

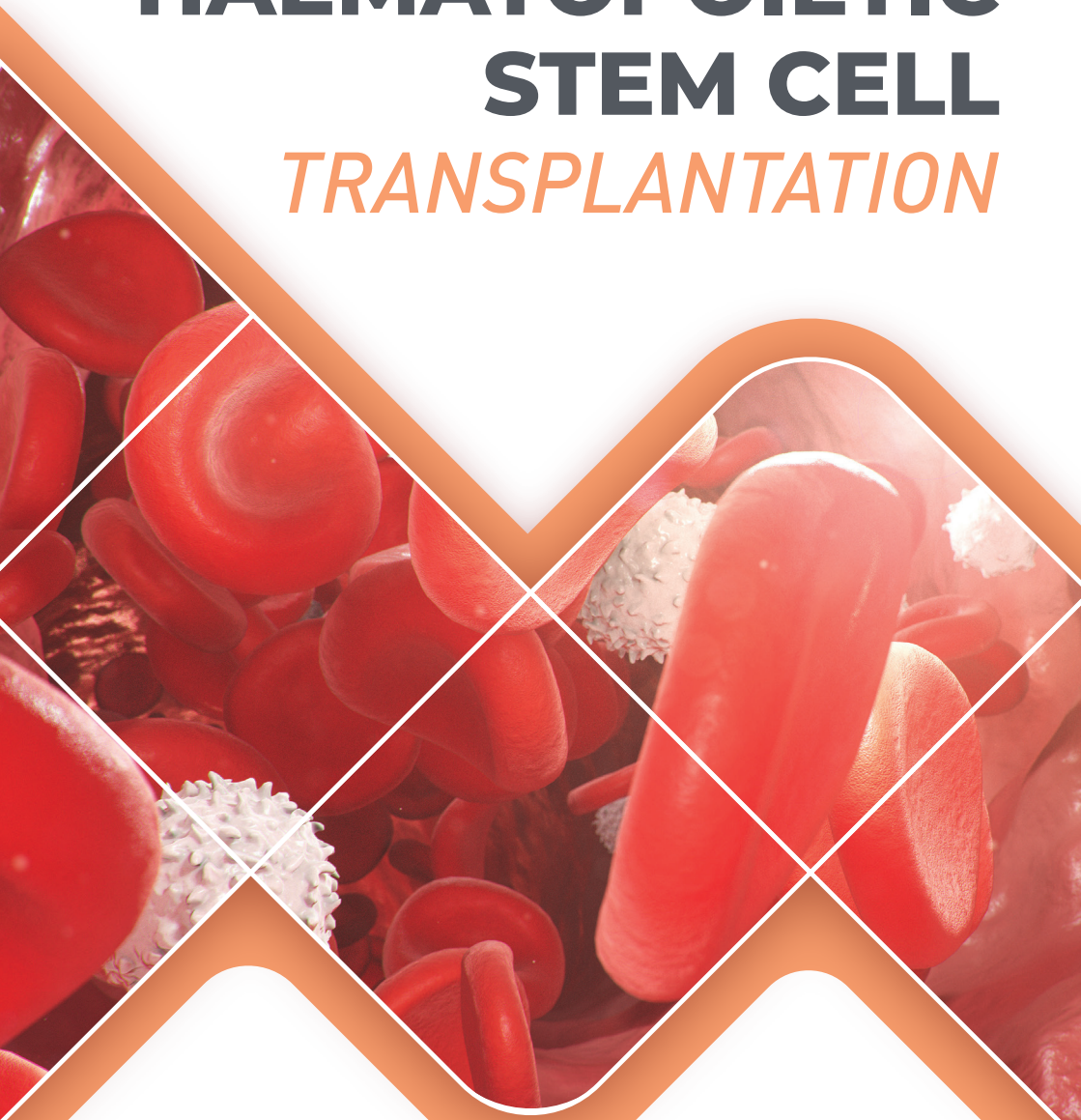


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Sunway City Kuala Lumpur

A Comprehensive Introduction To

# HAEMATOPOIETIC STEM CELL *TRANSPLANTATION*



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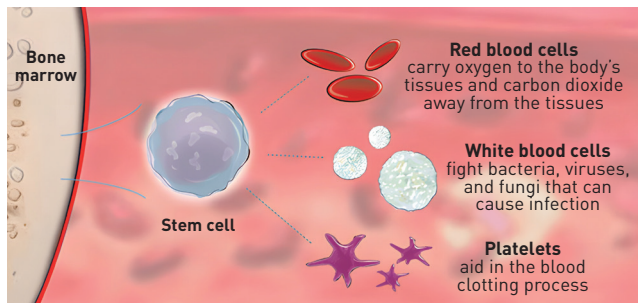
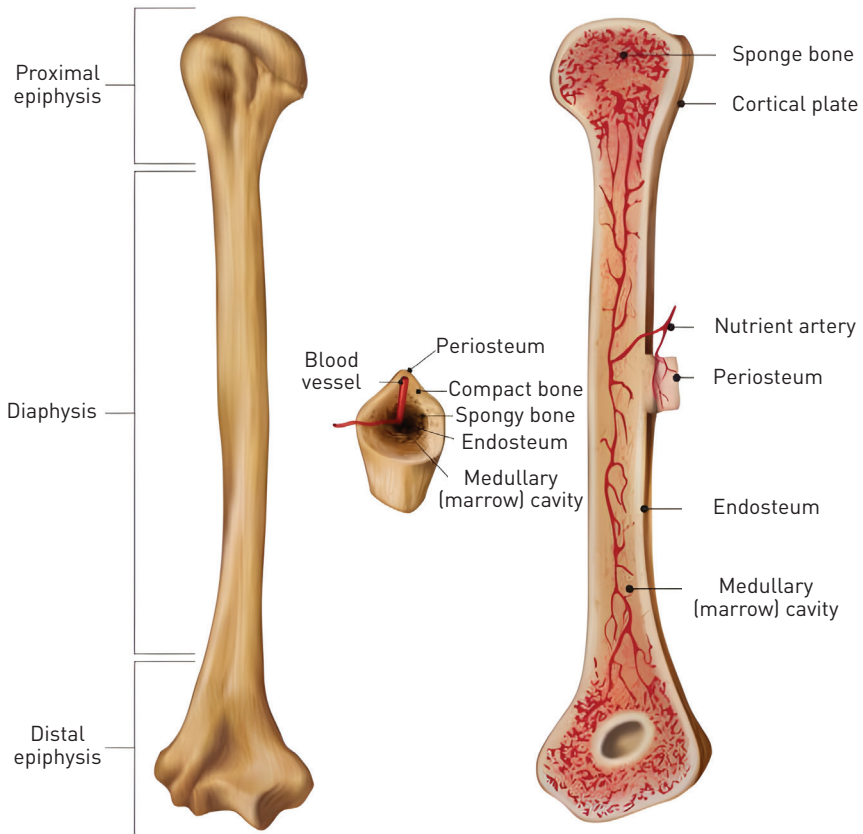
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# PART 1 UNDERSTANDING STEM CELL TRANSPLANTATION

Bone marrow is found in the center of most bones and has many blood vessels. There are two types of bone marrow: red and yellow. Red marrow contains blood stem cells that can become red blood cells, white blood cells and platelets. Yellow marrow is made mostly of fat.

Structure of a long bone. Humerus. Tube.



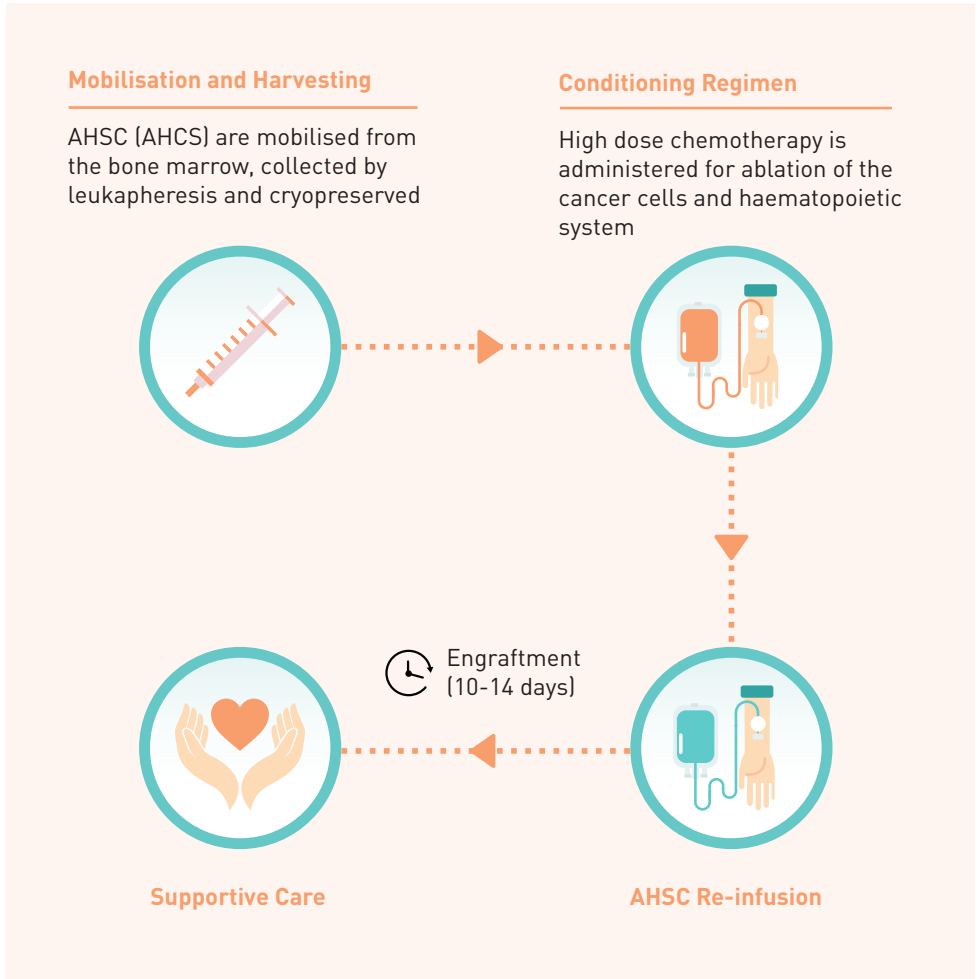
## Sources of Hematopoietic Stem Cell:

- ✓ Bone Marrow
- ✓ Peripheral Blood
- ✓ Cord Blood

# Types of Hematopoietic Stem Cell Transplantation

## 1) Autologous Stem Cell Transplantation

Stem cells are collected from your own body and stored in a freezer. Your stem cell will be infused back to you after receiving chemotherapy as known as conditioning regimen.

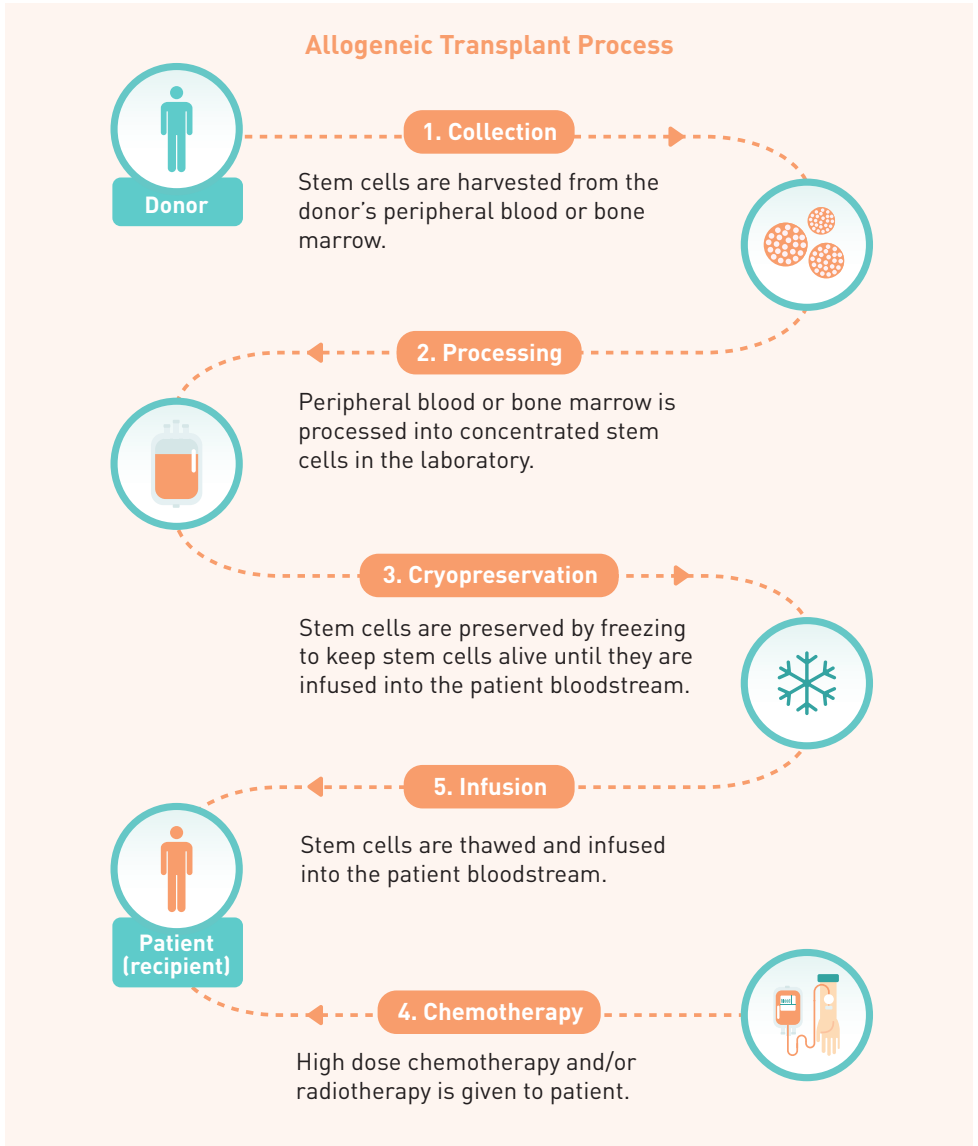


## 2) Allogeneic Stem Cell Transplantation

Stem cells are collected from a donor and stored in a freezer. The donor's stem cells will be infused into your body (recipient/patient) after you have received conditioning chemotherapy, radiation, or both.

Stem cell donors can be:

- Family – Parent, sibling, family members
- Matched unrelated donor - Voluntary donor

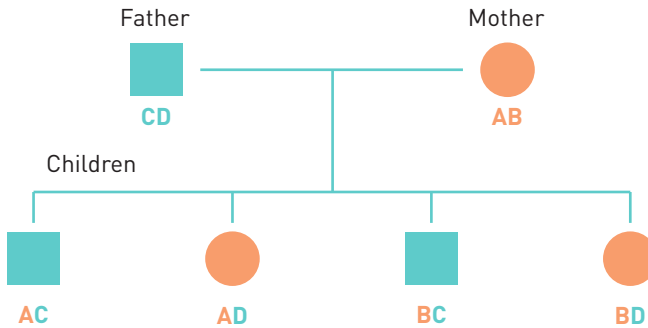


## Types of Donor

<b>Autologous</b>	Patient's own stem cell
<b>Allogenic</b>	Donor, based on Human Leukocyte Antigen (HLA) Type

## HLA Typing

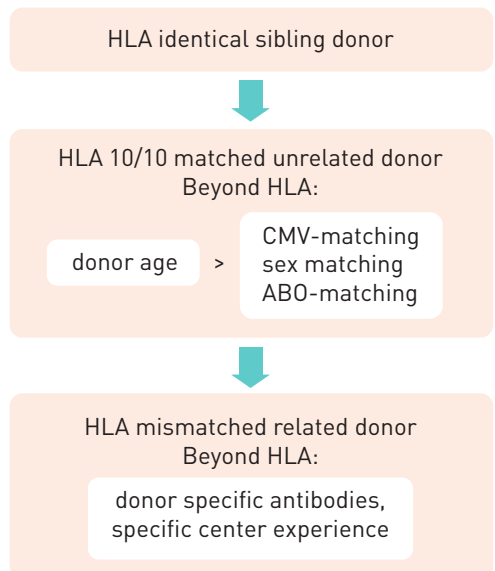
Human HLA type is inherited from our father and mother with one haplotype from each parent. There is a one-in-four chance (25%) that siblings may match another.



## Donor

- 1. Sibling donor**  
HLA matched brother or sister
- 2. Unrelated donor**  
From a donor registry
- 3. Haploidentical**  
Half-matched family member
- 4. Syngeneic**  
Genetically identical twin

## Algorithm for Donor Selection



## PART 2 PRE-TRANSPLANT EVALUATION

### Pre-transplant Workup, for RECIPIENT Only

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Before you become a transplant candidate, your overall physical condition will be evaluated. Components of the transplant evaluation process includes, but are not limited to, the following:



#### Blood tests

Blood tests are required as a baseline to compare to during your transplant.



#### Radiology tests

Radiology tests such as **Computed Tomography (CT) scan** that gives more detailed images of soft tissue and bone than a standard x-ray. **Position emission tomography (PET) scan** is used to look for certain types of cancer, as well as your organs and how they work in your body.



#### Bone marrow aspiration and biopsy

This is done to check how well your bone marrow is making cells and to look for any signs of cancer in the marrow.



#### Lumbar puncture (spinal tap)

A lumbar puncture is only done for certain types of leukemia and lymphoma. Sometimes, chemotherapy is injected into your cerebrospinal fluid (CSF) to keep the cancer from spreading there or to treat cancer if it's already there.



#### Diagnostic tests

Diagnostic tests such as **echocardiogram (echo)**, **electrocardiogram (ECG)** and **Pulmonary Function Test (PFTs)** are performed to assess your overall health condition.



#### Dental clearance

You are required to visit a dentist for dental assessment to establish general oral health status, and identify and manage existing or potential source of infection, trauma or injury.



#### Emotional / Mental health

It is also important to ensure your mental well-being. Please inform your caregiver if you need further counselling with our psychologists or psychiatrists.

## DONOR Evaluation

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Once you have been confirmed as a potential donor, you are required to undergo health evaluation to determine if you are fit and suitable for the stem cell donation procedure.

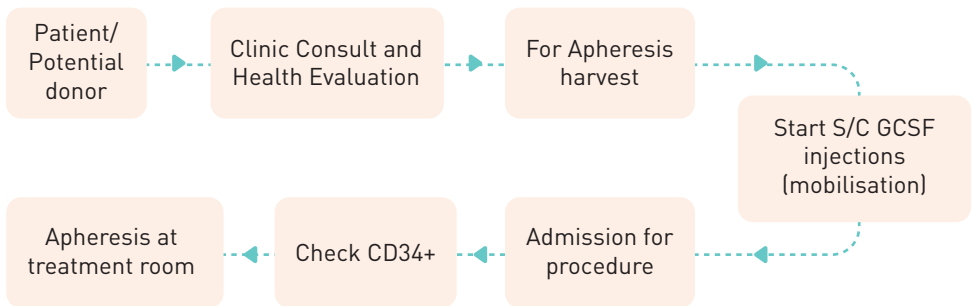
The health evaluation includes but is not limited to:

- ✓ Complete medical history and physical examination
- ✓ Chest x-ray
- ✓ Electrocardiogram
- ✓ Blood investigations, including tests for communicable disease
- ✓ Psychological assessment if requested

## PART 3 STEM CELL MOBILISATION AND COLLECTION

As stated earlier, stem cell sources are from patients themselves (AUTOLOGOUS) or matched-related sibling/ matched unrelated donor (ALLOGENEIC).

Below is an illustration that explains the process of stem cell collection:



## Mobilisation

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Although there are very few peripheral blood stem cells, their numbers can be increased through administering medications such as:

Growth factors, granulocyte-colony stimulating factor (GCSF)

GCSF is given daily and injected into the subcutaneous tissue usually at the abdomen area. Patient goes to the hospital daily for injection. You will be provided a timetable and simple instructions of what is needed to be done on a daily basis.

Some people may experience bone pain, low-grade temperature or discomfort following the injection, which is normally relieved by taking painkiller.

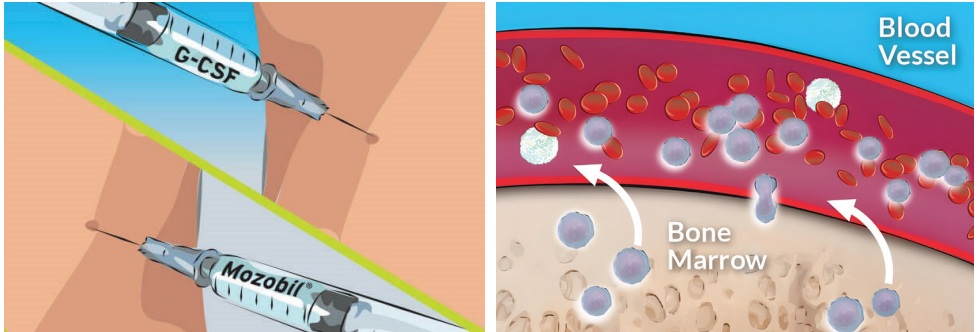


### Common side effects of G-CSF

- ✓ Tiredness
- ✓ Flu-like feeling
- ✓ Bone or muscle pain
- ✓ Fever
- ✓ Headache
- ✓ Dizziness

Less common side effects are chest pain, night sweats, difficulty in sleeping and dizziness. If these symptoms persist, you may need to inform the doctor-in-charge or transplant nurse.

Very rarely, it was reported worldwide causing stroke, myocardial infarction or splenic infarct. (< 3%)



### Plerixafor (Mozobil) injection

Plerixafor (Mozobil) is a drug used in combination with G-CSF for the patient who has poor bone marrow reserve (poor mobiliser). The use of Mozobil and G-CSF has been shown to improve the success rate of stem cell collection in certain patients.

Chemotherapy can serve as a stimulus for mobilising stem cells for stem cell collection. A combination of chemotherapy with G-CSF can mobilise stem cells better.

## Stem Cell Collection

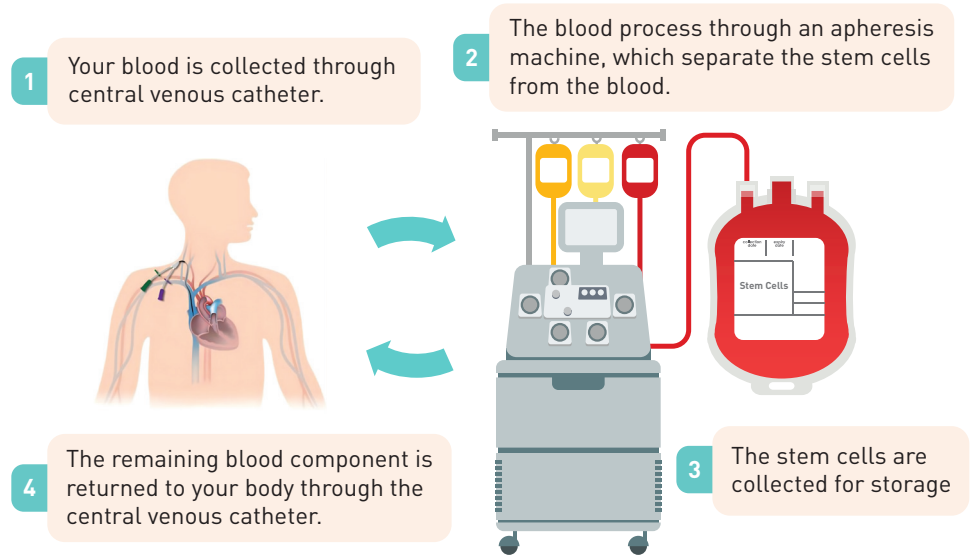
The timing of peripheral blood stem cell (PBSC) collection is critical. With the use of G-CSF alone, the peak of stem cell count (CD 34+) is on days 4 -5 which is the best time for stem cell collection.

2mls of peripheral blood will be taken to check whether the number of stem cells in the blood (CD34+) is sufficient for harvesting, on the scheduled collection day.

Once the CD34+ level is suitable for collection, patient/ donor will be prepared for stem cell harvesting through the process called APHERESIS.

A thin, flexible tube called Central Venous Catheter (CVC) will be inserted into a large vein either at the neck or groin under aseptic technique and local anaesthesia (LA). Some mild pain and mild bleeding are usually expected during the insertion. The CVC will be removed once adequate stem cell is collected, as determined by the doctor.

## Apheresis Process / PBSC Collection



A blood thinner called citrate may be added slowly to your blood during this process to help prevent blood clotting. This process may take approximately 4–6 hours to complete each session. A second collection may be needed if the first stem cell collection is inadequate.

These side effects of apheresis are temporary. They are due to changes in the blood volume of the patient as it circulates throughout the Apheresis machine. Citrate can reduce the blood calcium level which may cause the patient to experience tingling sensation, numbness around the lips or muscle cramp. This can be corrected by infusing Calcium Gluconate.

Below are the common side effects and they are normally transient and self-limiting:

### Common side effects of apheresis process

- ✓ Lightheadedness
- ✓ Coldness
- ✓ Tingling sensation at the hands and feet
- ✓ Numbness around the lips
- ✓ Muscle cramps
- ✓ Tremors

## Stem Cell Freezing and Storage

All stem cells that were harvested will be cryopreserved with Dimethyl Sulfoxide (DMSO) and stored in liquid nitrogen at  $-160$  to  $-196^{\circ}\text{C}$ . The collected stem cell will undergo microbiology culture upon collection and viability test will be done pre transplant.

Stem cells will be ready and waiting for you once you have completed your chemotherapy and/or radiation.

## PART 4 PREPARING FOR THE TRANSPLANT

Transplant preparation advice will be given to you and your family once transplant date is confirmed.

### Admission to Transplant Unit

- You will be admitted to a special and individual transplant room for about 3 weeks or more.
- One caregiver is allowed to be with you throughout the admission. However, to reduce the risk of infection, no visitors are allowed.
- Each room is equipped with telephone, television, cupboard and sofa bed.

#### Items to Bring



Slippers



A few pairs of warm and comfortable socks and jacket



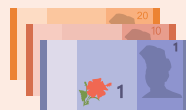
Hat or scarf



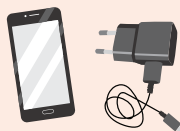
Individual packed biscuits and drinks



Thermos



Small amount of cash



Cell phone and charger

#### Items which are NOT permitted in the Transplant Unit



Fresh flowers and plants may contain bacteria and molds which can increase the risk for infection therefore are not allowed in the transplant unit

## What to Expect in the Hospital

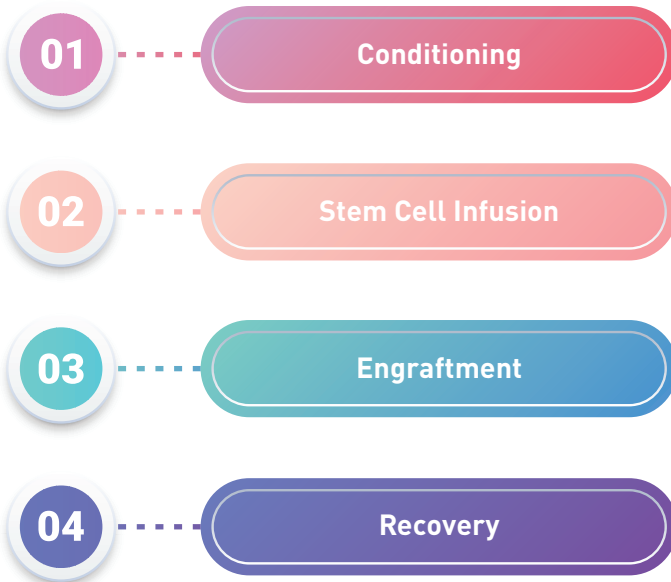
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- You will be connected to an IV pole with electronic pumps during most of the hospitalisation.
- Vital signs will be monitored every 4 hours or more frequent if necessary.
- Daily weight, fluid intake and urine output will be measured.
- Central line (catheter) would be inserted either at the neck or chest wall. This procedure will be done under local anesthesia by an Interventional Radiologist.
- You will be referred to a dietician and placed on a low-microbial diet (neutropenic diet).
- Blood test will be taken at a scheduled timing.
- You will be required to take medicines several times a day. Your nurse will be responsible for giving you your medicine at the prescribed times. Please bring a list of your current medicines when you are admitted.
- Meals will be served 3 times a day and snacks will be served during teatime.

## During Hospital Admission

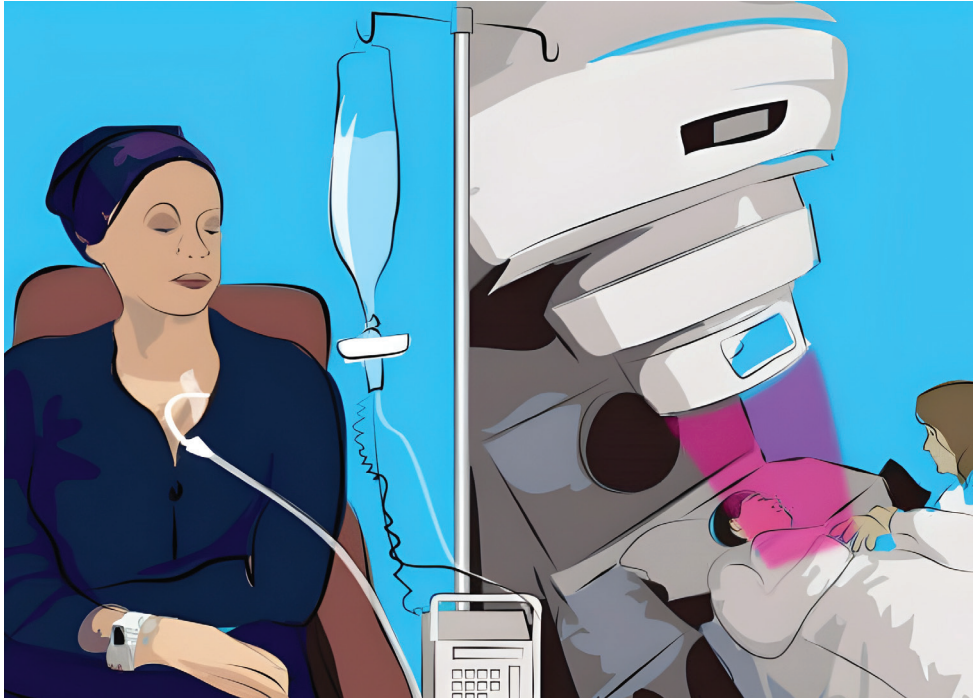
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- Stay active, walk around in the room and get out of bed every day. It reduces your risk of developing pneumonia.
- Keeping yourself clean is very important to help prevent infection, shower and change clothes daily.
- Keeping your mouth clean helps prevent mouth sores and infection. Bring your very soft toothbrush and fluoride toothpaste. Gargle with mouthwash.



## PART 5 CONDITIONING TREATMENT

Conditioning is the term used for the treatment rendered to patient in preparation for stem cell transplantation (SCT). Conditioning is usually a combination of two or more chemotherapy medications. Sometimes, it also includes radiotherapy.



Conditioning treatment is given to:

- Destroy the diseased cells in your bone marrow
- Suppress your immune system to allow the growing of donor's cells
- Create space in the bone marrow for the donor's cells

### Side effects

- ✓ Mouth sores
- ✓ Nausea and vomiting
- ✓ Diarrhea / Constipation
- ✓ Gastritis
- ✓ Fatigue
- ✓ Hair loss
- ✓ Risk of bleeding
- ✓ Organ toxicity
- ✓ Infertility
- ✓ Myelosuppression with neutropenic sepsis
- ✓ Transplant related mortality 5-10%
- ✓ Secondary malignancy in future

## Radiation Therapy

Total Body Irradiation (TBI) alongside high dose chemotherapy helps to kill off leukemia, lymphoma or myeloma cells in the bone marrow. TBI is widely used as part of myeloablative reduced intensive and non-myeloablative conditioning regimens to eradicate the disease, create immunosuppressive effect and space for donor cells to engraft. In addition, TBI is able to target sanctuary sites that some drugs cannot reach, such as central nervous system and gonads.

TBI is commonly given in fractions (2 doses each day) to minimise the side effects. A linear accelerator machine is used as a source of radiation. TBI is delivered in various doses and scheduling.

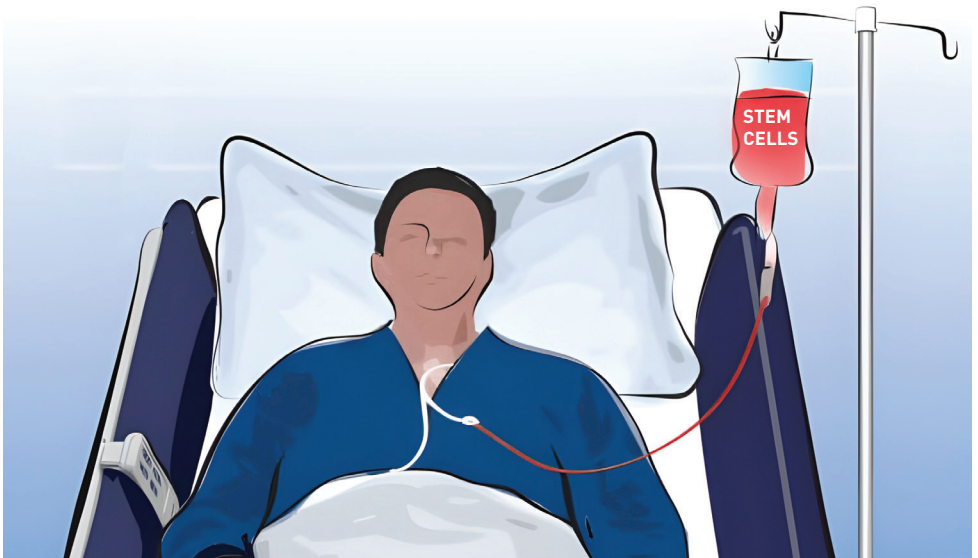
### Side effects of radiation therapy

- ✓ Dry skin
- ✓ Dry mouth
- ✓ Hair loss
- ✓ Nausea and Vomiting
- ✓ Parotid swelling
- ✓ Infertility

## PART 6 STEM CELL INFUSION

Transplant day is also known as Day 0.

On Day 0, the pre-collected stem cells will be re-infused into your bloodstream through your tunneled catheter. The stem cells will be transfused from a bag, just like a blood transfusion. The whole procedure will be done in the patient's room itself. Once they are infused, the stem cells will travel to your bone marrow and make new blood cells.



## Stem Cell Infusion

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- You will be given medications 30 minutes prior to the stem cell infusion to reduce the side effects of dimethyl sulfoxide (DMSO) which is a preservative used in the storage of stem cells.
- Your vital signs will be checked often during and after the infusion.  
You may have some side effects during and after your infusion such as nausea, flushing, headaches, low blood pressure and allergic reaction. The less common side effects are

Inform your transplant team if you have any side effects. If you do have side effects, your transplant team will treat them.

Your urine may look discoloured, ranging from pink-tinged to bloody. This can last for 24 hours after your stem cells are infused. This color change is caused by your body getting rid of extra red blood cells that may be with the stem cell infusion but aren't needed.

### **PART 7** IMMEDIATELY POST-TRANSPLANT PERIOD

This is the period where you would be experiencing the side effects from the conditioning treatment such as mucositis, diarrhea, gastritis, fatigue and loss of appetite. Your body takes time to recover.

It is extremely important to stay active. The more active you are, the stronger your body will be, and the more prepared you will be to return home. You are encouraged to walk in your room, sit in a chair for all your meals and walk to the bathroom to perform your daily grooming activities.

You are required to stay in hospital for another 2 to 3 weeks until:

- ✓ The engraftment has occurred - Sufficient & healthy white blood cell
- ✓ You can tolerate orally (solid and nourishing fluids)
- ✓ You can tolerate oral medications
- ✓ No signs of infection
- ✓ No treatment complications
- ✓ You are physically stable

## Graft-Versus-Host Disease (GVHD)

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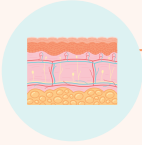
Graft-versus-host disease (GVHD) can happen in allogeneic stem cell transplant when the immune cells from the donor see your body as foreign. The donor immune cells may attack certain living organs, most commonly the skin, gastrointestinal (GI) tract and liver.

GVHD is very common. It can range from barely noticeable to life-threatening. There are two types of GVHD, acute GVHD and chronic GVHD. A person could have one, both, or neither type of GVHD.

## Acute Graft-Versus-Host Disease

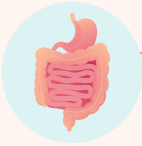
Acute GVHD can happen anytime during the first 100 days after allogeneic stem cell transplant. About one-third to one-half of allogeneic transplant recipients will develop acute GVHD. It is less common in younger patients and in those with closer HLA matches between donor and patient.

### Signs and symptoms of Acute GVHD



#### Skin

- Rashes (very faint to severe sunburn-like rashes)
- Blisters



#### Gastrointestinal Tract

- Nausea
- Vomiting
- Stomach discomfort and pain
- Diarrhea
- Belly pain that does not go away
- Bloating or full of gas
- Blood in stool



#### Liver

- Jaundice (yellowish skin or eye)
- Dark urine (tea colour)

Acute GVHD could be reduced by giving drugs that suppress the immune system, such as steroids (glucocorticoids), methotrexate, cyclosporine, tacrolimus, or certain monoclonal antibodies. These drugs are given before acute GVHD starts to prevent serious GVHD. Mild GVHD will almost always happen in allogeneic transplant patients. It is well documented that some level of acute GVHD is beneficial as the existing of graft versus tumour effect.



## Chronic Graft-Versus-Host Disease

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Chronic GVHD can happen any time after 100 days of allogeneic stem cell transplant. The extent of the disease can range from mild to severe.

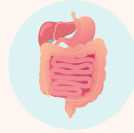
Chronic GVHD is treated with medicines that suppress the immune system, much like those used for acute GVHD. These drugs can increase your risk of infection for as long as you are treated for GVHD. Most patients with chronic GVHD can stop the immunosuppressive drugs after their symptoms improve.

### Signs and symptoms of Chronic GVHD



#### Skin and Nails

- Rashes
- Nail and skin texture changes



#### Digestive System

- Diarrhea
- Nausea and vomiting
- Stomach cramp



#### Joint and Muscles

- Pain and stiffness
- Muscle pain and cramps



#### Genitals

- Irritation or dryness
- Painful intercourse



#### Lungs

- Shortness of breath
- Cough that doesn't go away
- Trouble breathing

## Graft Failure

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Graft failure is a serious and fatal complication of allogeneic stem cell transplantation.

<b>Primary Graft Failure</b>	lack of initial engraftment of donor cells
<b>Secondary Graft Failure</b>	loss of donor cells after initial engraftment

Successful transplantation depends on the formation of engraftment, in which donor cells are integrated into the recipient's cell population.

## PART 8 DISCHARGE AND RECOVERY

You are advised to stay in a nearby amenity for 1 month post autologous transplant or 3 months post allogeneic transplant. You will be reviewed by the transplant team to ensure your health status is good.

Follow up appointment, in general, depends on patient's condition:

<b>Autologous stem cell transplant</b>	every 2 weeks for the 1st month
<b>Allogenic stem cell transplant</b>	every week for the 1st month

The frequency of follow up appointment will reduce according to your body's health status.

### Contact the Transplant Team If You Have

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- ✓ Fever with temperature above 38°C
- ✓ Change in the skin around the central line catheter
- ✓ Blood in urine or stool
- ✓ Coughing out blood
- ✓ Suspected graft vs host disease
- ✓ Persisting diarrhea, vomiting
- ✓ Painful in urination, tea colour urine
- ✓ Bleeding





## Transplant Medication

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It is important to know the names, dosage and timing of the medication.

You will be required to take your prescribed medications as directed. You may refer to the **medication list** from your pharmacist upon discharge for more information, and the medication list will be revised during outpatient appointment. Please inform your doctor or the transplant team if you experience any side effects.

For allogeneic stem cell transplant patient, please refer to **patient guide for medication in allogeneic stem cell transplant**.



## Dietary Advice

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After the stem cell transplant, you are encouraged to have adequate calories and protein in order to achieve and maintain your targeted body weight. You will need to practice Neutropenic diet, which is a low bacterial diet to reduce the risk of food-borne illness or food poisoning. You may refer to Neutropenic Diet Booklet for more information on dietary recommendation and meal plan. Please also follow dietary advice given by your dietitian.

Below is the general guidance:

- ✔ Eat 5 to 6 small portion meals daily instead of 3 large portion meals.
- ✔ Drink at least 2.5L to 3L of fluid daily.
- ✔ Avoid alcohol.
- ✔ Avoid raw and undercooked food such as salad, half-boiled egg, raw meat or fish.
- ✔ Wash and peel off the skin before eating the fruit.
- ✔ Do not purchase foods when foods or ingredients have been on the shelves for an unknown time.

## Sexual Activity

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- ✔ You should be able to engage in intimate sexual activities such as kissing, hugging, and touching after you are discharged from the hospital.
- ✔ Ensure partner has no infection and maintain hygiene
- ✔ Avoid sexual activity that involves penetration or contact with mucous membranes while platelet counts less than 50,000.
- ✔ Try using lubricant for vaginal dryness.
- ✔ Do not perform oral or anal sexual practices.



## Prevent Infection After Stem Cell Transplant

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### Mouth Care

Your white cell count may still be lower than normal, thus oral hygiene is important to protect the mouth from infections. You should let your doctor know if you notice any bleeding or ulcer in your mouth.

Good practice for mouth care:

- ✔ Brush teeth at least twice a day and when necessary
- ✔ Gargle with mouthwash after each meal and before bed
- ✔ Clean the dentures after each meal and keep in a container before going to bed. (if applicable)

### Hand Hygiene


Wash your hands often

- ✔ Before eating or cooking
- ✔ After going to the toilet
- ✔ After going outdoors and every time you return home



# HOW TO HANDWASH?

Wash hands when visibly soiled! Otherwise, use handrub

 Duration of the entire procedure: 40 - 60 seconds



Wet hands with water



Apply enough soap to cover all hand surfaces



Rub hands palm to palm



Right palm over left dorsum with interlaced fingers and vice versa



Palm to palm with fingers interlaced



Backs of fingers to opposing palms with fingers interlocked



Rotational rubbing of left thumb clasped in right palm and vice versa



Rotating rubbing, backwards and forwards with clasped fingers of right hand in left palm and vice versa



Rinse hands with water



Dry hands thoroughly with a single use towel



Use towel to turn off faucet



Your hands are now safe

## Caring of Your Tunneled Catheter / Hickman Catheter

**Redness, swelling, pain, fever and discharge** from the Hickman Catheter insertion site are the indications of infection. These photos below are infected Hickman Catheter. Contact the transplant team immediately if you suspect your Hickman line is infected. Do not apply cream or medication on the Hickman line insertion site without doctor's instruction.

Photos of the infected Hickman Catheter.



### Hickman Line Care

- ✓ Hickman Catheter is required to be flushed **ONCE A WEEK**.
- ✓ Keep the Hickman Catheter dry and clean.
- ✓ Cover the Hickman Catheter using clean plastic bag before shower.
- ✓ Avoid pulling the catheter or touching the Catheter site and the lumen.
- ✓ Never swim with Hickman line.
- ✓ Do not go into the bath tub.



## Home Environment and Pet

It is important to ensure the house is clean and tidy. Pets and plants could be a source of infection. You should avoid touching animal's saliva or faeces, remove all the plants from the bedroom and avoid touching soil from household plants. Wear gloves while gardening.



## Exercise

It is important to keep active even if you are feeling fatigue. This can help to prevent some of the complications of the transplant. You need to start gently and you will be able to build up your physical activity gradually within a couple months.



Get up, shower and dress, practise deep breathing exercise



Go for short walks around the garden



Build up your stamina gradually



## Going Back to Work

There isn't one rule for everyone when it comes to the right time to return to work. Usually the healthcare team will advise to take at least 3 months off work post transplantation and assess for fitness to resume work activities. This may be longer for those who have had GVHD or other complications.

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