Bone Marrow Transplantation Makes Comeback at NIH

By Rich McManus

Rejected nearly 20 years ago by NIH because it was toxic, expensive and seemed to have very limited use, bone marrow transplantation from one person to another is currently enjoying a renaissance both on campus and extramurally.

The therapy—always difficult for patients but finding more and more applications recently—is now used in clinical studies at NCI and in collaborative studies involving Children's National Medical Center and the Clinical Center's department of transfusion medicine. The latter department is fast becoming a national leader in automated marrow processing.

Other evidence suggests that marrow transplantation, following an initial period of rejection at NIH, is finally engrafting in this posttransplant period.

"There have been very few advances in this field that have come without tremendous effort," said Dr. Ronald E. Gress, senior investigator in NCI's Experimental Immunology.

The Final Rule, a guideline for scientists and institutions that receive PHS funding for their work, defines and details responsibilities for handling possible misconduct in science. The rule also officially recognizes the Office of Scientific Integrity Review (OSIR), a new PHS unit created under the Office of the Assistant Secretary for Health, DHHS. It will coordinate misconduct activities not only at NIH but also throughout PHS.

OSI is a centralized PHS-wide operation," explained Dr. Suzanne Hadley, OSI acting deputy director. "We are responsible for the pursuit by OSI of monitoring and investigative functions to be carried out by individuals who are themselves scientists, knowledgeable about the methods and standards of science and committed to preserving the integrity of scientific inquiry. At the same time, the OSI's unique location effectively removes it from ties to particular institutes and programs.

Independence of action and dispassionate pursuit by OSI of monitoring and investigative functions are further assured by the OSIR, Office of Scientific Integrity Review.

Established by HHS and located in the DHHF Office of the Assistant Secretary for Health, OSIR will review actions taken by OSI, insuring the fairness and thoroughness of investigations in addition to imposing any necessary sanctions.

Already there has been a great deal of interest about OSI from the press and from the scientific community.

"We've been extremely busy," admits Hadley, recounting the various activities in which OSI has been engaged. "We've been
OSI

(Continued from Page 1)

responding to congressional subcommittees and meeting with major NIH, PHS and HHS components in order to build good working relationships within the federal sector.

According to Hadley, establishing credibility and rapport with the research community is imperative to the success of OSI. Ultimately, PHS’s handling of activities involving misconduct in science will have a substantial impact on the credibility of the country’s biomedical science industry and could influence the public’s perception of all research. So far, OSI has been received well.

“We feel good about the reception thus far,” said Hadley. “We’re making an active effort to get the word out about the OSI and to be proactive in consulting with institutions dealing with inquiries and investigations of possible misconduct.”

OSI philosophy could be stated, “Act instead of react,” the new unit is already exploring prevention and education as possible cures for the malady of misconduct in science. Said Hadley, “We want to stop problems before they start.”

Developing plans for implementation of the policies outlined in the Final Rule was one of the first goals of OSI. Insuring that those policies are responsibly fulfilled is OSI’s primary mission.

“Under the Final Rule, the grantee or applicant institution has primary responsibility for conducting inquiries and investigations into allegations of scientific misconduct. Institutions are responsible for protecting the privacy of those who raise questions. Equally, those who conduct investigations and those trying to prove misconduct cases will also need to protect the privacy of those who conduct investigations,” Hadley said.

The rule is not entirely an original document. In July 1986, when news about scientific misconduct and research fraud dominated headlines, PHS prepared and published interim policies that provided guidance to its agencies and to grant applicants and awardees for dealing with allegations and subsequent investigations. The rule combines those interim policies with regulations prescribed by Department of Health and Human Services Secretary Dr. Louis Sullivan.

Before OSI was born, another NIH body, the Institutional Liaison Office (ILO) in the Office of Extramural Research, coordinated policy issues, primarily those involving grantee institutions.

Since its establishment, OSI has been setting up its physical space (located in Bldg. 31, BIC wing) and necessarily expanding its staff, which currently consists of eight employees, most of them detailed from various PHS agencies.

OSI acting director Dr. Brian Kimes, for example, has 14 years of research grant and contract program experience in NCI; acting deputy director Hadley not only has substantial research and program administrative experience but also served for several years as NIMH’s misconduct policy officer. Others among OSI’s professional staff come from NIGMS, DRR, NCI and ILO.

Besides responding to the deluge of interest from Congress and the press, revising policies defined in the Final Rule and meeting with representatives from PHS and grantee institutions, OSI is reviewing a number of cases that were passed to its hands for action.

OSI’s responsibilities will include also the coordination of all institutional assurances. Assurances, required by the HHS secretary, are documents certifying that institutions that receive federal funding understand and comply fully with scientific misconduct policies outlined in the Final Rule.

One reason for the strong interest in scientific misconduct is increased publicity and public awareness. Hadley explains: “There definitely has been more visibility in recent years of scientific misconduct cases. A couple of cases—the Steve Breuning case at ADAMHA and the John Darsee case—were extremely publicized.”

There is one other group that will help OSI accomplish its mission—BID misconduct policy advisors (MPOs). MPOs are individuals selected from each bureau, institute or division to act as liaisons between OSI and employees with misconduct questions.

“The MPOs are very important to us,” said Hadley. “There are some critical things that we will need to do. The MPOs will be our advisors, our consultants and a large part of any communication between OSI and the BIDs.”

Meeting on the Mind’s Clock

A conference titled “Suprachiasmatic Nucleus: The Mind’s Clock,” will be held Oct. 10-12 at Lister Hill Auditorium, Bldg. 38A.

The meeting will take place from 8:30 a.m. to 5:30 p.m. each day and will be organized by Dr. David C. Klein, NICHD, 496-6915. Registration fee is $100. For more information call 986-4886.

Correction

High school biology teacher Carl Eugene Keels was misquoted in a story on page 1 of the Aug. 8 issue of the Record. Rather than asking his class, "How many of you have a parent who goes to work every day?", as was reported in the story, Keels said, "How many of you have a father who goes to work every day?" Several working mothers objected to the misreported quote.

New Telephone Book in Press;
X, Y, Z Missing from Old One

Dr. James B. Wyngaarden was left out of the white pages in the NIH Telephone and Directory sections before he resigned as NIH director. Someone must have known of his plans (extrasensory perception, perhaps) even before he knew.

"Not so," says Lois Crider, chief of NIH’s telephone and directory section. "The end of the W's along with all the X, Y, and Z's were left out of the white pages in the Spring 1989 phone book. Also, the entire National Institute of Mental Health was left out of the green pages identifying the institutes.

"It was a printer’s error," she quickly explains. "In fact, they (the printers) were supposed to print a supplement to correct these mistakes. But it looks like the new fall directory may be published before we ever get the supplement." The new directory was sent to the printers at the end of July.

"In the meantime," she says, "you can call the telephone operator and we will be happy to give you the number; everything is on the computer."

As the Record went to press, the supplements arrived and were being distributed. For extra copies, call 496-3586.

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The NIH Record reserves the right to make corrections, changes, or deletions in submitted copy in conformity with the policies of the paper and NIH.

The Record
AZT Shown To Slow Progress of Early HIV Infection

By Patricia Randall

Zidovudine, commonly called AZT, significantly slows progression of HIV infection when given to persons with early AIDS-related complex (ARC), according to results from a placebo-controlled, multicenter clinical trial supported by NIAID in collaboration with Burroughs Wellcome Co.

Department of Health and Human Services secretary Dr. Louis W. Sullivan hailed these results as offering new hope in the struggle against AIDS. "We are on the threshold of a time when advances in biomedical research will enable HIV-infected individuals to live longer, more comfortable lives," he said.

NIAID director Dr. Anthony S. Fauci reported that NIAID has stopped the study on the recommendation of the data and safety monitoring board reviewing the trial data. The trial had been under way at 29 units of the NIAID AIDS clinical trials group since August 1987. All study participants will now be offered zidovudine. The board recently reviewed trial data at its regular August meeting.

"For the first time, the benefits of anti-retroviral treatment for patients with early symptomatic HIV infection have been clearly shown," Fauci said. "In this study, significantly fewer persons receiving zidovudine progressed to advanced ARC or AIDS. This finding could extend treatment to an estimated 100,000 to 200,000 persons with early symptoms of HIV infection. It also emphasizes how critical it is that persons at risk for HIV infection be tested and seek prompt medical care."

The randomized, double-blind trial was coordinated by Dr. Margaret Fischl of the University of Miami. It included 713 HIV-infected persons having T4 cell levels between 200 and 800/mm³ and one or two HIV-associated symptoms such as oral thrush, chronic rash or intermittent diarrhea. Participants received either placebo or 200 milligrams of zidovudine every 4 hours (1,200 milligrams per day) over a period of 3 to 20 months. Fewer than 5 percent of the participants experienced serious side effects.

As of July 1989, 50 of the 713 participants had progressed to advanced ARC or AIDS. Of these, 36 participants were in the placebo arm of the study, whereas only 14 were in the zidovudine arm. The benefit of zidovudine was demonstrated only in those participants who had T4 cell counts between 200 and 500 when they entered the study.

"This study clearly shows that early intervention is important in HIV infection and that zidovudine is well tolerated in persons with early ARC," Fischl said.

FDA commissioner Dr. Frank E. Young said, "The FDA will work closely with the NIAID and Burroughs Wellcome Co. to translate these important results into wider availability of zidovudine to this category of symptomatic HIV-infected persons."

Zidovudine is manufactured by Burroughs Wellcome Co. and is available under the trademark Retrovir. Its effectiveness in extending the lives of persons with AIDS was first announced in September 1986. It was approved in March 1987 for treatment of Pneumocystis carinii pneumonia and patients with advanced ARC.

Savings Bond Drive Deemed Successful

Winners of the raffle of the NIH U.S. Savings Bonds drive were announced at an informal ceremony held recently at the Lister Hill Center.

Before announcing the winners, Ken Carney, NLM executive officer, thanked all those responsible for participating in the drive.

"The results establish that the bond drive was very successful," said Carney, adding, "Each year, the goals of the department are optimistically high. This year, NIH employees have indeed looked out for their own financial futures."

Among the results were 50 percent increased allotments. "This represents 50 percent of the goal set by the department," said Carney. As for new bond buyers, the results were 60 percent.

Before announcing the winners of the raffle, Carney announced the photo contest winner.

Dr. Huber Warner of NIA won a $100 U.S. Savings Bond after correctly identifying the area/buildings of eight photos and naming the hidden phrase: "Buy Bonds."

The drive also included a raffle that awarded more than a dozen prizes donated by local businesses.

"I don't believe it!" said raffle winner Cheryl White, who captured two tickets to an Orioles game donated by the NIH R&W. White, also a savings bonds canvasser, said, "I came to the drawing to listen for names from my entire area and ended up hearing my own name. I hope we get good seats," she said.

Carol Cronin

Bond Drive Raffle Winners

Ann Adams/CC—NIH jogging outfit donated by the NIH R&W
Charles Butler/CC—$50 bond donated by the NIH R&W
Donna Dean/DRG—$50 gift basket full of exotic gourmet foods donated by Sutton Place Gourmet
Dorothy Harrison/DRG—Royal retreat weekend at Crowne Plaza Holiday Inn, Rockville
Ed Farley/DRG—$35 Gift certificate from O’Donnell’s Restaurant
Marie Glass/NLM—Four tickets to regular Washington Capitals game
Betsy Hebb/DRS—An evening for you and 10 of your friends at a K-B Theater donated by NIH R&W
Nancy Luppino/DRG—Four tickets to regular Washington Bullets game
Edwin May/CC—$15 gift certificate from Hechinger’s
Esther Peterson/NCI—Complimentary weekend night for two at Guest Quarters Hotel, Bethesda
Debbie Stitley/NCI—Complimentary Sunday champagne brunch for two at the Hyatt Regency, Bethesda
Denise Stoneman/NLM—Brunch for two at the Bethesda Marriott’s Kona Kai Restaurant
Cheryl White/NLM—Two tickets for an Orioles game donated by the NIH R&W
with a welcome by the staff of the NIH Visitor Information Center. The group of 75 was divided into smaller groups of 20, each of which had a translator. Though all of the students spoke English, their levels of proficiency varied. Included among the group were several high school student ambassadors, test-taker leaders of languages or international studies.

Walking beside this reporter was Anna, a 17-year-old from Moscow who learned to speak English 9 years ago. With curly brown hair and brown eyes, Anna was dressed in earth tone jeans and jacket. A student at Moscow's Power Institute, she is the daughter of parents who are both engineers.

This is Anna's first visit to the U.S. When asked about her impressions of America, she exclaims, "I was really shocked. I did not expect it to be so beautiful." Asked about her impression of American people, Anna replies, thoughtfully, in three words: "polite, hospitable, communicative." Anna wants to return to America next year to study computer science at the State University of New York at Stony Brook. "What do your parents think of this?" I ask. Anna gives me a sheepish smile. "They don't know about my idea yet, for it just came to me this week. But I think since it is a great idea, they will understand.

We visit the lab of Dr. John Daly, chief of the Laboratory of Bioorganic Chemistry, NIDDK. Daly talks about his research on Dendrobates auratus, a highly toxic frog found in South America. The little frogs come in a variety of colors—red, green, yellow, blue. Some are black-spotted and so toxic that, by rubbing the backs of the frogs with a dart tip, the natives yield enough poison for a particularly deadly blow dart. The frogs are being studied for their possible pharmacological benefits.

Concluding his talk, Daly leaves the room and reenters carrying a small terrarium that holds three frogs. Removing the glass cover, Daly reaches into the terrarium and takes out a green frog that he holds between his thumb and forefinger. This select group of frogs, Daly explains, were bred in captivity and are nonpoisonous. Thus, the mystery as to the source of their toxicity remains unsolved.

Our next stop is NLM. On the way, I meet Alex, who pushes back on his white golfer's cap, blushing, as I ask if he would mind talking with me. An 8th grader from School 171 in Moscow, Alex wants to study chemistry at the university. His interest in chemistry began when he was in 5th grade.

"My friend bought a chemistry set and it came with a book. We tried to understand the book. After that, my friend's mother got an idea for us to go to Pioneer Palace." A place where young people go to participate in after-school programs, Pioneer Palace has different "circles" for students at various levels of study in such fields as the arts, chemistry, computer science and astronomy. "There are 50 students in the chemistry circle. This includes general and organic chemistry," said Alex. Asked why he wants to become a chemist, Alex becomes very serious. "I like to train my mind to think about complex things," he says. "I like the process of synthesis and making a good blend." What will you do with this knowledge? I ask him. Alex's reply is certain: "Help people to live in this world. Improve the conditions of life for people."

At NLM, information officer Bob Mehnert demonstrates the Grateful Med system, performing a search of medical literature. References flash across the giant screen. A wave of whispering fills the auditorium after Mehnert tells the group that a search of the Grateful Med system reveals 1,497 articles that deal with medicine in the U.S.S.R.

Our last stop is the Clinical Center. The group is suddenly silent when told that there are young cancer patients and pediatric AIDS patients here. Someone comments, "If you ever come to Moscow, please visit me," he says earnestly. "And can we agree to exchange between our scientists from Moscow University and your scientists, here at NIH? If we can exchange, we can combine our efforts."

"Oh, and one more thing," he says with a smile, "If you ever come to Moscow, please stop at my house." He hands me his address, steps briskly on the down escalator and waves goodbye. "Nice to make your acquaintance," he says and fades into the crowd.

**NIDR Needs Volunteers**

NIDR seeks patients suffering from dry mouth caused by radiation therapy in the head/neck region. Patients must be between the ages of 18 and 70 and have no cardiovascular, respiratory, hepatic or gastrointestinal problems. For further information call Alice Macynski, 496-4371.
William Friedewald To Leave NIH After 24 Years

By Bill Hall

Dr. William T. Friedewald, the first NIH associate director for disease prevention, will resign his post and retire from the Commissioned Corps of the U.S. Public Health Service on Aug. 31 after 24 years of service.

He and his family will move to New York City where he will assume the position of chief medical director for the Metropolitan Life Insurance Co. He will oversee all of the company's medical activities and direct its health promotion and disease prevention education efforts. In addition, he will work with the company's programs in "managed health care."

Friedewald came to NIH in 1965 and spent all but 2 years of his PHS career here. Before his appointment as an associate director, he held a number of positions at NHLBI. In 1973 he became the first chief of NHLBI's Clinical Trials Branch. In 1979 he was appointed associate director of the Clinical Applications and Prevention Program in the Division of Heart and Vascular Diseases, and in 1984, he was named the first director of the Division of Epidemiology and Clinical Applications.

In retrospect, Friedewald's greatest satisfaction came from developing new organizational units and the science activities under them.

"To me, my greatest sense of accomplishment came from my work in developing new programs, such as the Clinical Trials Branch, and in bringing together several existing NHLBI programs to form a new administrative unit as I did with the Division of Epidemiology and Clinical Applications," he said.

To further expand NIH's interest in prevention research, NIH director Dr. James B. Wyngaarden established the congressionally mandated position of associate director for disease prevention in 1986 and named Friedewald to the post. In this position, Friedewald had the responsibility of overseeing the Office of Disease Prevention, the nutrition coordinating committee office, which later became the Division of Nutrition Research Coordination, and the Office of Medical Applications of Research (OMAR).

"We've been able to get a lot of things done in the time I've been here. We established the nutrition division, and we made sure OMAR continued working on solid ground. In the area of prevention, we now have an annual report of ongoing prevention activities in each BID, and we have an active disease prevention and health promotion seminar series in place," he said.

In providing advice for his successor,

Dr. William T. Friedewald

Friedewald said that the area of prevention will need the most attention in the future.

"I'd like to see an NIH-wide employee disease prevention program set up, and we have begun the early steps to establish such a program," he said.

Having been at NIH for 24 years, Friedewald has made many friends, and it is they who will miss the most. "I grew up as an adult here, I met my wife here, and all three of my children were born across the street at Bethesda Naval Hospital," he said. "The NIH is a wonderful place to work with a truly exciting group of people and important ongoing activities."

Although Friedewald says he is ready for changes in career, location and lifestyle, one of the main reasons for his leaving is financial. He said, "I have a daughter in college, a son who will start college this fall, and a second son who is starting high school in a private school. This creates an enormous financial need. The efforts by the NIH and administration to improve the pay scale for the federal employee at NIH are critical to retaining and, for that matter, attracting a good staff. This is especially true in the Washington area with its high cost of living and for people with children of college age. If it weren't for the money side of it, I'd probably stay at NIH."

Some people may cringe at the thought of living in New York City, but the Friedewalds are anxious and excited to move there. "We moved from Bethesda into downtown Washington several years ago. We love the urban setting, and we get to spend more time together as a family. Plus, I don't have to cut the lawn anymore and I no longer own a rake!"

Women's Equality Day Highlights
Career Enhancement Network

Aug. 26 is Women's Equality Day, which commemorates passage of the 19th Amendment to the U.S. Constitution. Women gaining the right to vote (suffrage) was a major goal of the women's movement from its inception in the early 1800's until the amendment's passage in 1920. With the right to vote came increased opportunity for women to improve their status in society. Education and employment too have yielded vast improvements in women's opportunities.

Improved employment opportunity for women is the overall goal of the women's advisory committee of the Federal Women's Program in the NIH Division of Equal Opportunity. One of the women's advisory committee's methods of increasing women's employment opportunity has been the Career Enhancement Network (CEN), which was established in 1987. The committee is using the occasion of Women's Equality Day to remind NIH employees of the CEN.

CEN is a network of NIH employees who serve as volunteer consultants or informal mentors for other NIH employees who desire information or assistance in an occupational field or specialty. CEN members are volunteers who have agreed to donate varying amounts of time on subjects that range from administration to veterinary medicine.

Employees desiring assistance or information contact the Federal Women's Program manager or a women's advisory committee representative. The employee receives a referral, which is made on an individual basis to best match the employee's needs with a CEN volunteer's expertise; the employee then contacts the CEN member. Meetings occur at the convenience of the two persons, usually during duty hours. Supervisors are encouraged to arrange work schedules so that employees can utilize this service for reasonable periods of time.

Reasons that employees may seek CEN involvement vary greatly. Some may wish advice on setting and achieving career objectives or guidance concerning entrance or advancement in a particular job series. Others may want to learn about career pathways or the best approach on a special project in a new field. The CEN process is primarily designed to meet short-term needs, but employees and CEN members may even develop long-term mentor relationships.

For more information about CEN, contact a women's advisory committee representative or the Federal Women's Program manager, 496-2112.—Linda Dugger
MARROW

(Continued from Page 1)

ogy Branch and an expert in the immunological aspects of BMT. "All of the success has been gradual."

Because it involves reconstitution not only of a patient’s entire blood supply, with all its complexity, but also his or her immune system, and because marrow is immunoreactive itself, BMT is the most difficult of all transplantations. More than heart, liver, kidney or other organ transplantation, BMT relies on a close match in the tissues of donor and recipient.

Bone marrow, a tissue that looks like thick blood, resides at the core of the larger bones in the human body. A rich repository of developing blood and immune cells, marrow is the font of a wholly competent hematopoietic (or blood) and immune system.

At present, BMT is the therapy of choice for certain patients under age 55 who have aplastic anemia, severe combined immune deficiency, or a variety of leukemias including acute lymphocytic leukemia, chronic myelogenous leukemia and acute non-lymphoblastic leukemia.

Unfortunately, only about one-third of the patients who have these diseases also have a relative whose tissue would make a suitable match for the patient. A transplant from an unrelated donor involves two potential risks: that the host’s immune system would recognize the new tissue as foreign and attack it (graft rejection), or that the graft would regard the host as foreign and mount an attack (graft versus host disease or “GVHD”).

To surmount these obstacles, donors are sought whose HLA (human leukocyte antigen) types are as closely matched to the recipient as possible.

In terms of simple tissue matching, the best marrow donor is a person who could donate to himself. In this situation, graft rejection and GVHD would not occur. This happens in a procedure called autologous (self-donated) BMT, a therapy that was never abandoned by NCI. After collecting and storing the patient’s own bone marrow, physicians treat the patient with drugs and radiation to eliminate all of the cancer they can reach at doses that destroy the patient’s remaining bone marrow. They then “rescue” the patient by returning his or her stored bone marrow. This process allows patients to tolerate what would otherwise be lethal doses of chemotherapy. In cases where cancer cells may be present in the bone marrow, additional procedures are carried out to “purge” the marrow of these unwanted cells.

In many diseases, however, the patient’s bone marrow is affected to the extent that autologous BMT is not possible, and a bone marrow donor must be found. This is called “allogeneic” (nonself) BMT. The ideal donor is an identical twin; both donor and recipient will be mirror images, genetically, of each other. Unfortunately, most patients do not have an identical twin.

The next best choice is a related donor whose HLA is closely matched to that of the recipient; a good match has a one in four chance of occurring between siblings. Partial matches that occur between parent and child or among siblings may be used, but frequently lead to rejection or GVHD.

Thanks to investigators such as Ron Gress, however, new studies using partially matched or even mismatched bone marrow may lead to an exponential expansion of the pool of available donors for allogeneic BMT.

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NIH colleagues Dr. Elizabeth J. Read and Dr. Ronald E. Gress discuss with Quinones details of a BMT case involving a 10-year-old leukemia patient.

A Brief Clinical History of BMT

The clinical history of bone marrow transplantation (BMT) goes back several decades. Each advancing year brings with it some refinement either of technique or application.

Begun as a treatment for aplastic anemia and severe combined immune deficiency (SCID), a disease recognized during infancy, BMT is now seen as a possible therapy for AIDS, assuming antiviral treatments improve.

The survival rate for aplastic anemia patients undergoing BMT is about 50-70 percent; in SCID, the rates are slightly higher—70 to 80 percent.

BMT was next used for a variety of acute and chronic leukemias.

When it was first employed against acute leukemia in the early 1970’s, allogeneic BMT was less than 10 percent effective.

By the mid-1970’s, BMT could cure about half of the patients with acute myelogenous leukemia (AML) who had low rates of relapse and controlled disease.

Its most recent application has been against chronic myelogenous leukemia (CML), a cancer that can’t be cured by drugs and the most common form of leukemia for which BMT is currently recommended. Some 50 to 60 percent of CML patients are cured by BMT; debate continues, however, about when, in the course of a chronic disease, to do a transplant.
Marrow Transplantation

Timing is also a major clinical issue in two other acute leukemias for which BMT is a therapy.

Acute lymphoblastic leukemia (ALL) can be cured 50 to 70 percent of the time with chemotherapy. If the disease recurs, drugs are usually used to induce a second remission. During second remission, BMT is recommended. Its cure rate at this stage is between 40 and 50 percent. Physicians are currently debating when BMT may be appropriate during first remission in ALL.

AML, also known as acute nonlymphoblastic lymphocytic leukemia (ANLL), is becoming somewhat more responsive to BMT in the 1980's. If performed during first remission, the therapy is 50-60 percent effective.

Other diseases treatable by BMT include both Hodgkin's and non-Hodgkin's lymphomas, Fanconi's anemia, a variant of aplastic anemia that is probably hereditary and that carries a high long-term risk of leukemia; myelodysplastic syndromes, a variety of nonhomogeneous, preleukemic problems; Cooley's anemia (thalassemia major), against which BMT is especially effective if done early in the patient's life.

"More and more diseases are amenable to BMT," observes Dr. Paul McCurdy of NHLBI, "maybe even sickle-cell anemia."

Quinones.

He explains that today's transplant, which involves a half dozen processing steps at NIH, will be the second that his young patient has undergone.

"The first one involved a little bit of rejection," he said. Rather than wait through a prolonged period of slow engraftment during which the patient would be vulnerable to infection, he decided to "boost" the patient's marrow with a second transplant. Since neither of the girl's two siblings were identical matches, the father was enlisted as donor. Out of six places on chromosome 6 that are important for tissue matching (paired sites at the so-called A, B and DR histocompatibility loci), dad and daughter share four.

Carter takes the bag of what looks like thick blood and divides it into three smaller bags that he inserts into a centrifuge. The spinning action separates the marrow into layers, the topmost one being a yellow rime of fat.

"Marrow has a lot of fat in it," explains Read, adding that older donors tend to have fattier marrow.

Below this top layer there is a layer of liquid plasma, and then a layer of cells that appear deep red toward the bottom of the collection bag.

After skimming off the fat, Carter reduces the volume of the suspension and eliminates unwanted cells through a process called mononuclear enrichment.

"It's sort of like separating the wheat from the chaff," explains Read.

By putting the fatless marrow through an apheresis machine, most of the packed red cells, platelets and granulocytes can be removed from the suspension, leaving lymphocytes, monocytes and bone marrow progenitor cells.

These latter cells, sometimes called stem cells, comprise only about 1 to 5 percent of the marrow but are its most critical component; from them will arise a mature and incredibly complex system of blood and immune cells.

Speaking of complexity, the apheresis machine is itself a wonder of fluid mechanics, classical physics and good old American plastic.

As Carter explains, the size and shape of metal chambers encasing the plastic-jacketed marrow as it spins in the machine's centrifuge help separate cells into layers.

"The strength of the centrifugal field and the shape of the chambers yield the desired layers," he said.

Cleverly threaded lengths of clear plastic hose permit unwanted cells to be siphoned off and the important cells to be retained. Because of the rate at which the plastic tube bundle spins in relation to the marrow, fluid flow is uninterrupted and no tangles complicate the process.

Notes Quinones, "Prior to our using this apheresis machine, the mononuclear enrichment process took 6 hours and several technicians—now it takes less than 2 hours and can be done by one person. It is also more sterile because it involves a closed system rather than many test tubes."

The physics don't get any easier as the marrow enters the next phase of automated processing. While mononuclear enrichment yields a single plastic bag of highly concen...
Gress. The proper number of T cells would assist in engraftment, provide the so-called "graft vs. leukemia effect," which protects against leukemic relapse, and contribute to immune system reconstitution.

In order to arrive at the precise number of lymphocytes needed for successful BMT, a process known as elutriation is employed. At the heart of an elutriator is a clear plastic chamber that spins inside a centrifuge. The proper number of T cells would process known as elutriation is employed. At

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In order to arrive at the precise number of lymphocytes needed for successful BMT, a process known as elutriation is employed. At the heart of an elutriator is a clear plastic chamber that spins inside a centrifuge.

"It's a physical method for separating T cells," explains Carter. "The cells in the chamber are exposed to two forces—centrifugal and fluid flow." Marrow and saline solution sail through the elutriator together at a variety of flow rates that result in "fractions"—individual bags of marrow concentrate that contain greater and lesser numbers of T cells.

"Elutriation is very gentle to cells," says Read. "Other methods of T cell removal are rougher on the bone marrow cells."

Using flow cytometry (the quick method) or a limiting dilution assay (longer, but more sensitive), researchers in the Experimental Immunology Branch count the number of T cells in each fraction and help Quinones determine which is best to add back to the patient.

Read knows of cases where infants under a year old were the most suitably matched donors for elder siblings in need of BMT; Quinones once harvested marrow from a 9-month-old.

**Female Volunteers Wanted**

The Biological Psychiatry Branch, NIMH, is currently seeking female volunteers between the ages of 45 and 53 to participate in studies of menstrual cycle irregularity and the menopause.

Volunteers must be free of medical illnesses and not taking any medication on a regular basis.

Volunteers will complete daily rating forms and will be asked to participate in one of several protocols; pay will be in accordance with the duration of each visit and the type of protocol. For further information, call 496-9675. □

JNCI News Team Receives Award

In recognition of their "extraordinary contributions" to the Journal of the National Cancer Institute news section, 14 NCI staff members received a group special achievement award recently.

The recipients are Linda F. Anderson, Gertrude P. Anthony, Florence S. Antoine, Maggie M. Bartlett, Elaine N. Blume, Francis X. Mahaney, Jr., Nancy S. Munro, Eleanor O'D. Nealon, Patricia A. Newman, Kathryn T. Ruddon, Kara L. Smigel, Corrine F. Vaccieri and Clarissa K. Wittenberg, all of the Office of Cancer Communications, and Dr. Mary C. Knipmeyer, who had been NCI's legislative liaison. Each received a certificate and a cash award.

The news section became a part of the journal in March 1988. The recent award recognizes the extra work done by these NCI employees, which has contributed to the success of the new journal, according to J. Paul Van Nevel, NCI's associate director for cancer communications.

Last year, the old JNCI combined with Cancer Treatment Reports, another NCI journal, to form the new, biweekly journal.

Comments from recipients of the journal reflect the popularity of the news section. Dr. Leo T. Furcht of the University of Minnesota Medical School said he likes the section because, "It keeps me in touch with what other people are doing in fields outside my own area."

Former NCI director Dr. Frank Rauscher, Jr., currently with the Thermal Insulation Manufacturer's Association, said, "Scientists need to know what is going on with the budget process in cancer research and in the sociological processes ... the news section provides the information." □
Dr. James Balow Named NIDDK Clinical Director

Dr. James E. Balow, chief, kidney disease section, NIDDK, has been named clinical director of NIDDK. He has been acting clinical director for the institute since August 1988.

A leader in the field of nephrology, Balow has been a senior investigator in NIDDK since 1977 and chief of the Clinical Center's nephrology service since 1976. He also served as acting director of NIDDK's Division of Kidney, Urologic, and Hematologic Diseases from 1983 to 1984.

"Dr. Balow has contributed in a very substantial way to the quality of care in the Clinical Center," said NIDDK director Dr. Phillip Gorden. "With his appointment, our clinical research program will continue to benefit from his scientific talent and his excellent administrative skills."

Balow and his colleagues in NIAMS were among the first to show that cytotoxic drugs were superior to prednisone in treating the kidney disease of systemic lupus erythematosus (SLE). Their studies in lupus nephritis also showed that intermittent, high-dose cyclophosphamide was more effective and had fewer side effects than standard treatment with daily low-dose cyclophosphamide. Balow also developed what has become a standard method of analyzing kidney tissue, which has enhanced the ability to gauge the prognosis of SLE patients. For his advances in lupus nephritis, he was the co-recipient of the 1983 Robecchi International Prize.

Balow's longstanding research interests focus on disorders of immunoregulation and mechanisms of immunosuppression. His studies have examined the action of corticosteroids and cyclophosphamide in experimental models and in human diseases. He and his colleagues in the kidney disease section have also described and studied several white cell abnormalities in patients with SLE and other forms of glomerulonephritis.

Balow is currently working on new approaches for treating lupus nephritis and other forms of immunologically mediated kidney diseases using immunosuppressive drugs such as cyclophosphamide and cyclosporine A. In other research, he is exploring the causes and treatment of membranous nephropyathy, which often leads to nephrotic syndrome (nephrosis) in adults.

He has authored and co-authored more than 140 scientific articles and book chapters. With colleagues in NCI, Balow contributed to landmark papers on treating the renal and metabolic complications of the acute tumor lysis syndrome in patients with lymphomas that are extremely sensitive to treatment. He is board certified in internal medicine and is a diplomate in nephrology.

After receiving his M.D. degree from the University of Minnesota Medical School in Minneapolis in 1968, Balow completed his training in internal medicine and nephrology at Georgetown University Hospital. In 1972, he joined NIH as a clinical associate in NIAID's Laboratory of Clinical Investigation.—Eileen Corrigan

Introduction to (NIH's) IRS

An introduction to the Inquiry and Reporting System (IRS) course will be taught by Carol Bleakley, DRG/ISB, 496-7711. The course will be taught Oct. 11, 12, 13, 19 and 20 from 9 a.m. until noon in Bldg. 12A, Rm. B45. Potential students should have completed the basic Wylbur course.

Students will learn how to extract data from the Information for Management, Planning, Analysis and Coordination (IMPAC) database. □

Dr. George Counts To Head New NIAID Branch

An authority on infectious diseases, Dr. George W. Counts has been named head of the new Clinical Research Management Branch in the treatment research program of NIAID's Division of AIDS.

"Dr. Counts brings enormous experience to this new position," said Dr. Daniel F. Hoth, DAIDS director. "He will strengthen our efforts to make each of the AIDS clinical trials units more effective, as well as lead our initiative to enroll patients from more diverse populations into clinical trials, especially African-Americans, Hispanics, women and intravenous drug users."

Prior to coming to NIAID, Counts was a professor of medicine at the University of Washington in Seattle, where he has been on the faculty since 1975. From 1985 to 1989, he also served as director of the clinical microbiology laboratory at the Fred Hutchinson Cancer Research Center.

Counts has published extensively on hospital-associated infections, on infections in immunocompromised patients and on the role of antimicrobial agents in the prevention and treatment of bacterial, fungal and protozoan infections. He is a member of the editorial board of the American Journal of Infection Control.

A diplomate of the American Board of Internal Medicine, Counts is a fellow of the Infectious Diseases Society of America and a member of the Society of Hospital Epidemiologists of America.

In 1983, he served as president of the 6,000-member Association for Practitioners in Infection Control. While in that office, he directed the process that resulted in a national certification examination for infection control practitioners.

Counts received his bachelor of science degree in 1957 and a master's degree in microbiology in 1960 from the University of Oklahoma. He earned his medical degree in 1965 from the University of Iowa.

His postgraduate training was completed at the Ohio State University Hospital, Columbus, and the University of Washington in Seattle. He was assistant professor at the University of Miami in Florida before accepting a position with the University of Washington. □
Human Genome Program Committee Named

Twelve members have been named to NIH's program advisory committee on the human genome.

The committee will advise the NIH director and NIH associate director for human genome research, Dr. James D. Watson, on the new NIH research initiative to map and sequence the human genome. It will help ensure coordination of NIH's human genome program with the private sector including industry, with various national and international scientific organizations, and with other federal agencies including the Department of Energy, the National Foundation and the Department of Agriculture.

The members include representatives from academia, industry and nonprofit organizations. Their terms are staggered, and range from 1 to 4 years.

The committee will advise Watson and NIH on how to organize and carry out this endeavor, which will mobilize the talents of scientists worldwide, to map and sequence the human genome and the genomes of important model organisms. Important components will also include training of scientists and provision of necessary resources. The advisory committee also will consider the massive data processing and data storage requirements that will be necessary to handle the knowledge gained through this program, as well as ethical and legal issues that may arise in the future.

Scientists have estimated that the total cost of the human genome initiative could be $3 billion over the next 20 years. The president's budget for NIH in FY 1990 includes approximately $100 million for this project.

Gene mapping, the process of determining the locations of genes on chromosomes, helps scientists understand inherited disorders and may lead to new ways to diagnose, treat and prevent such disorders. Genome analysis involves the development of new tools for and approaches to the study of the genomes—the complete genetic endowments—of humans and other organisms such as bacteria, viruses, plants and animals. Comparisons between the human genome and those of other organisms will help provide understanding of the function of the human genes.

The committee will be chaired by Dr. Nor­ton D. Zinder, professor at Rockefeller University. Serving as executive secretary will be Dr. Elke Jordan, director, NIH Office of Human Genome Research.

Members of the committee are: Dr. Bruce M. Alberts, chairman, department of biochemistry and biophysics, University of California, San Francisco; Dr. David Botstein, vice president-science, Genentech Inc.; Dr. Jaime G. Carbonell, associate professor, computer science department, Carnegie-Mellon University; Dr. Joseph L. Goldstein, chairman, department of molecular genetics, University of Texas; Dr. Leroy Hood, chairman, division of biology, California Institute of Technology; Dr. Victor A. McKusick, university professor, division of medical genetics, Johns Hopkins Hospital; Dr. Maynard V. Olson, professor, department of genetics, Washington University School of Medicine; Dr. Mark L. Pearson, director, molecular biology central research and development department, du Pont Co.; Dr. Cecil B. Pickett, executive director of research, Merck Frost Centre for Therapeutic Research; Dr. Philip A. Sharp, professor and director, Center for Cancer Research, Massachusetts Institute of Technology; and Dr. Nancy S. Wexler, president, Hereditary Disease Foundation and associate professor, department of neurology and psychology, Columbia University.

Mays, NCI Researcher, Dies

Dr. Charles W. Mays, 59, a radiobiologist at the Radiation Epidemiology Branch, National Cancer Institute, died of cancer Aug. 3 at Washington Hospital Center.

Mays, a leading radiobiologist at NCI, was a specialist in the area of cancer risk from exposure to ionizing radiation. He had served on National Academy of Sciences committees on biological effects of ionizing radiation and federal research on its biological and health effects. From 1978 to 1983, he was chairman of the scientific advisory committee to the United States Transuranium Registry.

He was author or coauthor of more than 185 scientific papers, 75 research abstracts and 164 technical reports and was editor of two books on the radiobiology of internal emitters.

Mays, who lived in Gaithersburg, was born in Corsicana, Tex. He served in the Army during the Korean War and was awarded a Bronze Star.

He graduated from the University of Utah, where he also received a doctorate in physics. He was physics group leader in the radiobiology laboratory at Utah and research professor of pharmacology until 1987, when he moved to the Washington area and joined the staff of NCI.

In 1962, he was among the first to express concern about possible detrimental effects to Utah residents of radioactive fallout from the Nevada atomic bomb test site.

In 1988, Mays received the Distinguished Scientific Achievement Award from the Health Physics Society.

He was a long-distance runner and enjoyed hiking.

Survivors include his wife, Desiree Mays, and their two sons, David and Rory Mays, all of Gaithersburg; three daughters of his first marriage, Shelby Box, Sharon McGough and Susan Kinsel, all of Salt Lake City; and nine grandchildren.

Free Family Portraits

As part of its ongoing program to enhance employee benefits, R&W has made arrangements with Executive Color Studios to provide any NIH employee, contractor, retiree, etc. with a free 10" x 13" canvas family portrait. Sittings will be scheduled from 1 to 8 p.m. on Sept. 16 only, in the Clinical Center's Lipsett Amphitheater.

To schedule your appointment, call Kelly in the R&W office at 496-6061. A limited number of sittings can be scheduled, so call early to ensure availability.
TRAINING TIPS

The NIH Training Center of the Division of Personnel Management offers the following:

**Courses and Programs**

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<td>cost to NIH employees for these hands-on sessions. The</td>
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NOW AVAILABLE ON SHARE TRAINING FY 89 Training Center courses. Access Wylbur and enter SHARE TRAINING. First time users only, enter:

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**Hydrofluoric Acid First Aid**

Several burns involving hydrofluoric (HF) acid have recently been reported to the Occupational Medical Service (OMS). HF in gas or liquid form is extremely corrosive and can easily penetrate the skin or mucous membrane. It acts by coagulating protein and may cause serious injury as it diffuses into the tissues. Damage, however, may not be readily apparent. To help reduce the extent of the injury it is important to institute first aid measures following a spill or splash.

There are three steps involved in first aid at the worksite: Immediately wash the skin and/or eyes with water for 15 minutes; apply a 2.5 percent calcium gluconate gel to skin to limit tissue damage (Omit this step for eye treatment); report to the OMS clinic (6th floor clinic, hours 8 a.m. - 12:30 a.m. weekdays) or afterhours call the fire department emergency number 116 for transport to Suburban Hospital emergency room.

First aid kits with 2.5 percent calcium gluconate gel are available to all HF users from OMS. Employees who use HF should obtain a burn kit by contacting the OMS triage nurse, 496-4411.

**Judo Beginners Class**

The NIH Judo Club will hold its fall beginners class on Tuesdays and Thursdays from 6:15 to 7:30 p.m. starting on Tuesday, Sept. 12 at the Malone Judo Center in Bldg. 31C. The cost is $35 for 10 weeks. For more information contact Stephanie Harrison, 496-9490.

**Volunteers Needed for Test**

Researchers at NIH are testing a new vaccine against herpes simplex virus. People who have never had either oral or genital herpes are sought. Interested, healthy heterosexual people, ages 18-35, may call 496-1836 for information.

Recognition awards were presented at the recent R&W annual meeting to (front row, from l) Alan Moore, R&W president; Erny & Liz Beile, Special Love Ski Programs; Myra Darrow, Camp Fantastic Barbecue; back row (from l) Margaret Foster, NIH R&W Theatre Group; Clare Markham, R&W executive council; Deborah Parshall, NIH Sailing Association; Mary Roberts, Friends of the Clinical Center. Award winners not pictured: Robert & Elaine Sose and Steve & Brenda Wood, Special Love Ski Programs; Mary Ann Williamson and John Spagno, NIH R&W Theatre Group; Daniel Zaharko, NIH Sailing Association; Ed Wellner, NIH R&W Tennis Club; Tom Roach, NIH Health's Angels Running Club.

Evan Major (r), representing the campers, helped throw out the first ball at the “Fantastic Night” with the Baltimore Orioles, recently. At a bullpen party before the game, players joined the group and signed autographs. The names of the campers were also displayed on the lighted scoreboard. More than 500 persons attended the game and approximately $2,000 was raised to help fund Camp Fantastic, a summer camp for kids with cancer. The fundraiser is an annual event sponsored by the R&W Association at NIH.
High School Sophomore Jumps to College Freshman

By Anne Barber

From Singapore to Washington, D.C., and then on to Chicago — 15-year-old Chin-Shan Chuang is moving forward fast.

Chuang, a summer intern working in the tumor biology section of NCI's Laboratory of Biology, is here on a Katherine Dulin Folger Summer Scholarship from the D.C. division of the American Cancer Society. The program sponsors 20 high school students in laboratories at local universities and government research institutions. A stipend of $500 is given for their daily travel and lunch expenses. The students are required to submit a typed report at the end of the program and arrange a cancer education program for their school.

Chuang, however, will not have much time to produce his cancer report because on Oct. 2, he leaves for the University of Chicago. While a sophomore attending St. Alban's School last year, he applied to the university through its early admissions program. He took the SAT's, completed the application forms and placed them in the mail last April. "In June, the university started calling my teachers and in July I received my letter of acceptance."

A native of Singapore (his mother and father still live there), Chuang came to Washington to attend St. Alban's for his freshman and sophomore years. Receiving early admission to college is nothing new to his family; both his brothers graduated early. "In fact," he says, "my brother in New York was the youngest graduate of New York University (3 years early)."

Chuang (his friends call him Sean) chose NIH because of its reputation as one of the largest research institutions around. Last summer, he was named "Scholar of the Week" by the Johns Hopkins University Center for Talented Youth during his studies in chemistry at Scripps College in California.

According to Dr. Charles H. Evans, chief of the tumor biology section, Chuang is investigating the secretion of leukoregulin, a cytokine and immunologic hormone, that was discovered in his laboratory. "He is participating in experiments to determine the time of leukoregulin secretion after stimulation of normal human lymphocytes."

"In fact," Evans continues, "Chuang is working on something new. He is studying the rate of leukoregulin secretion by cells from when it first appears to when it reaches its peak. This has not been done before."

Chuang is working with Dr. Esme Farley, a Fogarty visiting fellow from whom he has learned a variety of assays. "This reflects the range of his abilities," Evans continues. "He is quite good not just for a high school student, but for a college student also."

"I picked cancer because my main concern was to get an overall view of research and not go into anything specific," Chuang says. "This program gives me a pretty good idea of what research is really like. I'm actually doing something worthwhile and getting hands-on experience."

According to Evans, the laboratory frequently has interns for short periods of time. "We make the work opportunity available when we can," he says. "We try to give the students current research so they can actually see what NCI is doing. They really get to see the wave of new research."

"Chuang," Evans continued, "absorbed every opportunity we offered. He attended seminars and cancer rounds. We trained him in chemical and laboratory safety. He understands what he is doing extremely well and is always busy working on something."

"As happens when all our other interns enter into our office, we didn't know much about him. As it turned out, Chuang proved to be very exceptional. I hope he found this job stimulating. If we are going to get young people interested in science we need to offer them this opportunity as much as we can. The financial incentives aren't as appealing as other careers."

As for Chuang, "This job gave me the opportunity to participate and evaluate the experimental process of research first-hand. It was great. I'm not sure yet what my major in college will be but it will definitely be math or science."