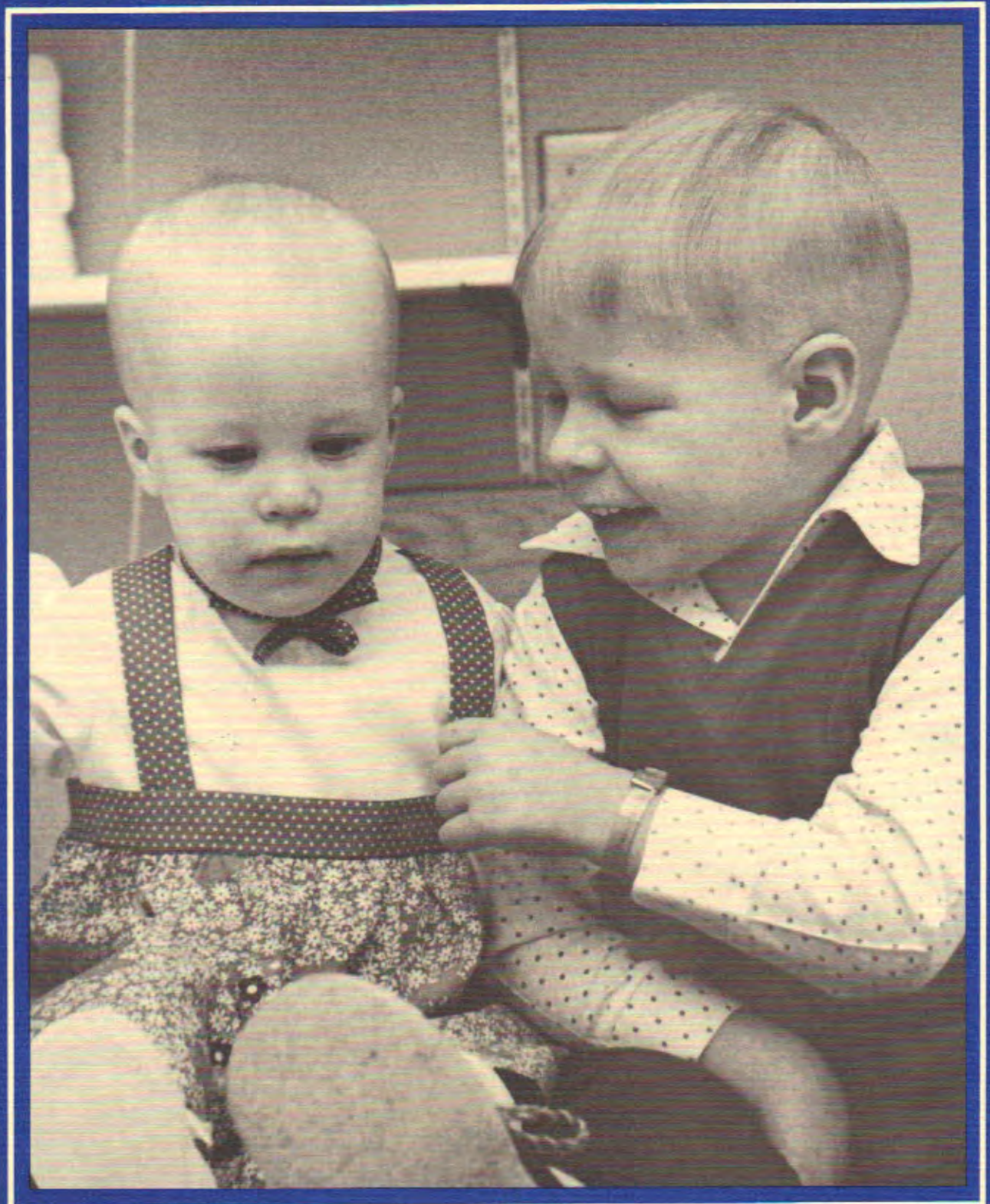
Milwaukee
Children's
Hospital

SUI GENERIS



A Gift For Matthew: The Future

As the recipient of Wisconsin's first successful bone marrow transplant, five year old Matthew Goerg has suddenly been given another chance to combat his leukemia.

The son of Michael and Cynthia Goerg, Matthew was diagnosed as having acute lymphocytic leukemia when he was first brought to Milwaukee Children's Hospital two and a half years ago. In that time, under the care of Bruce M. Camitta, M.D., director of the Midwest Children's Cancer Center at Milwaukee Children's Hospital and associate professor of pediatrics at the Medical College of Wisconsin, Matthew has undergone a myriad of treatments from drugs to radiation therapy. None provided any lasting success.

Finally in October, 1980, Matthew became Milwaukee Children's Hospital's first bone marrow transplant recipient with marrow donated by his 14-month-old sister Erin. Now, several months later, both are doing fine.

"In most of the children's leukemias now, we can make the patient 40-50 percent disease-free with nothing but chemotherapy," said Camitta. "After they've failed once with chemotherapy, however, their prognosis drops to between two and five percent chance of survival with just chemotherapy alone."

Matthew had been in remission for a year and eight months when his white blood counts became unstable. This is when Camitta began to think seriously about the possiblity of a transplant.

"In acute lymphocytic leukemia," Camitta explained, "the disease-free survival rate after a transplant is 30 percent if the patient is in remission. The guiding principle in making the decision, however, is to balance the prognosis of the disease treated with standard medical means versus the prognosis with the transplant. Generally speaking, there's a higher initial rate of mortality with the transplant, but the long-term success is much greater than with standard medical means."

According to Camitta, transplants were tried as early as the 1950's, but without much success. "People didn't appreciate then the need for compatibility between a donor and a recipient," he said.

"We now know that this is one of the most crucial aspects of the transplant process."

Most of the necessary matching information can be found on chromosome #6, therefore two separate blood tests are performed to determine compatibility. One is a blood serum test to detect specific proteins. The other is called a mixed lymphocytic culture (MLC) and tests compatibility by the reaction produced when blood from donor and recipient are combined in a test tube.

In Matthew's case, testing determined that his sister Erin would be a compatible donor. As Camitta pointed out, it is important that the patient and donor match in both tests since the more closely matched they are, the more successful the transplant is likely to be.

Siblings are generally the most likely donors as parents would rarely meet the chromosome requirements. "Some people suggest looking for donors in the random community," said Camitta, "but again, it is difficult to find a perfect match using this method. In fact, to achieve even a 50 percent chance of finding one person of the same race who matches at the A, B and D protein, you'd need samples from 100,000 donor types. And if the patient is from a minority race the chances are even slimmer."

Physical risk to the donor as a result of the transplant is minimal. The transplant is not dangerous and the donor need only be in the hospital for 48 hours. There is a minor risk of bleeding or infection at the puncture site, but according to Camitta, that is very unlikely.

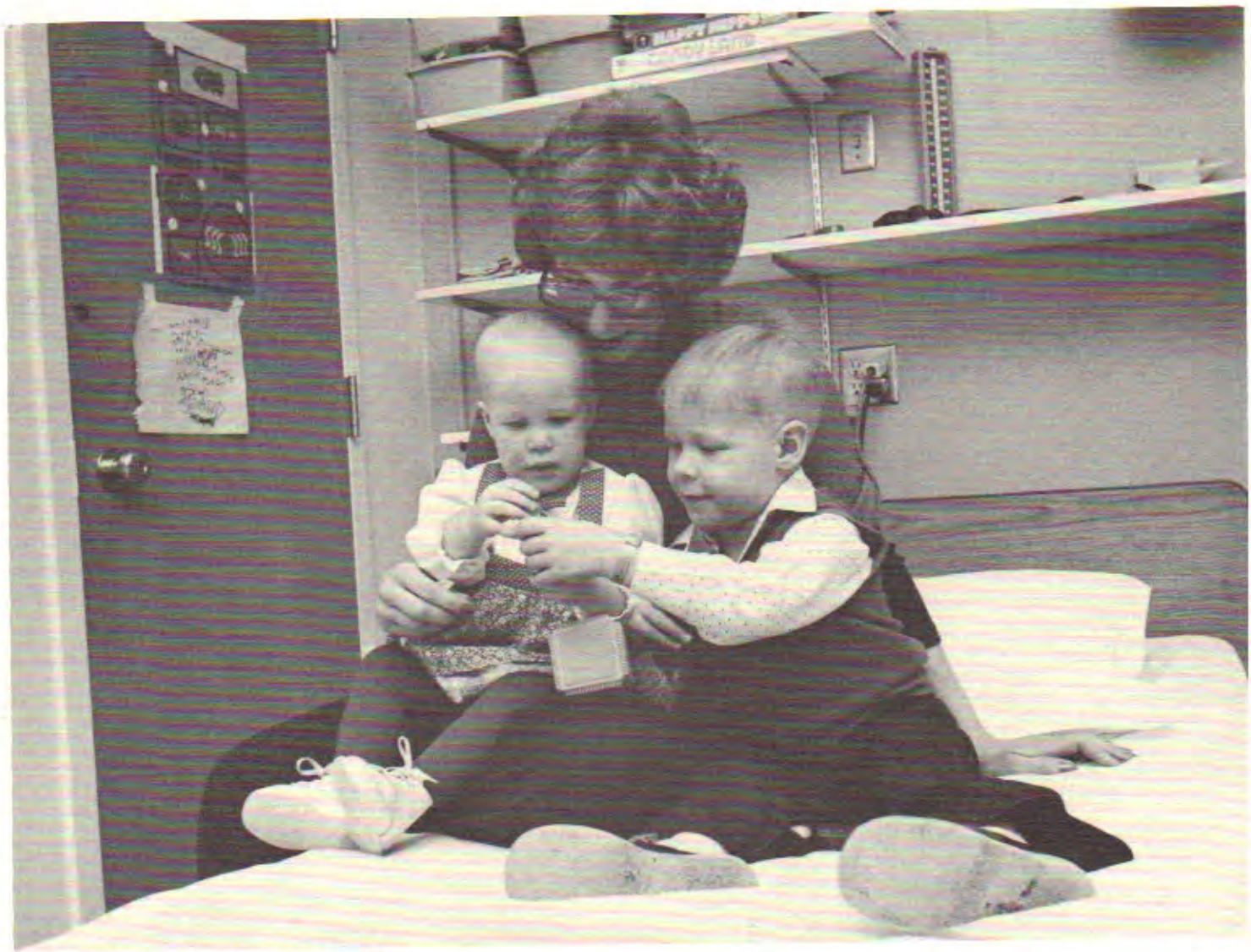
As a precaution, donors take iron pills for a month or two following the transplant to help restore the blood taken. The marrow itself, should grow back totally within four weeks.

The whole process is not quite so easy for the recipient. Although the actual transplant is a relatively easy procedure, the pre-transplant regimen is extremely difficult. Before the patient is even admitted to the hospital, two to three weeks of testing goes on to ensure that the transplant team knows all they need to know about the patient. Recipients are checked for infections and donors are assessed for both physical and psychological health at this time. "We want to make sure that the family understands and can tolerate the procedure," said Camitta.

The patient's own immunity is destroyed by the preparative process so they are less likely to reject the transplant. For leukemia, this process serves a double purpose: the chemotherapy not only destroys immunity, but also kills the leukemia cells and makes space for the new ones to grow.

"For both aplastic anemia and leukemia patients, the preparation regimen is so difficult, so intense, that it is extremely unlikely that the person's own bone marrow will ever grow again," said Camitta. If the new marrow does not grow, the patient will be unable to survive."

There are some immediate side effects that the patient may experience as a result of the preparative regimen as well. High doses of cytoxan can cause nausea, vomiting, diarrhea, blood fluid and salt



The Goerg's share a special moment together.

problems, plus bleeding from the bladder and long-term bladder troubles.

Total body radiation leads to a high risk of developing cataracts on the eyes within five or six years after exposure, but these can eventually be removed.

A more severe problem stemming from the radiation treatment is that the patient will not be able to have children of their own, although their normal gland function can be preserved.

And finally, there is still the risk of a second tumor developing. "That is why we only give the radiation treatment to patients with a malignancy," explained Camitta. "It's a low risk, but it's still a risk."

Matthew tolerated the procedure exceptionally well. Although he underwent intense chemotherapy treatments the week prior to the transplant, his most noticeable side effect was loss of appetite in the initial stages.

The day before the transplant Matthew had a total body transfusion to convert his type O blood to Erin's type A. This was just one more step to discourage the rejection of her marrow when it was introduced in his system.

For Matthew, the transplant was one of the easiest parts of the entire procedure. The marrow is taken from the donor through multiple aspirations, filtered to remove fat and cell clumps and administered intravenously to the patient. He was awake through the entire process.

Immediately after the transplant, work is begun to make the adjustment as easy as possible for the patient. "Blood samples are sent to the lab to try to determine what makes the immune system tolerant of its new body," said Camitta. "We want to know what will make the patient survive to be healthy and happy."

Once the marrow has been injected, several things can happen. One possibility is that the marrow will be rejected. This is due to prior sensitization against the donor, usually caused by a blood transfusion.

This is rare in leukemia according to Camitta. The patients are constantly getting medications that tend to suppress their immunity, therefore, it's hard to get them sensitized.

If the marrow begins to grow, it takes three to five weeks before the blood counts start looking normal. During that time, the

patient is under high risk of infection from bacteria and fungus.

Unfortunately, the patient's immunity is destroyed by the preparation regimen and the immunity of the donor is not carried over in the transplant. "The patient has to start from scratch, just like a baby does, to build up immunities," said Camitta. An additional complication is that from four to twelve months, the immune system is unable to build immunities even if it is exposed to infection.

The most common — and severe — complication is Graft versus Host Disease (GVHD). GVHD is an immune reaction by the new blood cells (from the donor) against the patient. "No matter how well the patient and donor were matched up, it can't be a perfect match," said Camitta. "The cells try to remodel the new environment to make it just like it was." Despite matching, 70 percent develop some Graft versus Host Disease and in ten to twenty percent of these it can be fatal. Low doses of methotrexate are administered for about three months after the transplant to mitigate the disease.

Symptoms include fever, watery diarrhea, abnormal liver tests (that could lead to cirrhosis), and a bad skin rash. Almost all organs of the body can be target organs for GVHD.

As he did in the preparation regimen, Matthew came through the transplant with little difficulty. He experienced both good and bad days during the first month following the transplant. Initially, he had chills, fever and lack of appetite, but as Erin's bone marrow began to grow, he began to improve steadily.

The marrow grew slowly in the beginning; it took almost three weeks before new cells were detected and a month before doctors were certain it was actually beginning to grow.

Graft versus Host Disease also had a mild effect on Matthew. His only noticeable reaction was a skin rash that was kept under control by low doses of methotrexate.

Finally, forty days after the transplant, Matthew was able to go home. He now visits the Hematology/Oncology clinic at Milwaukee Children's Hospital once a week for check-ups and blood work. If things continue to go well, he may be able to start school in the fall.

Camitta is pleased with the success of the transplant and Matthew's progress at this point. "The most important thing is that a bone marrow transplant requires an intensely alert, educated and coordinated team," stressed Camitta. "It starts at bedside and eventually includes practically every hospital department. Without the entire team working, you can't do the proper job."

Transplantation rounds are now held weekly at Children's Hospital to discuss what's currently happening with specific patients and what more can be done from a research standpoint. Selection and preparation of potential patients is also discussed.

"Matthew's case is a success story in itself, but right now we're looking toward the future," said Camitta. "Our program here has turned into a major team effort and we're very pleased."

Dr. Camitta discusses Matthew's case with another physician.