, but a new protocol at M. D. Anderson aims to expand umbilical cord blood transplantation to more adults by combining umbilical cord blood from two or three donors and transplanting it into a single patient.

"In adult single-donor umbilical cord blood transplants, especially when the HLA mismatch is large, the engrafting is very delayed," said Marcos de Lima, M.D., an assistant professor in the Department of Blood and Marrow Transplantation and principal investigator of the study. "The majority of cases will engraft, but instead of the usual 10

to 20 days for bone marrow and blood stem cell transplants, umbilical cord blood transplants may take 40 to 60 days to engraft," said Dr. de Lima.

Dr. de Lima hypothesizes that combining umbilical cord blood donors will increase the number of stem cells available and decrease the time it takes for the transplant to engraft. This hypothesis is supported by preclinical animal experiments. While there have been verbal reports of this type of study elsewhere, there have been no published results.

Dr. de Lima stressed that the protocol is an option for patients who otherwise would not be able to receive a transplant of any kind.

"The major eligibility criteria for this protocol is patients who don't have an available bone marrow or blood stem cell donor," Dr. de Lima said. "This treatment is very intensive, so it's mainly for patients age 50 and younger."

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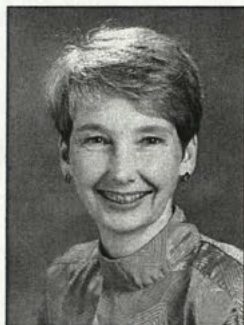
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Protecting the Interests of Young Donors

Rebecca Pentz, Ph.D.
Clinical Ethicist

A 42-year-old woman had a relapse of acute myelogenous leukemia and desperately needed a bone marrow transplant. Each member of her family was tested, and the closest human leukocyte antigen match was her two-year-old son. But who should provide consent for the child to donate? Both the patient and her husband had a conflict of interest—the patient's life was at stake. Also, the bone marrow donation would provide no medical benefit and pose some risk to the child.



At M. D. Anderson, pediatric donors have a separate health care team: a social worker, a child life worker, a pediatrician, and an anesthesiologist or apheresis physician. These team members provide a safe harbor for the child to voice dissent. Each member of the team interviews the prospective donor—alone if the child is six or older—to discover any fears or misconceptions the child might have, as well as to gauge the child's willingness to proceed with the donation. If a member of the team has any concerns about the child's motivation or state of mind, a special task force of the Clinical Ethics Committee meets with the health care team to discuss the case.

Since the Minor Bone Marrow Donor Policy was adopted six years ago, the ethics committee has been called to review eight cases and has recommended against donation in only one case. A six-year-old child refused to give stem cells for her biological mother, whom she had not lived with for four years. The child's guardian requested that the ethics team support the child's decision not to donate; the ethics team concurred. This case illustrates two things: (1) our procedure allows a child the freedom to refuse to donate, and (2) our operative definition of family is not biological but relational.

This case triggered the formation of a multidisciplinary task force to review The University of Texas M. D. Anderson Cancer Center's approach to transplantations using donors of minor age. In creating a Minor Bone Marrow Donor Policy, the task force addressed three main concerns: (1) benefit to the recipient must be balanced with risk to the donor; (2) the child must have the freedom to refuse to donate; and (3) some mechanism must be in place to help decide who warrants a familial obligation.

Since the patient's health care team should focus only on benefiting the patient, having these team members weigh benefits and risks for the donor may represent a conflict of interest.

Despite the complicated issues surrounding bone marrow donation by minors, it is possible to develop a policy that protects child donors and gives them an independent voice in the process.

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