Hematopoietic Stem Cell Transplantation in Children and Adolescents

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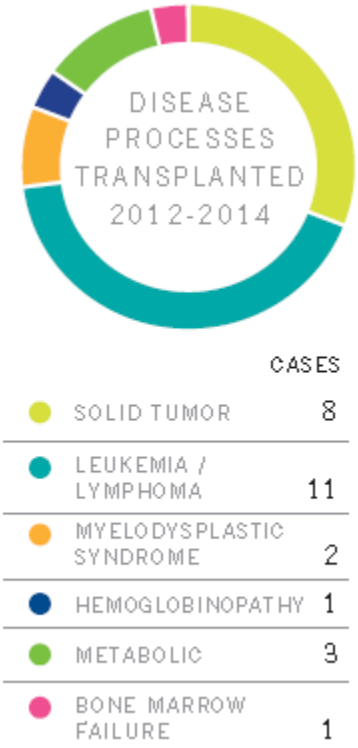
In 1958, Georges Mathé, a French oncologist, performed the first successful infusions of bone marrow in Vinca, Yugoslavia, when 6 physicists developed bone marrow failure following radiation exposure. After they were infused with donor bone marrow, the donor cells were rejected and the patients' own bone marrow recovered.

The next major advancement in transplantation came with the discovery of the human leukocyte antigen (HLA) histocompatibility system in the late 1960s. Applying this discovery resulted in decreased rates of rejection and graft versus host disease (GvHD). During the 1970s, efforts were made to develop conditioning regimens that reduced toxicity, yet limited later relapses of disease. While the majority of initial transplants were performed on patients with malignant conditions, the last several decades have expanded the focus of transplantation for non-malignant conditions1,2. Now, approximately 2,000 pediatric hematopoieticstem cell transplants are being performed annually in the United States3,4.



All blood cells – red blood cells, white blood cells and platelets – are derived from the hematopoietic stem cell (HSC) that resides in the bone marrow. Hematopoietic stem cell transplantation (HSCT) is a therapeutic modality used to replace a defective blood-forming system (due to intrinsic disease or as a result of disease therapy) with one that is fully functional. Thus, HSCT has been used to treat malignancies, immune deficiency syndromes, metabolic disorders, hemoglobinopathies, myelodysplastic syndromes, autoimmune disorders, and bone marrow failure.

In the treatment of malignancy, the patient may receive high doses of "conditioning" chemotherapy and/or radiation to eradicate cancer cells. Stem cells are then given to repopulate the bone marrow, thereby "rescuing" the patient from chemo/radiotherapy injury to the HSCs. Importantly, recognition of patients' (host) cells as "non-self" by the donor immune cells also targets cancer cells, and this "graft-versus-tumor" effect may be exploited to eradicate cancer with lower (i.e., less toxic) doses of conditioning chemotherapy.

Stem cell transplantation can also be used in non-malignant diseases to replace defective marrow and in the treatment of metabolic diseases, where the donor blood system supplies a critical enzyme that's deficient in the patient.

Hematopoietic stem cells may be collected from the patient (autologous), from a related or unrelated donor (allogeneic), or, in rare cases, from an identical twin (syngeneic). HSCs can be obtained from bone marrow, peripheral blood or umbilical cord blood. The source of the stem cells is based on the disease process being treated and on donor preference. In pediatrics, autologous stem cell transplantation is used primarily in the treatment of solid tumors, while allogeneic transplantation is used for many other disease processes, as described above.

Complications of stem cell transplantation include infection (bacterial, viral, fungal and protozoal), mucositis, malnutrition, organ dysfunction and GvHD (acute and chronic). Infections are common in hematopoietic stem cell transplant patients due to disruption of mucosal (e.g., skin and gastrointestinal) barriers.

Experience at Akron Children's

The first autologous stem cell transplant at Akron Children's Hospital was performed in 2000. Since that time, over 100 hematopoietic stem cell transplants have been performed. These include autologous, matched sibling donor, matched unrelated donor and cord blood stem cell transplants. HSCT has been used in the treatment of bone marrow failure syndromes, immunodeficiencies, metabolic disorders, hemoglobinopathies, myelodysplastic syndrome, leukemia/lymphoma and solid tumors (see chart on page 6).

From July 2003 to December 2014, the survival rate for Akron Children's HSCT patients at 100 days post-transplant is 96 percent. The table below outlines our institution's 100-day post-transplant survival compared to national benchmarks by disease group. During the 3-year period spanning from 2012 through 2014, 26 transplants were performed at Akron Children's including 8 autologous, 6 allogeneic matched sibling donor and 12 allogeneic matched unrelated donor transplants.

100-DAY POST-TRANSPLANT SURVIVAL

DISEASE PROCESS	TRANSPLANT TYPE	AKRON CHILDREN'S HOSPITAL	NATIONAL AVERAGE[5]
NEUROBLASTOMA	AUTOLOGOUS	100%	96.3%
SICKLE CELL DISEASE	ALLOGENEIC MSD	100%	99%
ACUTE LYMPHOID LEUKEMIA	ALLOGENEIC MSD AND MUD	100%	86.9% TO 98.4%
ACUTE MYELOID LEUKEMIA	ALLOGENEIC MSD AND MUD	88%	83.3% TO 97.7%

MSD = Matched Sibling Donor
MUD = Matched Unrelated Donor

References

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6.) Barrell C, Covington L, Bhatia M, et al. Prevention strategies for central line-associated bloodstream infections in pediatric hematopoietic stem cell transplant recipients. *American Journal of Infection Control*. 40: 434-439, 2012.