

AMPATHCHAT

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Haematopoietic stem cell transplantation: An overview



Haematopoietic stem cell transplantation (HSCT) is any procedure where haematopoietic stem cells of any donor and any source are given to a recipient with the intention of repopulating the haematopoietic system in total or in part. Haematopoietic stem cell formation starts during embryonic development and is found in the bone marrow and umbilical cord blood. It expresses a unique marker

called CD34. This marker is used to identify haematopoietic stem cells in blood and bone marrow samples using flow cytometry technology. These cells are multipotent and can differentiate into a variety of specialised cells. They have the ability to mobilise from the bone marrow into the peripheral blood (Figure 1).

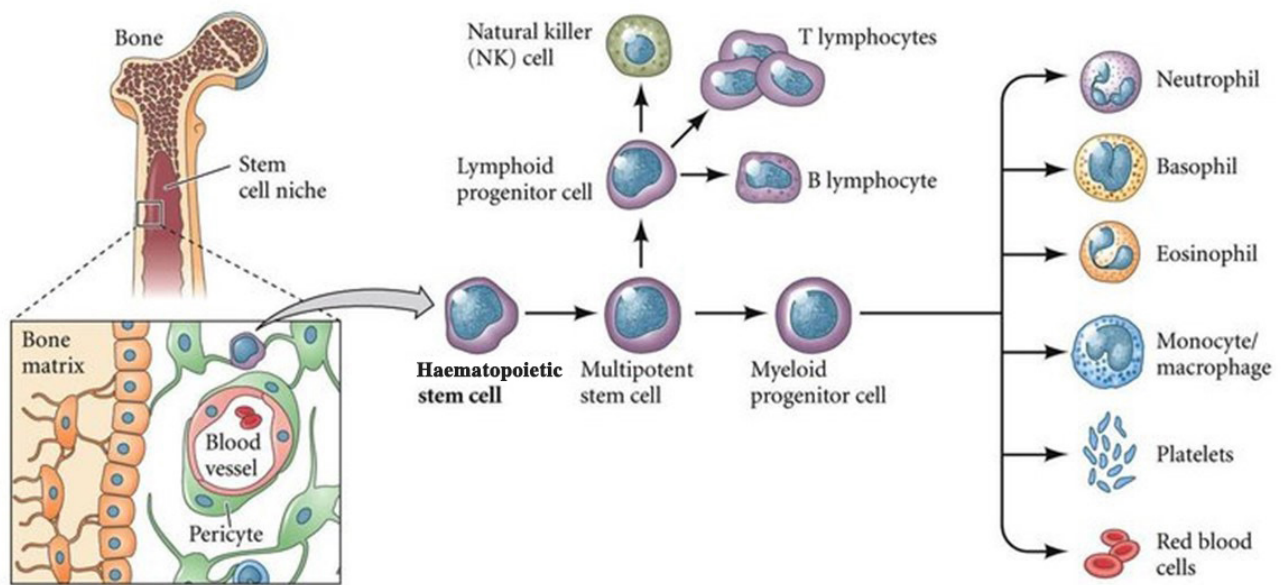


Figure 1: Differentiation of haematopoietic stem cells

INDICATIONS

Stem cell transplantation is a procedure used in the following conditions:

Malignant		Non-malignant	
<i>Haematological</i>	<i>Non-haematological</i>	<i>Haematological</i>	<i>Immunodeficiency</i>
Acute myeloid leukaemia	Neuroblastoma	Aplastic anaemia	Severe combined immunodeficiency syndrome
Acute lymphoblastic leukaemia	Germ cell tumours	Fanconi anaemia	
Non-Hodgkin lymphoma		Thalassaemia	
Hodgkin lymphoma		Sickle cell disease	
Multiple myeloma		<i>Autoimmune</i>	<i>Miscellaneous</i>
Chronic myeloid leukaemia		Systemic lupus erythematosus	Glycogen storage diseases
Myelodysplastic syndrome		Systemic sclerosis	Gaucher syndrome

TYPES OF DONORS

There are two types of donors:

Autologous: Stem cells are obtained from an individual's blood or marrow, and are infused back into the same individual (Figure 2)

Allogeneic: Stem cells are collected from a matching donor and transplanted into the patient to suppress the disease and restore the patient's immune system (Figure 3).

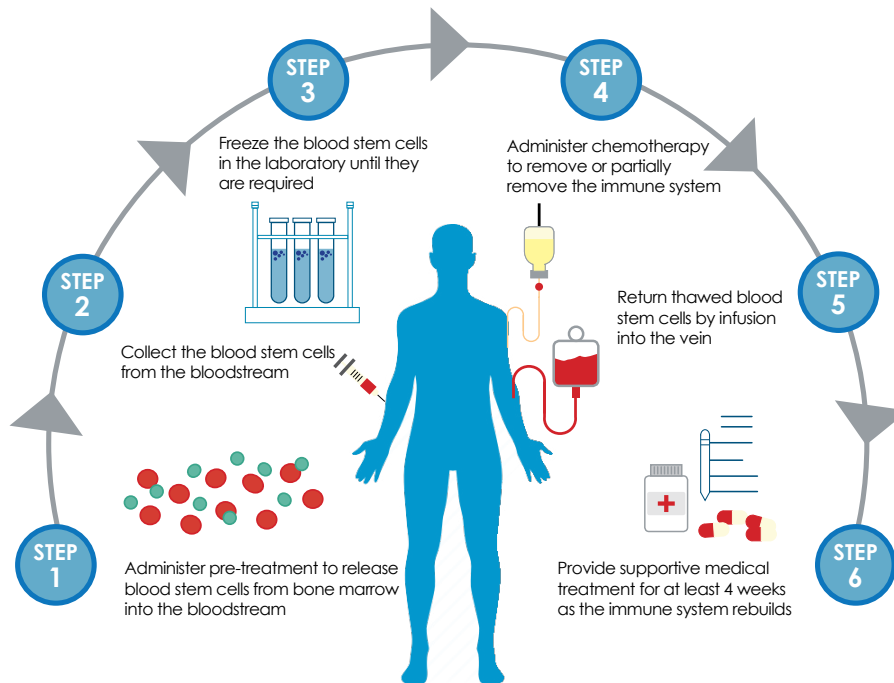


Figure 2: Autologous donors

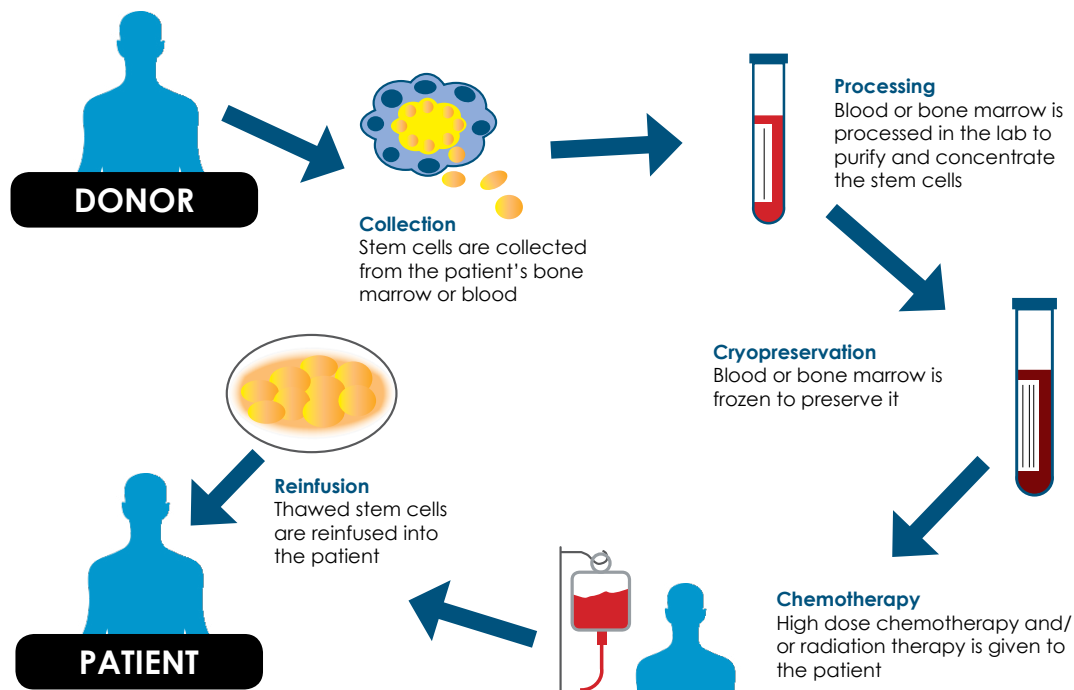


Figure 3: Allogeneic donors

DONORS

Donors can be HLA matched or HLA mismatched based on the human leukocyte antigen (HLA) complex, which is a gene complex encoding the major histocompatibility complex (MHC) proteins in humans. These proteins are responsible for the regulation of the immune system in humans. HLA are proteins found on the short arm of chromosome 6.

Three antigens are important in stem cell transplantation: HLA-A, HLA-B and HLA-DR.

One set of three is inherited from each parent.

Donors can be:

- Identical twins: HLA matched
- Related donors (sibling or relative): HLA matched, HLA mismatched or haploidentical (half-matched donor)
- Unrelated donor: HLA matched or HLA mismatched

Stem cell sources for transplant are as follows (Table 1):

- Bone marrow
- Peripheral blood
- Umbilical cord blood

Table 1: Clinical characteristics related to allogeneic transplants

	Bone marrow	Peripheral blood (PB)	Cord blood (CB)
HLA typing	Restrictive	Restrictive	Less restrictive
Yield	Best	Less	Limited number of cells
Engraftment	Faster than CB	Fastest	Slowest
Acute GVHD	++	++/+++	+
Chronic GVHD	++	+++	+
Graft vs tumour	++	++/+++	+++
Availability	Depends on donor type	Depends on donor type	Immediate access Cord blood banks
Donor's risk	Anaesthesia Surgical procedure	Use of granulocyte colony stimulating factor (G-CSF) injections Apheresis	None

Graft versus tumour effect occurs when the graft contains donor T cells that can be beneficial to the recipient by eliminating the residual malignant cells.

Graft versus host disease (GVHD)

In GVHD the donor cells view the recipient's body as foreign, and the donated cells attack the body. Classic acute GVHD occurs within the first 100 days. It affects the skin, gastrointestinal tract and the liver.

Chronic GVHD may be found in the skin, mouth, gastrointestinal tract, lung, fascia and genitalia (for example, lichen planus or lichen sclerosis, poikiloderma, sclerosis, or esophageal web).

Table 2: Classic acute, classic chronic and overlap syndrome

	Symptoms post-HSCT	Presence of acute features	Presence of chronic features
Classic acute	≤ 100 days	Yes	No
Acute Persistent Recurrent Late onset	> 100 days	Yes	No
Classic chronic	No time limit	No	Yes
Overlap syndrome	No time limit	Yes	Yes

Transplantation process for allogeneic transplants

Conditioning

Chemotherapy is given to eliminate malignant cells (7 to 10 days)

Stem cell infusion

Takes 20 minutes to 1 hour

Neutropaenic Phase (2 to 4 weeks)

No immune system, supportive measures

Engraftment Phase

Management of GVHD and prevention of viral infections

Post-engraftment period (months to years)

Reconstitution of the immune system

Post-engraftment monitoring

Chimerism testing (engraftment analysis): the test involves identifying the genetic profiles of the recipient and the donor and then evaluating the extent of mixture in the recipient's blood or bone marrow.

Factors influencing outcome

Disease factors

Staging

Patient-related factors

Age, co-morbidity

Donor-related factors

Histocompatibility (HLA)

Viral status (cytomegalovirus)

Peri-transplant

Conditioning

GVHD prevention

Stem cell source and content

Post-transplant

GVHD

Practical challenges

Finding a donor

This is administered by the South African Bone Marrow Registry (SABMR).

Financial

Facilities available both in state and private.

Emotional strain on patient and family

Need for clinical psychologist intervention.

Disruption of routine and family life, schooling, work.

Fertility can be affected.

South African Bone Marrow Registry (SABMR)

The SABMR was established in 1991, and is a member of the World Marrow Donor Association (WMDA).

The SABMR searches both locally and internationally for donors.

Its mission is to save lives and provide hope for all patients in need of bone marrow stem cell transplantation.

Why should you become a donor?

- Presently there are more than 73 000 donors on the SABMR's database.
- More than 450 patients have received matched unrelated bone marrow transplants in South Africa.
- The Registry works with more than 75 international registries with approximately 33 million donors worldwide.
- Donor matches depend on tissues types. These inherited genetic characteristics are often more frequent in a particular group. Therefore, it is important that people of all races register as donors.
- There is a 1:100 000 chance of finding a match.
- Testing is painless with no cost to you.

How to become a donor?

- Visit www.sabmr.co.za/become-a-donor.
- Read the criteria so that you are eligible to be a donor and register online.
- Fill out the donor application form and return the completed form to donors@sabmr.co.za.
- If you are eligible, a buccal swab kit will be sent to you or you will be directed to one of the SABMR's locations where the buccal swabs are kept.
- Follow the buccal swab kit instructions.
- Samples will be analysed and results will be available in four to eight weeks.
- You will receive a membership card.

REFERENCES

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