Pediatric Blood and Marrow Transplant

Since 1980, there have been approximately 600 Blood and Marrow transplants (BMTs) performed at BC Children’s Hospital. There have been countless scientific and medical advances in this field in the past 45 years that make up the modern era of hematopoietic (blood) stem cell transplantation, and it gets more and more complex with each passing year as we learn how to make them more successful.

The reason that a child undergoes a blood or marrow transplant depends on the underlying illness, and the underlying illness is not always a malignancy. In fact, up to 40% of all pediatric BMTs are now performed for non-malignant diseases.

In the early years of the modern era of transplantation, most patients had leukemia or lymphoma. Once the basic process of BMT was established, other conditions we call marrow failure syndromes were considered for BMT. A common example in children is severe aplastic anemia. Other conditions that involve blood cells that do not function properly, like thalassemia, were also added to the list. The list of indications progressed quite quickly to the immune deficiency syndromes, like severe combined immune deficiency (SCID). The list of immune deficiency syndromes that are treated with BMT grows every year. Since the cells of the bone marrow travel to every part of the body, and share some of the proteins they make with other cells of the body, it was discovered that certain metabolic diseases could be treated with replacement of the marrow. Once the process of collecting and storing hematopoietic or blood stem cells was established, the idea of ‘rescuing’ the marrow after very high doses of chemotherapy was developed for many malignant diseases (autologous BMT procedure). Thus, today, there are many indications for hematopoietic stem cell transplantation, which are listed in Table 1. Although it has been shown that hematopoietic stem cells can differentiate into other organ cells, like heart muscle and neurons, we have not figured out how to use stem cells to replace these cells in large numbers to repair another organ. Thus, hematopoietic stem cell transplantation in 2015 remains a treatment to replace a person’s bone marrow, thereby giving a patient a new immune system and in some conditions providing needed enzymes to adjacent tissue cells.

The purpose of BMT is essentially this: to replace absent, diseased, or damaged stem cells with a healthy bone marrow. Usually, the BMT process begins with assessing the patient’s health to undergo the stem cell transplant and identifying the donor source of stem cells. The recipient continued on page 2
is then admitted for approximately one week of intensive chemotherapy, called the conditioning or preparative regimen. The dual purpose of this preparative regimen is to remove the “immunogenic” cells that can cause rejection of the graft and in the case of malignancy to remove any residual malignant cells. The stem cell infusion occurs on what is known as “day 0”. The stem cells, which have been collected previously and frozen in the case of donating one’s own stem cells (called autologous), or collected the same day as the infusion (if the stem cells are from a related donor), are infused via a central intravenous catheter which has been surgically implanted. This is generally uneventful and tolerated well. After the stem cell infusion, we await recovery of healthy new cells over the weeks.

There are two types of BMT: autologous, which means the stem cell source is the recipient him/herself; and allogeneic, which means the stem cell source is from someone other than the recipient. This can be a related sibling, parent, unrelated adult or unrelated umbilical cord blood.

Autologous transplants are somewhat less complicated than allogeneic BMTs, and the purpose of them is also somewhat different. Autologous transplants are generally used in the treatment of solid tumors. Very high doses of intensive chemotherapy are given to treat the malignant tumor, so high that recovery of healthy bone marrow cells would take months. The risk of infection is very high during this period of recovery. Therefore, these patients undergo a stem cell collection prior to this procedure, after which the cells are cryopreserved (frozen) and stored in a lab at the BCCH site. When the stem cells are due to be infused, the cells are thawed and infused directly into the patient. This allows very high doses of chemotherapy to be given for solid tumors; the stem cell infusion hastens blood count recovery to usually less than two weeks.

In allogeneic BMT, stem cells are collected from a source other than the patient. Donors are assessed by a special typing called human leukocyte antigen typing, and these antigens (or proteins) are inherited as a grouping from each biological parent. Therefore, the best chance for well-matched donors is from a full sibling. Otherwise, an alternative donor may be used either from a cord blood bank or from unrelated adult donor registries e.g. OneMatch. Using a fully matched donor decreases the risk of engraftment failure (failure of the new stem cells to make healthy blood cells) as well as graft vs host disease (GVHD).

Graft versus Host Disease (GVHD) is a disease whereby the new immune system of the donor (graft) recognizes the recipient’s (host’s) body as foreign and attacks the host. Almost all patients are given prophylactic medication called immune suppression to prevent GVHD. Despite this medication, a significant proportion of patients still develop GVHD; from 30% in full matched sibling donor transplants to more than 70% using unrelated or less fully matched donors. There are two forms of GVHD, an early form (acute) and late onset form (chronic).

In the first few months after day 0, acute GVHD can develop as an immune response against the skin causing a rash, the gut in the form of diarrhea or pain, or the liver causing increased liver enzymes and jaundice. This can be a potentially debilitating and devastating condition. It is generally treated with systemic steroids, and/or changes to immune suppressive therapy. While we have become very good at treating and minimizing the effects of the acute form of GVHD, we still have a significant problems treating chronic GVHD.

Chronic GVHD develops slowly and is very slow to resolve. Sometimes it never goes away and stays the rest of a person’s life. Chronic GVHD is a very complicated disease and can affect any organ or tissue in the body resulting in decreased quality of life or inability to return to normal physical activity. We have been able to significantly decrease the impact of GVHD partially by using antibodies called alemtuzumab and antithymocyte. Based on research done at BCCH, another antibody therapy called rituximab has been found to be a major step forward in the treatment armamentarium. Another newer treatment is the drug imatinib, which is used to treat chronic myelogenous leukemia, but has been found to have anti-fibrotic or anti-scarring properties in the treatment of chronic GVHD. Recently, we have begun a new therapy using interleukin-2. Other treatments that have been developed include a process called extracorporeal photopheresis.

None of the agents work for all of the children and teenagers as we are just now starting to understand the biology of this complex disease in Dr. Schultz’s lab here at BCCH as well as others around the world. Chronic GVHD is the primary cause of long term health issues suffered by BMT patients and after the first two years is the primary cause of death. Thus, chronic GVHD is now a major focus of research worldwide to make BMT safer for all patients. The Michael Cuccione Childhood Cancer Research program has been partnering and supporting our laboratory at the Child and Family Research Institute (CFRI), one of the laboratories studying this terrible complication.

The transplant team consists of a team of multidisciplinary health care professionals who ensures that the transplant patients get the care they need during this life saving and sometimes life threatening treatment. In 2007, Juliana Roden, a Nurse Practitioner has joined the BMT program.

As the BMT nurse practitioner, she is responsible for patient and family education, evaluation of the donor and recipients prior the transplant hospitalization, as well as post BMT follow-up. Her focus and priority are those receiving allogeneic transplants, with follow-up up to 2 years post BMT. In addition, she is integral to the operation of the chronic GVHD Clinic with Dr. Kirk Schultz. As many of these children go to their home communities after a more than 3 months stay in Vancouver, we must rely on our community health care teams to perform appropriate follow up post-BMT. Much of the system-specific follow-up with regards to GVHD and disease monitoring will be performed here in Vancouver, but unforeseen infections and other longer term side effects of the treatment and GVHD (heart, eyes, endocrine, and other organs) may need to be monitored and treated in the home community. It is important to note that full cellular immunity is not restored until continued on page 3
How does one begin to thank a man who has dedicated his life to Pediatric Oncology and who has selflessly served the children of British Columbia? After 42 years as a pediatrician and 37 as a pediatric oncologist, Dr. Fryer is retiring. He shall leave a huge gap and we humbly thank him.

Dr. Fryer graduated in 1965 from the University of London, had his first job as a consultant pediatrician in Halifax in 1973 and came to BC in 1977. Chris was dual certified in pediatric oncology as well as radiation oncology and he served as Division Head in the Division of Pediatric Hematology / Oncology and BMT from 1992-1998. Upon his return to BC after a short sojourn in the Middle East, he became the Medical Director of the Provincial Pediatric Oncology Hematology Network (POHN) in 2002. In this role he provided clinical service, taught, developed policies and advocated for the children of BC. The Network that has flourished under his direction.

Dr. Fryer has achieved numerous academic accolades, has published over 100 journal articles and been a member on many tumor research groups. His passion for children and the commitment to holistic care shows in his co-founding Camp Goodtimes and serving on the boards of Canuck Place and the Zajak Foundation.

From all the patients, families and health care professionals from across the Province we wish him well and thank him from the bottom of our hearts! His wisdom and compassion will be missed…

Dr. Caron Strahlendorf, MB, BCh, FCP, FRCPC
Division Head of Oncology Hematology BMT
Welcome Dr. Malcolm Moore

We welcome Dr. Malcolm Moore the new President of the BC Cancer Agency. Previously he was head of the Division of Medical Oncology and Hematology at the Princess Margaret Cancer Centre and director of the Bras Family Drug Development Program at the Ontario Cancer Institute. His clinical and laboratory research has focused on the development and testing of new cancer therapies, particularly in the areas of prostate and pancreatic cancers. He recently completed the EXTRA Fellowship Training Program with the Canadian Health Services Research Foundation and the Program for Chiefs of Clinical Services at the Harvard School of Public Health. To read more about Dr. Moore, please visit the Journal of Family Practice Oncology (Fall 2015). www.bccancer.bc.ca/family-oncology-network-site/Documents/2015FallFPONjournal_webSep10.pdf

SAVE THE DATE

Pediatric Oncology Hematology Conference
Thursday, October 27 and Friday, October 28, 2016
BC Children’s Hospital, Vancouver, BC

More information to come...

The 2015-2016 flu guidelines are posted at:
www.bcchildrens.ca/Oncology-Site/Documents/Flu%20Vaccine%202015.pdf

Wishing you a Merry Christmas and Healthy New Year!

THE PROVINCIAL PEDIATRIC ONCOLOGY/HEMATOLOGY NETWORK

The Network is an interdisciplinary organization whose goal is to ensure appropriate diagnosis, management, follow-up, and end-of-life care for pediatric patients with malignancies and blood disorders.

The Network supports community hospitals and practitioners, and develops partnerships with other healthcare facilities to enable seamless and integrated care for patients and families on treatment and off treatment.

It will further develop and enhance the research programs of basic, translational, and clinical research to better childhood cancer control and improve outcomes for these patients and their families.

FOR MORE INFORMATION

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Our mission is to improve the health and welfare of children in BC with cancer and blood disorders through research, education, and care.