

A fact sheet

UNRELATED BONE MARROW AND CORD BLOOD STEM CELL TRANSPLANTS

Each year, thousands of patients are diagnosed with diseases treatable by a blood stem cell transplant. These blood stem cells can come from bone marrow donation, either from a tissue type matched relative or from an unrelated volunteer donor. 60-70% of patients, however, have no relative that matches their HLA tissue type. Millions of volunteer donors are listed with the registries around the world in case they can help by providing blood stem cells to patients who have no matched relatives. An alternative source of those stem cells is from the placenta after delivery. This blood is rich in blood stem cells, so only about 100 millilitres is enough to transplant.

Bone Marrow Donors Worldwide is an international database where physicians can search for volunteer donors and cord blood units. Registries worldwide celebrate the 10,000,000th donor on November 16th, 2005.

HISTORY OF BONE MARROW TRANSPLANTATION

Performing blood stem cell transplants in humans was not attempted until after a number of critical discoveries were made about the human immune system in the late 1950s, when scientists first described the human histocompatibility antigens. These are proteins found on the surface of most cells in the body and are called human leukocyte antigens, or HLA antigens. HLA antigens can be compared to the ABO blood groups, the typing of which is essential to make blood transfusions safe, but they are of much greater complexity.

The body's immune system uses these HLA antigens to identify which cells belong in the body and which do not. The immune system uses this to recognise and destroy foreign cells such as bacteria, viruses, tumor cells and transplants. In this way, the immune system defends the body against threats that can enter the body and cause harm. The importance of these findings was acknowledged when Jean Dausset, Baruj Benacerraf and George D. Snell received the Nobel Prize in 1980.

For a blood stem cell transplant to be a success, the recipient's immune system must accept the donated cells. This is accomplished by making sure that the HLA antigens on the donated blood stem cells are identical, or very similar to, the antigens on the cells of the recipient.

A transplant between identical twins guarantees complete HLA compatibility between donor and recipient and these were the first kinds of transplants performed in humans. It wasn't until the 1960s that physicians knew enough about HLA compatibility to perform transplants between siblings who were not identical twins.

In the 1970s, physicians performed the first transplants using HLA-matched donors who were unrelated to the transplant recipient. By this time, physicians had gained enough experience with bone marrow transplantation to determine that at least three types of antigens – called the HLA-A, HLA-B and HLA-DR – were crucial when determining a match between a donor and recipient. An individual inherits one of each of these three antigens from each parent. Therefore, a total of six antigens from the donor must match the six antigens of the recipient.

In 1990, Dr. E. Donnall Thomas was awarded the Nobel Prize in Medicine for his pioneering work in transplantation. During the early to mid-1970s, Thomas had performed more than 100 transplants for patients with aplastic anemia and leukemia with HLA-A, HLA-B and HLA-DR identical siblings. He was awarded the prize because of his many successful endeavours in both clinical and experimental bone marrow transplantation.

As two out of three patients have no related donor, transplant physicians realised it was important to be able to search for a matched donor amongst volunteers everywhere in the world.

ESTABLISHING THE REGISTRIES

The concept of registries dated back to 1970, when Prof. Dr. Jon J. van Rood proposed at the meeting of the Deutsche Gesellschaft für Bluttransfusion in Munich to set up a file of HLA typed volunteer blood transfusion donors to be used for HLA matched platelet transfusions and bone marrow transplantation.

The first active dedicated bone marrow donor registry was, the Anthony Nolan Trust, United Kingdom. The Charity was initially set up in 1974 to find a donor for Anthony Nolan, born in 1971 with an immune deficiency disease, Wiskott Aldrich syndrome. Anthony died in 1979 without a transplant, but numerous patients have benefited from his legacy. The Register of unrelated donors inspired by his mother, Shirley Nolan, continued to grow and prosper over the years. It was Shirley Nolan's intent to offer hope of a donor to any patient in need of a blood stem cell transplant in any part of the world.

The register of volunteer donors that Shirley Nolan created served as a model for establishing numerous registries in almost every developed country of the world.

Jon J. van Rood created a collaboration between several bone marrow donor registries worldwide to produce the global search engine for donors, "Bone Marrow Donors Worldwide". The first edition of this "yellow pages of bone marrow donors and cord blood units" published in 1989, had 150,000 bone marrow donors coming from 8 countries.

Today, Bone Marrow Donors Worldwide is a web based search engine which has just listed the 10,000,000th volunteer stem cell donor and is a collaboration of 42 countries.

Despite having 10,000,000 chances, there are still an estimated 10,000 to 15,000 of patients that cannot find a sufficiently close match. They need a different answer.

ESTABLISHING THE CORD BLOOD BANKS

The first transplant using blood stem cells from placental cord blood was performed in 1988. The donor was his HLA-identical sister. The cord blood was collected and frozen at birth. The transplant was successful and the recipient is alive and free of disease more than 15 years after transplant.

In 1993 Bone Marrow Donors Worldwide welcomed the first public cord blood bank: New York Cord Blood Bank. Nowadays more than 200,000 cord blood units from 37 cord blood banks and cord blood registries are available for transplantation.

Collecting blood from the umbilical cord after delivery carries no risk to mother or child. Umbilical cord blood can be frozen and stored in cryogenic freezers, ready for use when needed. Because the blood stem cells in cord blood are not developed fully, they carry a much lower risk of graft versus host disease (GVHD), a condition in which the blood stem cells attack and sometimes kill the recipient. The lower risk makes it possible to perform transplants with less perfectly tissue type matched cells. However, a typical cord blood harvest only contains enough stem cells to transplant a child or small adult. Because the stem cells in cord blood are more primitive than those in marrow, the engraftment process takes longer with cord blood, leaving the patient vulnerable to infection for a longer period of time.

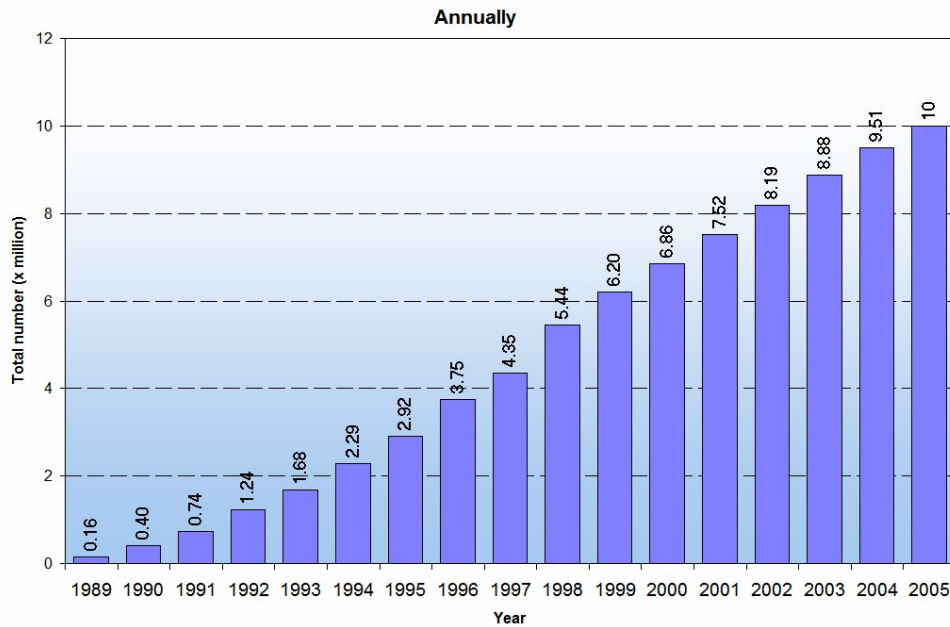
INTERNATIONAL CO-OPERATION

The World Marrow Donor Association (WMDA) developed guidelines to facilitate international exchange of blood stem cells. The WMDA has initiated an accreditation program for national donor registries to ensure uniform standards for international donor exchange. In 2004, 35% of the 7,266 unrelated blood stem cell donations were provided to patients in another country.

DONOR DATA

Because a person's HLA characteristics are inherited, a patient is more likely to find a matching donor from within his or her own racial or ethnic group. Donors of all ethnic groups other than North Western European origin are still underrepresented in the database of blood stem cell donors. The chance of finding a potential donor for patients of North Western European origin is much higher than for patients from other ethnic groups.

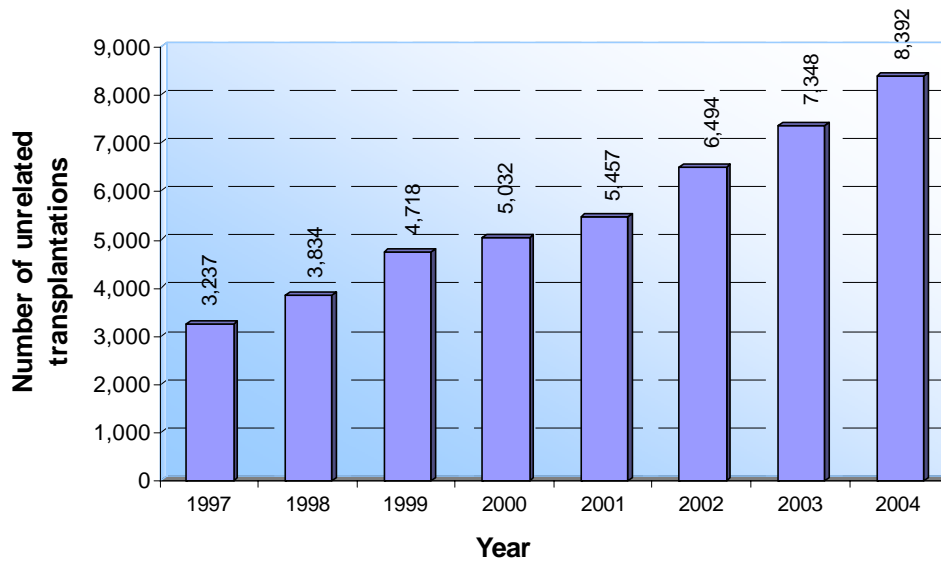
Total number of donors and CB units



The World Marrow Donor Association produces annual statistics on worldwide unrelated stem cell transplantation activity. In 2004: 7,266 blood stem cell donations and 1,126 cord blood units were provided for patients in desperate need.

More than 50,000 patients worldwide have received blood stem cells from an unrelated donor. More than 5,000 patients worldwide have received an unrelated cord blood transplant.

Total number of unrelated blood stem cell transplantations



no data available before 1997

USEFUL WEBLINKS AND REFERENCES

1. Website of Bone Marrow Donors Worldwide: www.bmdw.org (central database of stem cell donors worldwide)
2. Website of World Marrow Donor Association: www.worldmarrow.org (quality guidelines for recruiting blood stem cell donors, collection and transport of blood stem cell products between the different countries).
3. *Bone Marrow Transplantation* (2002) 30, 627 (information about Shirley Nolan 1942-2002)
4. Website of the New York Cord Blood Program: www.nationalcordbloodprogram.org (the first public active cord blood bank)
5. Website of the National Marrow Donor Program: www.marrow.org (general information about blood stem cell donation; the largest blood stem cell donor registry)
6. Website of Anthony Nolan Trust: www.anthonynolan.com (the first active registry)
7. WMDA Annual Report Stem Cell Donor Registries 2004
8. WMDA Annual Report Cord Blood Banks/Registries 2004
9. Bone Marrow Donors Worldwide Annual Report 2004: www.bmdw.org