## **Blood Donation and Beyond**

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World Blood Donor Day is celebrated on 14 June every year.<sup>1</sup> On that day, countries all around the world express their appreciation for blood donors, whose generous gift of blood have saved the lives of millions of people they have never met. It is a precious gift indeed as the donated red blood cells help to carry sufficient oxygen to critical tissues during anaemia or blood loss while the derived platelets and plasma help to prevent uncontrolled bleeding in selected situations. Yet, the global need for blood transfusion is far greater than the current available supply. This situation is most acutely felt in developing countries, which have 82% of the world's population, but which only collect 38% of the world's blood units.<sup>2</sup>

While history is filled with many exciting and, sometimes horrific encounters of both successful and failed blood transfusions, the 20th century saw many new breakthroughs for blood transfusion. In 1900, Karl Landstenier discovered human blood groups,<sup>3</sup> paving the way for the first direct human blood transfusion<sup>4</sup> and a century of development in safe and rational blood transfusion. Currently, the whole blood transfusion has been largely replaced by transfusion of specific blood components like packed red blood cells, plasma or platelets are carried out instead. This increases the efficiency of blood banking and helps deliver the appropriate blood product to the patient most in need of it. The advent of pheresis devices that perform dynamic separation of blood components have further facilitated the collection of specific blood components leading to more efficient platelet and granulocyte donation.5

The discovery of transfusion transmissible diseases like the viral hepatitis and the human immunodeficiency virus led to a new wave of awareness in the screening of donors and blood products. The threat of continually emerging infectious diseases further threatens our access to safe blood. Fortunately, scientific advances in blood processing, storage and testing technologies, as well as numerous efforts to promote and enhance blood donation have helped to meet these challenges. However, increased need of testing also means escalating costs – which developing countries can ill afford.

The last 60 years have also seen the development of a new type of "blood" donation: that of blood-forming (haematopoietic) cells. In the late 1950s, a group of clinician investigators performed the first successful transplant of haematopoietic stem cells (HSC) derived from the bone marrow of a healthy twin donor.<sup>6</sup> This set the stage for many decades of exciting development in these so-called bone marrow transplants (BMT). However, some of the first patients undergoing BMTs came down with an unusual plethora of symptoms including skin rash, jaundice and diarrhoea. This syndrome was later termed graft versus host disease (GVHD) and identified as being caused by donor immune cells attacking the patient's cells and tissues.<sup>7</sup> With the advent of effective immunosuppressive drugs like cyclosporine as well as a better understanding of histocompatibility and human leukocyte antigens (HLA),<sup>8</sup> the risk of this disease was substantially reduced. The 1980's saw further development of 2 other sources of haematopoietic stem cells (HSC): peripheral blood stem cells (PBSC) and umbilical cord blood (UCB) stem cells. The former was associated with faster rates of haematopoietic recovery in the patient and higher rates of GVHD, while the latter was associated with slower engraftment, but lower rates of GVHD and increased ability to tolerate HLA mismatches. Currently, several hundred thousand HSCTs have been performed around the world and about 50,000 more are being performed every year.

UCB transplants have enjoyed recent popularity because of the rapid availability, lack of GVHD and relative ease of finding a donor. Results of partially mismatched unrelated donor UCB transplants have also been shown to be equivalent to that of fully matched bone marrow transplants.<sup>9</sup> Currently, there are more than 20,000 UCB transplants that have been performed from public UCB banks around the world which store and test donated UCB units in readiness for any patients who might be found to be a suitable match and require them later. The banking of UCB has also gained particular interest because of the advent of UCB banks which store UCB for personal and family use. It is important to note statements from societies like

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the American Academy of Pediatrics (AAP), which state that "the chances of a child needing his or her own cord blood stem cells in the future are estimated to range from one in 1000 to one in 200,000. Private cord blood banks target parents at an emotionally vulnerable time when the reality is most conditions that might be helped by cord blood stem cells already exist in the infant's cord blood."10 Many genetic disorders are also currently untreatable by a child's own UCB as the genetic abnormality is also present in the UCB. On the other hand, donation of UCB for public use is encouraged as there is substantial evidence of that unrelated donor UCB will be of benefit to patients who cannot find a suitable bone marrow or PBSC donor. Nevertheless, the decision to publicly donate or privately bank a UCB unit is a very individual decision based either on a sense of altruism and an assessment of current recommendations versus an unknown potential for new advances in future.

In this century, cellular therapy of blood components has extended beyond the mere transplantation of HSC and now includes the transfusion of ex vivo expanded T cells, NK cells, mesenchymal cells and various cellular subsets to selectively enhance and or suppress immune reactions. These modalities of treatment are under intensive study and some will likely prove useful in enhancing the power and precision of haematopoietic cell therapy. Thus, while many challenges continue to exist, the future of transfusion and transplantation of blood and blood-forming cells is bright.

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