

# Bone Marrow Transplantation: A Gift to Society

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The advent of the 21<sup>st</sup> century has seen great developments in our society. The focus of medicine in the developed world has shifted from the treatment of communicable diseases—such as malaria and TB—to the treatment of diseases of affluence, such as cardiovascular disease and cancer. As our standard of living improves and our life span increases, the incidence of leukaemia has also gone up (1). Leukaemia is a form of cancer which can affect the very foundations of our blood system: our bone marrow (2) (See diagram 1) In the UK alone, a staggering 7,000 people are diagnosed with leukaemia every year, with 4,300 deaths annually (1).

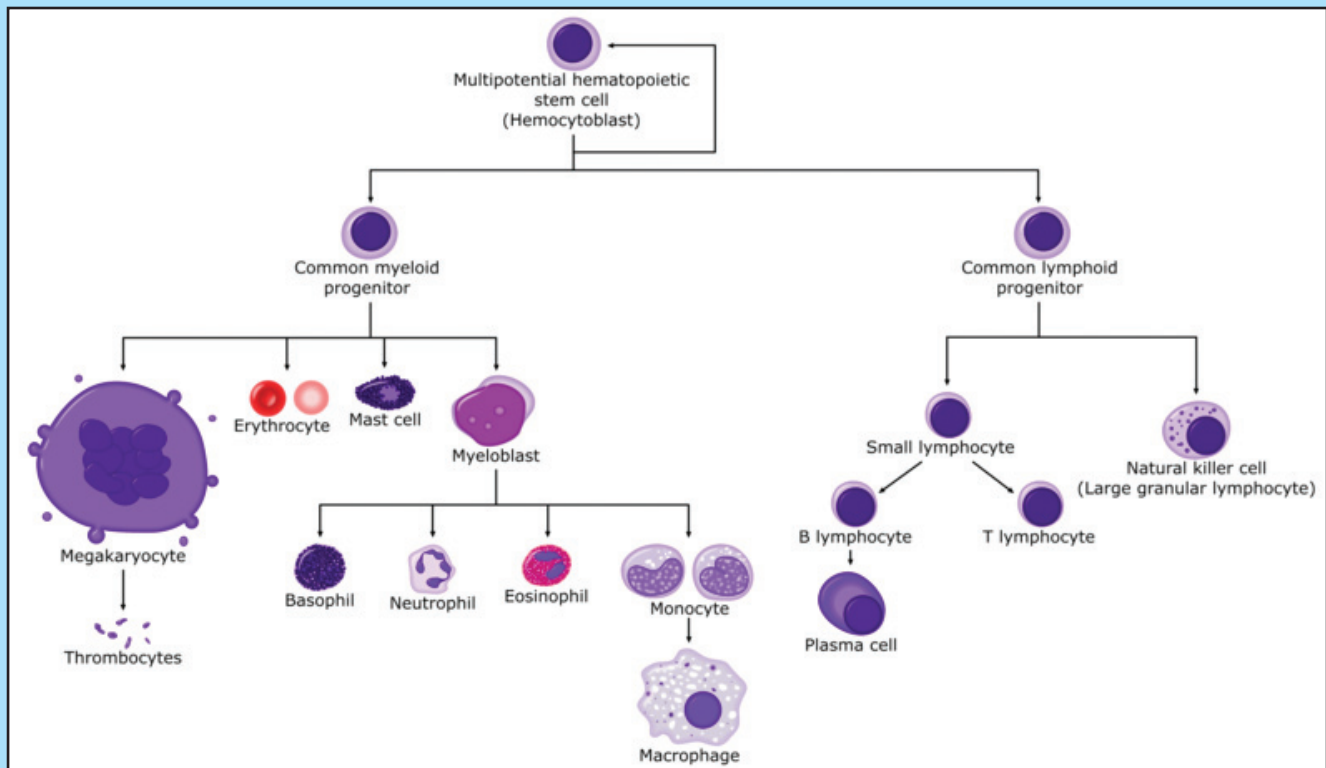
As always, medical research teams raced to the rescue. After several attempts to keep leukaemia at bay, researchers finally hit upon marrow transplantation as a key to patient survival. Pioneered by E. Donnall Thomas and his team at the Fred Hutchinson Cancer Research Centre in the 1950s, bone marrow transplantation (BMT) is a therapy for patients with certain cancers or other diseases which affect the bone marrow and therefore constituents of the blood (3). The goal of BMT is to obtain healthy blood stem cells from the

donor, and use these to replace the malfunctioning cells of the recipient or to replenish the cells of patients whose own bone marrow has been destroyed by harsh treatments such as chemotherapy.

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There are two types of bone marrow transplantation: autologous BMT and allogeneic BMT. In autologous BMT, the more common treatment, the donor is the patient himself. Healthy stem cells are either 'rescued' before cancer therapy and re-introduced after treatment, or harvested after chemotherapy once the patient is in remission from leukaemia. The donor in allogeneic BMT, on the other hand, is a family member or a non-related person whose 'Human-Leukocyte Antigens' (HLAs) match those of the patient. A

## Bone Marrow



This diagram shows the role of the bone marrow in the immune system. Bone marrow contains 2 types of progenitor stem cells, including haematopoietic stem cells which can multiply and differentiate into cells which make up our immune system, including macrophages, lymphocytes and natural killer cells. Haematopoietic stem cells can also differentiate into red blood cells and platelets, meaning bone marrow transplants can also help people with certain blood disorders such as aplastic anaemia

perfect match is needed in all clinical scenarios in order to prevent *graft-versus-host disease* (GVHD), a complication in which the immune cells contained within the donor's injected cells can attack a range of different organs in the recipient, having serious consequences (4). With conventional tissue typing, there may be subtle differences between host and recipient HLA molecules which are not picked up, but are enough to cause GVHD, so DNA sequencing methods are now used instead (5). If, even after searching through international registers, a complete match cannot be found, some partial matches might be accepted, depending on the nature and degree of the differences (6).

Apheresis is a typical, modern procedure that involves harvesting peripheral blood that has been enriched for peripheral blood stem cells (PBSC) following a cytokine injection (7). Blood is taken from the donor and the stem cells are filtered out and collected, whilst the remaining blood is directed back to the donor. As this procedure does not involve general anaesthesia, there is a quicker recovery time (8). An older, more traditional method involves extraction of bone marrow from the hip bone of the donor, who is usually placed under general anaesthesia throughout the procedure (9). In both cases, the recipient's own unhealthy bone marrow is destroyed via full body irradiation or chemotherapy, before it is replaced with the healthy marrow from the donor via intravenous injection.

Since its full introduction in 1968, bone marrow transplantation has been heralded by patients as the gift of life. As more and more patients turn to marrow transplantation as a cure, this treatment has gained its own special place in 21<sup>st</sup> century society. BMT is not only a life-saver for leukaemia, but also for a wide-range of conditions including severe combined immunodeficiency or 'baby in the bubble' syndrome, named after the sterile plastic sphere protecting the baby from infection. Bone marrow transplantation, more recently in combination with gene therapy, has finally enabled some affected children to lead relatively normal lives (10).

For allogeneic transplants, bone marrow donors generally comprise of family members with matching HLA-haplotypes (usually siblings since they have a 25% chance of a match (11)). Genetic compatibility is vital to prevent rejection of donated stem cells by the patients' body. However, family members are not always genetically compatible with the patient. This is when the need for an unrelated donor arises.

Finding an unrelated, genetically-compatible donor is a Herculean task for the individual patient as the HLA genes are highly *polymorphic*, meaning that there are many hundreds of different versions

of these genes in the general population; and *polygenic*, meaning individuals have more than one HLA gene (six), making the chances of finding a donor with the same haplotype, or set of HLA genes, extremely difficult (12).

To aid this search, several countries have set up donor registers, which contain details of prospective donors. The Anthony Nolan Trust (ANT) (13) was the first such register in the world. Based in the UK, it searches for compatible donors on behalf of at least 3000 newly diagnosed patients each year. In fact, the ANT can be looking for donors for up to 7000 people worldwide at any one time. To become a new donor, you need to be between 18 and 40 years of age (14), making university students the most eligible proportion of our population. According to current donors, it is a humbling experience to know that students can make a great difference in society so easily.

Despite the simple donation procedures, registering as

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### Registering as a donor can be a huge responsibility

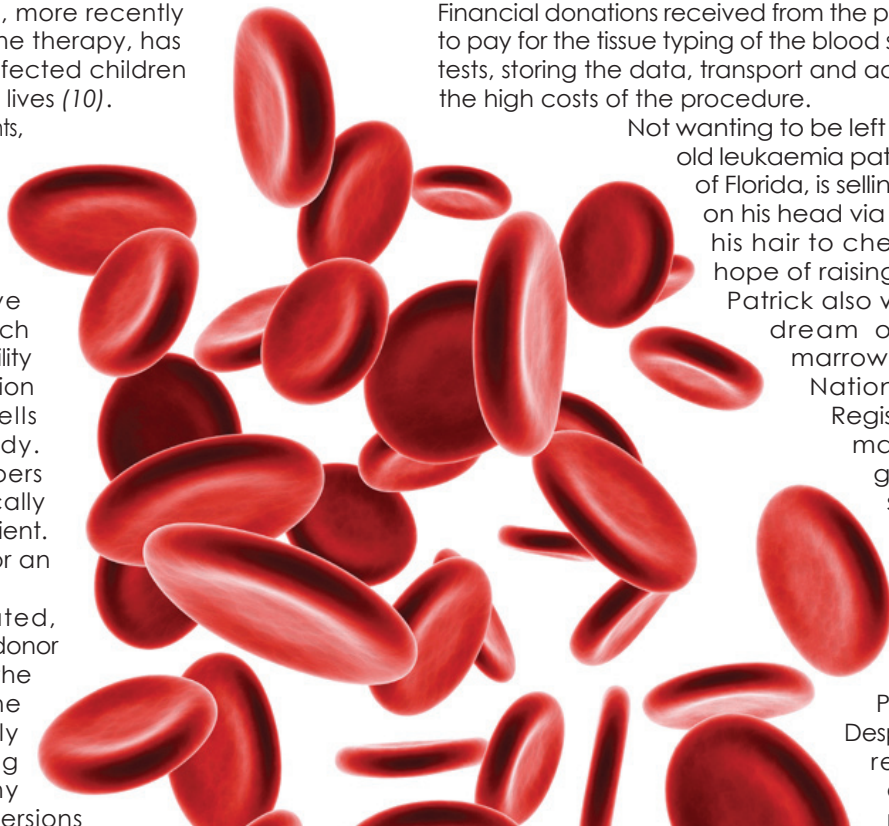
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a donor can be a huge responsibility. A donor needs to be available to a patient at any time, and joining the registry is a lifelong commitment. Although the donor is able to opt out of the BMT procedures at any time, doing so can be devastating news for expectant recipients who, at an early stage, will have been informed that a suitable match has been found. Not everyone can register as a donor as there are certain exclusion criteria including medical conditions and high risk sexual behaviour (14). But these criteria do not deter generous community members from helping out. Many of those who are not able to donate have campaigned to help raise awareness, or have raised funds for the ANT. Financial donations received from the public are channelled to pay for the tissue typing of the blood samples, other blood tests, storing the data, transport and accommodation, and the high costs of the procedure.

Not wanting to be left behind, an 11-year-old leukaemia patient, Patrick Pedraja of Florida, is selling advertising space on his head via eBay after losing all his hair to chemotherapy, in the hope of raising funds for patients.

Patrick also wishes to realise his dream of recruiting 2007 marrow donors to the USA National Donor Program Registry in 2007. "All that matters to me is if we give one person a second chance at life," said Patrick during a recent chemotherapy session (15).

Unfortunately, not everyone shares Patrick's awareness. Despite the considerable reservoir of donors, ethnic minority patients are still



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### How You Can Help

'Marrow' is the student run wing of the ANT. We are different from the ANT in that we use medical students to counsel potential donors, explaining to them the commitments required and the pros and cons of joining the register. Firstly, Cambridge University Marrow runs clinics at least once a term, providing plenty of opportunities for people wishing to join the register. We provide prospective donors with as much information about the procedures and implications of joining the register as we can, and help them fill out their form and answer any questions. Secondly, medical students can train as counsellors and provide support at the clinics. Thirdly, clinical students can volunteer as phlebotomists, who take blood samples. Last but not least, we are a charity, so fundraising and raising awareness are key parts of what we do. Thus, whether it be volunteering at our street collections, attending charity events like the annual Ceilidh, or signing up to be a college representative, your involvement is very much welcome.

### Bone marrow transplantation has been heralded by patients as the gift of life

For more information about all of our activities, please visit our website: [www.srcf.ucam.org/marrow](http://www.srcf.ucam.org/marrow)

thirsty for help. There are very few African and Asian donors, and although it is possible for a minority patient to match a donor from any racial group, the most likely match is a person who shares the patient's same racial background. Currently, an African-American searching for a matching donor is 30% less likely to be successful compared to a Caucasian (16).

#### Donors to the Rescue

Bone marrow transplantation (BMT) has been highly successful in combating leukaemia and other diseases, and demand for BMT is increasing in the healthcare market. As desperate patients try their best to get to the limited number of donors, some irresponsible parties have taken advantage of this 'lucrative' procedure, creating the need for law enforcement.

In 2006, it was revealed that certain Ukrainian hospitals might have been involved in what looked like an illegal trade of bone marrow and organs for transplantation taken from aborted fetuses and babies snatched at birth. These incidents may have been taking place since the autumn of 2002. This could also be more widespread, including other Eastern European countries, such as Moldova where some single mothers are offered up to 3,000 euros for their babies (17, 18).

Limited numbers of adult donors have also driven some to consider foetal bone marrow transplantation as an alternative. However, this raises many ethical issues regarding

the morality of harvesting stem cells from foetuses (obtained via induced abortion). In some countries, laws similar to the Fetal Protection Act of the US have been enacted to protect foetal rights. However, there are also other stem cell sources, such as umbilical cord stem cells, which are more ethical and are beginning to be used (19).

An increase in adult bone marrow donors will help reduce these problems.

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