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# What's New with Stem Cell Transplants?

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Once reserved as a last resort when chemotherapy was no longer effective, hematopoietic stem cell transplantation (HCT) for blood cancers has improved remarkably over the past 30 years, and the field continues to evolve.

Even among advanced cancer patients whose disease did not respond to other treatments, some are cured by HCT. “There are patients who are surviving more than 20 or 30 years after HCT who would have died within a few weeks or months had they not received transplants,” says H. Joachim Deeg, MD, of the Fred Hutchinson Cancer Research Center in Seattle.

### Improving Transplantation

Transplants are used to treat patients with a variety of blood cancers, including leukemia, lymphoma, and myeloma. There are two main types of HCT: allogeneic and autologous. An allogeneic transplant uses stem cells from a healthy donor whose tissue type ideally matches that of the patient. High-dose chemotherapy is given prior to the transplant to kill off cancer cells, but it also damages the patient’s healthy stem cells. To replace those stem cells, donor cells are infused into the patient. Autologous transplantation, on the other hand, uses the patient’s own stem cells, which are collected before high-dose treatment, frozen, and then thawed and returned to the patient after high-dose therapy with chemotherapy, radiation, or both.

It has long been recognized that radiation or chemotherapy at doses that are tolerated by patients will not kill all cancer cells. To eliminate residual cancer cells, “We’re relying heavily on the immunotherapy provided by allogeneic donor cells,” says Deeg.

In transplants that use reduced-intensity conditioning regimens (sometimes referred to as “mini-transplants”), patients are given lower, less toxic doses of chemotherapy or radiation, which makes the regimen more tolerable for older patients or for those with other medical problems who may not be able to withstand high-dose treatments.

Another innovation, according to Deeg, involves the use of high-dose therapy with autologous stem cell rescue (with the intent of reducing the amount of cancer cells in a patient’s body, followed by a reduced-intensity allogeneic transplant. This strategy combines the anti-cancer effects of high dose therapy with the immunotherapeutic effect of allogeneic donor cells.

There are also more recent developments of interest. The Food and Drug Administration approved Mozobil (plerixafor) late last year. This drug, which “mobilizes” stem cells from the marrow into the bloodstream, given alone or in combination with granulocyte-colony stimulating factor (G-CSF), allows the collection of sufficient numbers of stem cells even in patients in whom more established methods were not successful. As a result more patients with diseases such as non-Hodgkin lymphoma or multiple myeloma are able to undergo an autologous transplant. Side effects of the drug include nausea, fatigue, and diarrhea.

## Tackling Graft-Versus-Host Disease

A major obstacle to allogeneic stem cell transplantation has been graft-versus-host disease (GVHD), a clinical disease that is triggered by donor cells, which recognize the recipient’s cells and tissues as foreign and attack them. Patients are treated with steroids and immunosuppressive drugs, including mycophenolate mofetil, tacrolimus, sirolimus, and others.

An immunosuppressive antibody preparation called antithymocyte globulin is now being tested in certain stem cell transplant patients. Although currently approved to prevent kidney transplant rejection, it may also reduce chronic GVHD when it is given as part of the conditioning regimen in preparation of HCT.

As of late, the chemotherapy drug Cytoxan (cyclophosphamide) is also being used after transplantation in an effort to prevent GVHD. “We infuse the donor cells, allow them to become activated for a couple of days, and then give cyclophosphamide. This strategy appears to be able to eliminate activated cells T cells that react against the patient and leave non-activated T cells intact. Those cells are expected to speed up the recovery of the immune system and to help fight cancer cells,” Deeg says.

Campath (alemtuzumab), approved for the treatment of B-cell chronic lymphocytic leukemia, is also used to prevent or treat GVHD. Current studies are investigating whether Campath, combined with other immunosuppressive drugs, can further prevent or manage GVHD in transplant patients.

## Changing Landscape

In addition to the developments described above, the landscape for treating blood cancers has undergone many changes in recent years. This includes changes in when transplantation should be used.

“Myeloma has become sort of a poster child for what has been happening in the non-transplant field. Overall survival has probably doubled over the last couple of decades,” Deeg says, partly due to treatment options, such as Thalomid (thalidomide) or Revlimid (lenalidomide), which help fight anemia, decrease the blood supply to tumors, and induce changes in the immune system.

A class of drugs called proteasome inhibitors, which interfere with the breakdown of proteins thus killing cancer cells, has also made an impact on multiple

myeloma. Velcade (bortezomib), approved in 2003, has improved survival for myeloma patients. “As a result, transplants are now typically used later in the disease course,” he says.

Even more striking, in chronic myeloid leukemia (CML), the arrival of Gleevec (imatinib) and next-generation drugs such as Sprycel (dasatinib) have improved patient outcomes, with a majority of individuals able to sustain long-term remissions on chronic therapy.

“Now that tyrosine kinase inhibitors [such as Gleevec] have become available, the frequency of transplants for that disease have decreased considerably,” says Edward Copelan, MD, director of the Acute Leukemia Program at the Cleveland Clinic in Ohio. As a result, relatively few patients with CML are now treated with stem cell transplantation.

With the combination of improved drugs and the recent and ongoing advancements in stem cell transplantation, patients—and their physicians—are welcoming the many options in treating blood cancers.

For more information on stem cell transplantation, read “[Cell Restoration](#)” from *CURE's* 2008 Special Issue.