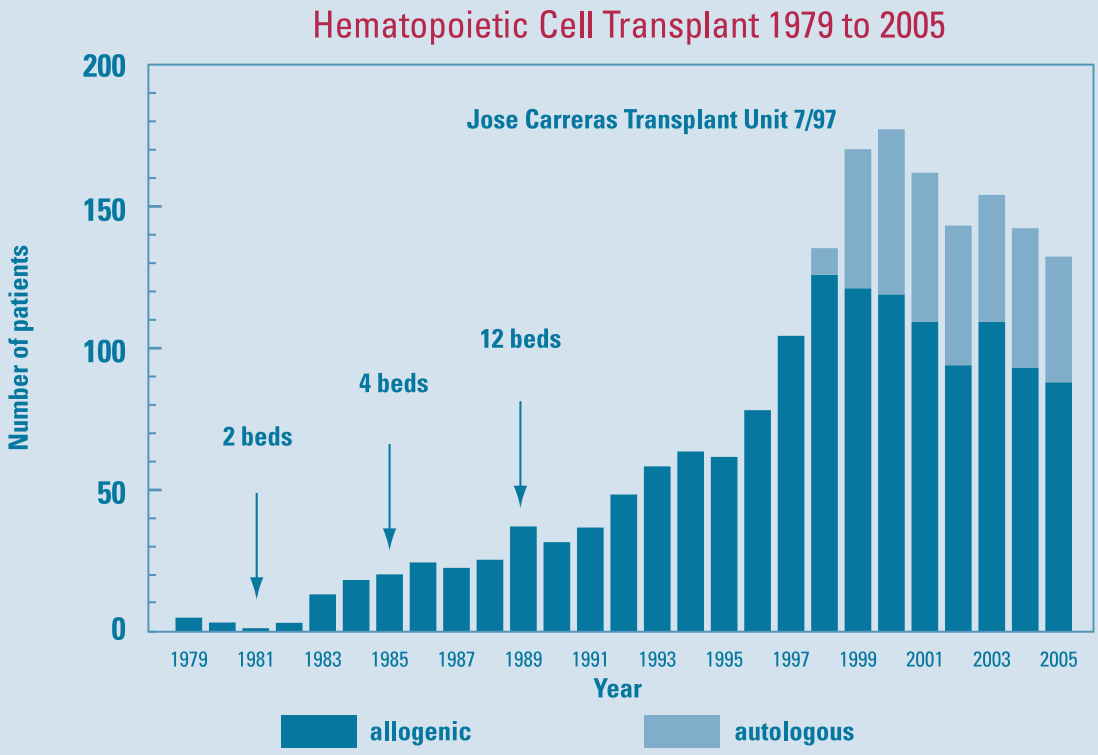
Pioneers of Bone Marrow Transplantation

Particularly it is due to the close interaction of laboratory and clinic that scientists in basic research and physicians of the GSF could become pioneers of bone marrow transplantation: in 1975 Prof. Hans-Jochem Kolb, now head of the Clinical Cooperation Group "Hematopoietic Cell Transplantation," together with a colleague from the Municipal Munich Schwabing hospital saved the life of a youth with bone marrow failure by transferring healthy bone marrow. It was the first successful transplantation of this kind in Germany.

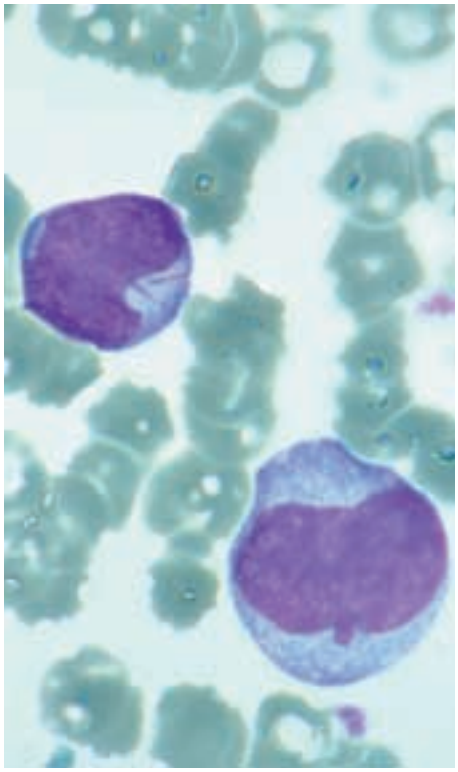
If left untreated, leukemia, a blood cell production (hematopoiesis) disorder in the bone marrow, inevitably causes the patient's death. Therefore, attempts to destroy the patient's diseased bone marrow and to replace it with healthy bone marrow from a suitable donor were made very early on. In 1975 Prof. Hans-Jochem Kolb together with colleagues from the Hospital of Schwabing of the City of Munich succeeded in saving the life of a youth with bone marrow failure (aplastic anaemia) by transferring healthy bone marrow.



Since the first successful bone marrow transplant in 1975 the number of transplants carried out under Prof. Kolb in Munich has been rising continuously. In 1987 there was a steep increase, when a new transplant unit was established with funds from the German Jose Carreras Leukemia Foundation. While patients had to wait for a bed in Munich for an average of one year before that, there have been hardly any waiting times since then. Today up to 170 patients a year can receive transplants.

T-Cells Put out of Action

The spectacular treatment had been preceded by years of experimental work at what was then the GSF Institute of Immunology, headed by Prof. Stefan Thierfelder. First suitable radiation methods had to be developed in animal experiments. They could destroy the degenerate blood cells in the bodies of leukemia patients and at the same time make space for the healthy cells of the transplant. But this was not all. Because the donated bone marrow does not only contain the vital blood-cell-forming stem cells, but also so-called T-cells, which consider the recipient as foreign and attack his/her organs and tissues. "Prof. Thierfelder had shown in experiments that the treatment of the donor with antiserum against T-cells can prevent this dangerous immune reaction of the donor against the recipient," Prof. Kolb remembers: "But the human donor cannot really be treated with antiserum in order to prevent the reaction of the patient. Prof. Thierfelder had the idea to simply remove the T-cells from the



Leukemia cells in the bone marrow of a patient with myeloblastic leukemia

bone marrow before the transfusion is made." For the first time ever the GSF physicians at Haunersches Kinderspital (pediatric clinic) treated a girl suffering from leukemia with T-cell-depleted donor bone marrow in 1978; today "T-cell depletion" has become an established method in bone marrow transplantation.

Adoptive Immunotherapy Helps

Just a year later Prof. Thierfelder introduced another innovation: the removal of leukemia cells from the bone marrow. This means that the patient's own bone marrow can be used for the transplant. It is taken during a quiescent phase of the leukemia and treated with an anti-leukemia serum which eradicates any remaining leukemia cells. The prepared bone marrow is returned to the patient after whole body irradiation. This method does show success, but it cannot eliminate all remaining leukemia cells. Looking for a better solution to this problem, the doctors benefited from a special feature which distinguishes the bone marrow from all other organs: it is only combated by the recipient's immune system as a foreign body at the beginning and then tolerated only a few months after the transfer. This "tolerance" of the patient to the donor bone marrow was used by Prof. Kolb and his working group to follow a new approach to leukemia treatment: adoptive immunotherapy. The donor's T-cells which had been removed from the bone marrow before the transplant are reintroduced into the patient who has now become "tolerant" in a second step, so that they specifically destroy his remaining leukemia cells. "We first showed that in a patient who has had a transplant and who has had recurrent leukemia this leukemia can be eliminated by the administration of T-cells of the donor – without chemotherapy or radiation," Prof. Kolb stresses. Although the classical weapons against cancer, chemicals and radiation, are still indispensable for the preparation of any bone marrow transplant, subsequent adoptive immunotherapy can considerably reduce the dosage of the preceding chemotherapy and irradiation – and thus the stress the patient is exposed to.

Apart from the treatment of leukemia, the method developed by Kolb may be able to help solve yet another problem in the future: transplanting organs which do not match as yet. For as opposed to the classical bone marrow transplant, where maximum correspondence between the donor and the recipients is required, Kolb's method also allows the transfer of bone marrow which does not match. Patients whose body has accepted such a transplant could also have another organ of the bone marrow donor transplanted without rejection as a foreign organ – a new chance for transplant medicine.

KKG Hematopoietic Cell Transplant

Third Party Funds

Deutsche Forschungsgemeinschaft

Krebshilfe

Deutsche Jose Carreras-Leukämie-Stiftung e.V.

Federal Ministry for Education and Research

Kröner Stiftung

Wilhelm Sander Stiftung

European Union (Transeurope, Transnet, Eurocord)

National Genome Research Network

Third-party funds raised by the KKG are an important supporting pillar of the Clinical Cooperation Group "Hematopoietic Cell Transplant" in addition to contributions from GSF and Ludwig-Maximilians-University.

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