

INFORMATION ON HAEMATOPOIETIC STEM CELL TRANSPLANTATION

Difference tissue sources of haematopoietic stem cells (HSC) for transplantation

HSCs are characterized by the ability of self-renewing replication and differentiation into blood cells of various lineages. In adult, HSCs normally reside in bone marrow (BM) but can be mobilized into peripheral circulation upon stimulation with growth factors and/or chemotherapy (mobilized peripheral blood stem cell, mPBSC). Both sources of HSCs are currently used for transplantation with comparable outcomes. BM stem cells are aspirated from the donors at the back of the pelvis in the operation theatre under general anaesthesia and transfused into the patients via intravenous route. After mobilization, mPBSCs are obtained by apheresis and transfused into patients intravenously. No general anaesthesia is required.

Different donor sources for haematopoietic stem cells transplantation (HSCT)?

HSCTs can be classified according to the type of donors. Donors can be the patients himself/herself (autologous) or it can be from another person (allogeneic), which can be patient's siblings or matched unrelated donors (MUD). In general, autologous HSCT is less toxic than allogeneic HSCT with less risk of severe infection, graft rejection and graft-versus-host disease (GVHD). However, only certain groups of patients may benefit from autologous HSCT:

1. Lymphoma or other solid tumours WITHOUT bone marrow involvement.
2. Certain groups of patients with multiple myeloma.
3. Autoimmune diseases.

Allogeneic HSCT is indicated for leukemia, severe aplastic anaemia, lymphoma with BM involvement, young patients with multiple myeloma as well as thalassaemia and primary immunodeficiency.

The following are the prerequisites for allogeneic HSCT:

1. HLA-matched donors (at least 5/6 HLA antigens for sibling and 6/6 for MUDs) available.
2. Patient aged 55 or below for sibling and 45 or below for MUD transplantation.
3. Patient who can give consent to the transplantation.

In recent years, allogeneic HSCT may be performed using reduced intensity of chemotherapy (mini-transplantation) in certain groups of patients. As a result, more elderly patients of older age group may benefit from transplantation.

Who can benefit from HSC transplantation?

Patients with the following diseases may benefit from HSC transplantation:

1. High risk acute myeloid (AML) or lymphoblastic leukaemia (ALL).
2. Advanced stage lymphoma.
3. Non-elderly patients (aged 65 or below) with multiple myeloma.
4. Chronic myeloid leukemia (CML) opted for transplantation.
5. Severe aplastic anaemia.
6. Congenital immunodeficiency and thalassaemia.
7. Solid organ tumours.

For patients with haematological malignancies (1-4), the best transplantation outcome can be accomplished when the underlying diseases are under adequate control. Patients with significant residual diseases are more susceptible to relapse after transplantation.

For children who are suffering from end stage neuroblastoma or rhabdomyosarcoma, and adults with breast cancer, HSC transplantation will be considered to improve the treatment successful rate.

Who can be the donor?

Donors for HSC transplantation may be siblings of patients or unrelated volunteer donors. In both cases, blood tests are performed on the donors for typing of human leukocyte antigen (HLA). This is the most important determinant for donor choices and the occurrence of HSCT complications, including infection, graft rejection and graft-versus-host disease. In Hong Kong as well as in many major BMT centers world-wide, HLA-matching is performed against the three major HLA pairs (i.e. 2 HLA-A, 2 HLA-B, 2 HLA-DR) located on the same chromosome. Under this system, the best matching between the patient and the donor would be a six-out-of-six match. For sibling donors, there is a 1/4 chance of having identical HLA-typing (6/6 match) with the patients. Siblings who have a 5/6 match with the patient would also be considered for transplantation. For unrelated donors, information on HLA-typing will be stored in the Hong Kong Bone Marrow Donor Registry (HKBMDR). Patients without a suitable sibling donor will be matched against the HKBMDR database for unrelated donors. Oversea databases will also be searched for patients without a suitable donor from Hong Kong. In all cases, unrelated donors will have to be 6/6 matched with the patients. Under exceptional circumstances, parents or children of patients may also be considered as donors for transplantation.

What donors have to do before transplantation?

HLA-matched sibling or unrelated donors will be interviewed. Detail procedures and potential risks associated with bone marrow (BM) harvest or PBSC mobilization will be explained. After the interview, potential donors will need to sign a written consent for HSC donation. Prospective donors will have to come to QMH in a separate occasion for physical examination and blood tests including blood grouping, complete blood picture, liver and renal function tests, hepatitis and HIV screening. Chest X ray and electrocardiogram will also be performed.

For BM donors, 300-500 ml autologous blood will be venesected in Hong Kong Red Cross about two weeks before the transplantation. To replenish blood loss during BM harvest, BM donors will be given iron supplement two weeks before and four weeks after the harvest. One day before the operation, donors will be admitted to the hospital for final assessment by haematologists and anaesthetists.

For allogeneic PBSC donors, they will have to come to QMH three days before the harvest for daily growth factor injection through subcutaneous route. On the fourth to fifth days of injection, they will also need to come to the apheresis centre for collection of peripheral blood stem cells.

For autologous PBSC collection, the patients will receive growth factors and chemotherapy eight days before the harvest. On the ninth to tenth days, the mPBSCs are collected in the same way by apheresis. Then the collected stem cells are cryopreserved in liquid nitrogen for later use.

Investigations for patients before transplant

Patients will be worked-up one to two months before transplantation. The following investigations and work-ups will be performed before transplant:

- Blood test: complete blood picture, biochemistry, viral screening and others. These tests will be repeated during hospitalization.
- Specimen from throat, ear, rectum, urine, stool and sputum for bacterial and viral culture.
- 24 hours urine for renal assessment.
- Chest X ray.
- Lung function test and electrocardiogram.
- Bone marrow aspiration to assess the pre-transplant disease status.
- Insertion of Hickman catheter (central venous catheter) to facilitate blood taking and nutrition supply so as to diminish peripheral vein access and painful needle pricks.
- Dental assessment or detection of other potential sites for infection, if needed specialist will be consulted for appropriate treatment.
- Dietitian consultation to optimize the nutritional status before transplantation.

Protective isolation room

During HSC transplantation, patients will have low white cell count for three to four weeks, hence the risk of infection. The BMT centre provides protective isolation rooms with positive pressure ventilation in which air is filtered through high efficacy particulate air filter. All personnel need to wash their hands thoroughly before entering the room. To facilitate patient care and to reduce the stress of isolation, up to three designated family members or relatives can take turn to accompany the patient during daytime. Any person with influenza, gastroenteritis or other infection will be prohibited from visiting.



On average each patient has to stay in the isolation room for five to six weeks. Each room is equipped with television, telephone, radio, VCD and DVD for the patient to relieve the sense of isolation during the treatment process. No fruit or flower is allowed in the isolation room to reduce the risk of bringing infection to the patients.

Treatment before transplant

All patients undergoing HSCT will undergo a course of chemotherapy. Chemotherapy will be given by mouth and by intravenous means. Some patients may also receive a course of total body irradiation. The total duration of chemo-irradiation will last about five to seven days. The purpose of chemo-irradiation (conditioning) is to remove the patients' diseased bone marrow and to facilitate engraftment of donor HSC. HSC will be infused intravenously about one day after the conditioning.

Day of haematopoietic stem cell transplant

1. Bone marrow stem cell transplant

The donor side:

Bone marrow from the donor will be aspirated under general anesthesia in the operation theatre by experienced haematologists. Site of marrow aspiration is on both sides of the pelvic bone. The volume of bone marrow needed will depend on the body weight of the patients and will be around one liter. The whole procedure takes about an hour. There will be a small wound on each side of the buttocks with the size of about half a centimeter long. No stitching will be needed in most cases.



After recovery, the donor will be transferred back to the ward. If the post operation haemoglobin level is low, autologous blood will be transfused to replace the loss during marrow aspiration. Normally there will be pain over the pelvis and it can be relieved by simple analgesics. In most circumstances the donor can be discharged the next day.

The patient side:

The harvested bone marrow will be processed in the laboratory before transfusion to the patient through the Hickman catheter. In most cases, engraftment is expected in three to four weeks. By then the patient's blood counts will recover.

2. Peripheral blood stem cell (PBSC) transplant:

Two catheters will be inserted one on each arm of the donor for the collection of PBSC in the apheresis centre. For donors without prominent arm veins, a single catheter may be inserted into the neck for the same purpose. The collection takes about four hours and the total volume withdrawn is about 100 ml. The catheters will be removed and the donor can go home the same day after PBSC collection. Sometimes, one to three consecutive days of apheresis may be needed for adequate PBSC collection. PBSC will either be infused into the patient immediately through the Hickman catheter or cryopreserved in liquid nitrogen until the patient is ready for the transplantation.

What happen after HSC transplantation?

Most complaints during early post-HSCT are related to the side-effects of chemotherapy given before the infusion of HSC. These include hair loss, poor appetite, nausea and vomiting, as well as sore throat and oral mucositis. They are mostly transient and are amenable to medical treatment. In particular, oral mucositis is a common morbidity and source of distress to the patient. Very often, mucositis is so severe that oral intake of food or liquid becomes impossible. In these circumstances, nutrition and fluid will be given parenterally via the Hickman's catheter. Maintenance of oral hygiene is particularly important, as the inflamed and bleeding buccal cavity is a portal of entry for bacteria and fungus, causing systemic and often life-threatening infection.

In addition, the patients will also suffer from the complications resulting from cytopenia. These include:

1. Low white blood cells - causing fever, chills and rigors.
2. Low platelets - causing gum and nose bleeding, bruises and excessive menstruation in female.
3. Anaemia - causing tiredness, breathless and palpitation.

While most complications are amenable to medical treatment, close monitoring of patient's symptoms, temperature, urine sampling and blood checking as well as radiological images is important for them to be treated preemptively. Despite the close surveillance and aggressive treatment, some patients would die of fatal complications, notably due to fulminant infection and intracranial bleeding.

Most patients can survive the initial stage of HSCT. After about three to four weeks, most of the above complaints will resolve as the infused HSCs begin to engraft in the patient's bone marrow. Arbitrarily, we define success engraftment as the day when the absolute neutrophil count can be maintained above $0.5 \times 10^9/L$ for more than three consecutive days. By then, patients may be allowed to come out of the isolation room - and the first step towards a successful treatment.

Discharge planning

The length of stay in hospital can be variable depending on the clinical course of transplantation. On average, most patients would have to stay for five to seven weeks. After discharge, they will need to come back for regular follow-up, at weekly intervals in the first few visits and at longer intervals thereafter. Regular blood tests will be performed at each visit and special tests including radiological imaging and tissue biopsies may be needed when necessary.

Special notes after discharge

Before discharge, the patient will be advised in detail about their care outside the hospital. They will also be alerted of the early sign of infection and GVHD (refer to the chapter on Graft Versus Host Disease) so that prompt medical attention can be sought. In particular, all patients are considered severely immunosuppressed at least in the first six months after HSCT and very often much longer. As a result, patients should avoid exposure to crowded public areas, such as cinema, restaurant and public transportation and N95 mask should be worn in these areas. Domiciliary and dietary hygiene should be maintained at high standard to reduce the risk of infection. Smoking and alcoholic beverages are strictly forbidden which will inevitably damage the already impaired lung and liver functions. For allogeneic HSCT patients, excessive sunlight exposure should be avoided at least for the first year after HSCT to prevent the triggering and aggravation of skin GVHD. Persistent diarrhea and abdominal pain are symptoms of gut GVHD and immediate medical attention should be sought.

Emotional and social problems

Hospitalization, separation from family members, interruption of work and daily routines and most importantly the uncertainties of the treatment outcome are understandably sources of severe psychosocial stress to the patients. The following services are available to patients before, during and after HSCT who may need assistance beside medical care:

1. Clinical psychologist - for psychological counseling, stress management etc.
2. Medical Social Worker - for financial and social difficulties related to HSCT.
3. QMH Cancer Center - CancerCare and Support Unit situated in 2/F, Cancer Center, Queen Mary Hospital. It provides cancer counseling and support services, as well as palliative care consultative services to patients and their families. A convalescent home for bone marrow transplant patients is also managed by the unit. Enquiries number is 2855-3900.
Website: <http://www3ha.org.hk/hkwc/community/ccsu/index.htm>
4. The 'BMT Patients Association' - a patient self-help group organized by patients who had recovered from their diseases after HSCT - for sharing of experience and support from patients' perspective. Hotline number is 6239-0025.
Website: <http://www.bmthk.net/firms.com>

POINTS TO NOTE AFTER DISCHARGE

Clothing, Shoes & Socks, Bedding, Wig and Cap

1. Clothing

- Choose cotton material especially the underwear.
- Change if it gets wet.
- Changed clothing must be thoroughly washed and sun dried. Ironing is only needed if neutrophil count is less than $1 \times 10^9/L$.
- All daily wear after going out should be changed and washed. As for those heavy ones please wash at least weekly.
- Sun heated those that have kept for a long time in the cupboard

2. Shoes and Socks

- Place shoes in well-ventilated place to keep it dry and clean. Do not wear those that are wet or of other person. Choose the right size and close-head type.
- As for socks, choose cotton material and change daily.

3. Bedding

- Bed sheet, pillowcase and quilt cover should be changed twice weekly. Whereas pillow, mattress, and quilt (wool or summer blanket) should best be sun heated once weekly (these recommendations only applied to when neutrophil count is less than $1 \times 10^9/L$).

4. Wig

- Send to hair dresser weekly for washing.

5. Cap

- Choose cap that is easily to wash and dry, and must be washed at least weekly and keep dry at all times.

Food

1. Food to avoid

- Shellfish, as there might be parasites e.g. crab.
- Uncooked food e.g. salad or raw seafood.
- Stimulant e.g. coffee, tea, wine, hot and spicy food.
- Water that has been left overnight, left over and take-away food.
- Preserved food such as raw instant noodles, beef jerky and sliced cuttlefish.
- Fermented food such as salty fish, fermented bean curd and preserved duck egg.
- Dairy products such as fresh milk, cheese, ice-cream, and yoghurt.
- Health products or food with Chinese herbal components e.g. Ginseng, Yuzhi and Lingzhi.



2. Food to take

In general, food should be thoroughly and well cooked. They should be fresh and easily digestible. Frequent and small meals are always better than those that are irregular and full. A balanced diet should be adhered to. In addition, food rich in iron such as egg white, spinach, apple, and lean meat, is encouraged. Fruits with thick outer skin are allowed three months after HSCT.

3. Handling of food and eating utensils

Eating utensils must be rinsed with hot water before use and thoroughly washed and dried after meal. Food from market should be properly washed and stored in refrigerator until cooking.

Living environment

Keep inside house well ventilated with daily cleansing. Try to minimize visitors.

Vaccination

Patients should be vaccinated exclusively under our program one year after HSCT. Self vaccination outside the program and vaccination of close family members should be extremely cautious as some vaccines may paradoxically cause severe viral infection in HSCT patients. The patients should consult BMT physicians in advance.

PHYSICAL



What may be the problems of oral intake and bowel function after HSCT? How can we deal with them?

Most patients will develop gastrointestinal problems to various extents, usually a few days after transplantation. These include dry mouth, lack of appetite, oral mucositis, change of taste, diarrhoea or constipation. These are related to the use of high dose chemotherapy and irradiation during conditioning.

1. Dry mouth leading to eating difficulty

- Solutions:
- drink plenty of water and frequent gargling to moisten the oral cavity
 - try sucking citric candy to stimulate salivary secretion
 - take more liquid or fluid diet

2. Lack of appetite leading to weight loss

- Solutions:
- small and frequent feed
 - have nutritious food
 - eat after light exercise to stimulate the appetite
 - try to increase appetite by imagining the food being your favourite
 - try to relax or seek help from professionals if there is emotional distress

3. Oral mucositis leading to difficulty in eating

- Solutions:
- take or drink icy or cold food
 - take soft food
 - drink fluid with a straw
 - take high protein and calories food to speed up the healing of oral mucositis
 - take blend or fluid diet
 - maintain good oral hygiene
 - use pain-killer to relieve pain if needed

4. Change of taste leading to a lack of appetite

- Solutions:
- take foods or beverages at room temperature
 - take strong flavoured food or fluid

5. Diarrhoea leading to weight loss or dehydration

- Solutions:
- small intake at each meal
 - drink plenty of water to avoid dehydration
 - avoid taking high fiber food
 - if needed, doctors will prescribe medication to control the symptom

6. Constipation leading to abdominal distension and discomfort

- Solutions:
- take more warm water
 - take food high in fibre content
 - have appropriate exercises
 - stool softener may help if needed

Why is there a change of taste?

Taste change is quite obvious especially in the first few weeks after transplantation. This is because the intensive conditioning leads to damage of the oral mucosa and taste buds. This will gradually improve upon engraftment. Sometimes medications for treatment of chronic GVHD and infection may also affect the taste buds.

Why is there dry mouth after transplantation?

Dry mouth may be caused by chronic GVHD affecting saliva secretion from the salivary glands. It may also be caused by dehydration due to inadequate fluid intake. Sometimes nutritional deficiency may also cause cracking at the mouth corner.

Why is there oral mucositis after neutrophil engraftment?

It could be due to infection such as herpes simplex or candidiasis or chronic GVHD.

How can nausea and vomiting be relieved?

This is a common side effect related to conditioning. It can be relieved by medications and by having small but frequent meals. Sometimes, soothing music and psychologically counselling may help.

Why is the loose stool and frequent bowel opening after transplantation?

It may be the side effect of chemo-irradiation, signs of GVHD or infection. Please pay attention to quality and quantity of the stool, and inform doctors for diarrhoea as soon as possible.

Why is the newly grown hair darker, denser and curlier?

This is due to cyclosporin A that is used for preventing GVHD. The hair will become normal again after the course of cyclosporin A is finished.

Why does the skin become darker with many tiny hairs after transplantation?

This is due to the use of chemo-irradiation and cyclosporin A or the occurrence of chronic GVHD. The condition is usually reversible after treatment. Avoidance of exposure to sunlight may also alleviate the skin coloration due to chronic GVHD.

Why is there a feeling of dizziness after transplantation?

It can be due to anaemia, medications, lack of physical strength or hypotension.

Why is there dry and gritty eye after transplantation?

This is due to chronic GVHD that leads to reduced tear secretion and can be relieved by artificial tears. Other eye conditions, e.g. photosensitivity, blurred vision or painful red eye should be seen by medical doctors immediately.

Why is there hearing loss after transplantation?

Antibiotics for infection might affect the hearing ability. Sometimes it may be due to other reasons such as otitis media.

Why are there frequent mosquito bites after transplantation which are slow to resolve?

Immune function after allogeneic transplant will gradually be replaced by the newly developed haematopoietic system. Therefore the above peculiar immune response will be seen during this transition period.

Why is newly grown fingernails so fragile after transplantation?

High dose chemotherapy can damage the nail beds and the new fingernail may be fragile. This is more severe in patients with chronic GVHD. This condition will improve gradually.

Why there is poor memory after transplant?

In most cases, the subjective feeling of poor memory is due to distraction by physical weakness and mental stress during the course of transplantation that impede the concentration of patients. This will improve with the physical recovery of patients. In severe cases, discuss with your doctors about the problem.

What psychological problems will transplant patients encounter? How to deal with them?

The physical disabilities and uncertainties about treatment complications and disease relapse are understandably sources of stress to the patients. Some of them may have fear, discomfort and worry; while others may have a sense of helplessness, loneliness or despair. We suggest the following coping strategies:

1. Learn and cultivate your ways of expressing the emotion so as to develop your pattern of relaxation. Relatives can also provide appropriate emotional support to the patient.
2. Learn the ways of open communication - Some will subconsciously suppress their negative emotions which will block communication and have difficulty to share with the family.
3. Learn to have self-acceptance, and do not neglect your daily achievement such as attending follow up as scheduled, taking drug as prescribed, and actively showing your concern and help to others.
4. Learn to adjust the acceptable expectation to the disease prognosis and treatment so as to avoid disappointment by the unresolved.
5. Get relevant information at hand that includes related health care service, social resources and emotional support. More correct information brings about greater sense of control which will in turn minimize the worry of future uncertainty.
6. Join support or educational groups which not only increase public assistance, but also through knowing, encouraging and sharing experience with other patients, one can have social support, learn new ways to cope with the disease and better use of the social system.
7. Rearrange family responsibilities - Illness complicates and confuses a patient's roles, duties and responsibilities. Family members need to share the patient's responsibilities appropriately. However, over protection and care for the patient is a kind of pressure and will easily lead to a stressful relationship. Therefore patient should be allowed to maintain their functions appropriately, and learn to adapt their new role and responsibilities.
8. Seek for the meaning of life - If you can accept your present experience and emotion totally including the feeling of pain and happiness, learning to accept your wholly self, and caring your surrounding people and things with love so as to build up a trusting relationship; then your heart will be filled with love and not hard feeling. In that case your life will be more meaningful and colorful.

Is it necessary for the transplant patients to worry about their recovery after high dose chemotherapy? How to deal with it?

Worries in fact could not improve the disease condition, yet easy to put the patient into fear, discomfort or depression. Nevertheless, a certain degree of worry is unavoidable. Try adopting other ways to overcome the psychological problems to decrease or diminish the degree of worry.

How to improve the quality of sleep?

1. Maintain a stable emotion, regular life-style and appropriate exercise.
2. Have body massage before sleep to allow emotional balancing and muscle relaxation which can help to fall into sleep.
3. Form a habit of having a relaxing mood before sleep, such as having a warm water shower and listening to soft music.
4. Avoid strong drinks such as tea and coffee.
5. Seek medical advice and receive appropriate medication to assist sleeping if there is a long history of insomnia that affects daily life.

How to manage when the male transplanted patient has dryness, soreness, redness, pain and itchiness over the penis?

These are mostly caused by infection, mucositis or GVHD. Patients need to seek medical advice.

Why would female transplanted patients have rash and itchiness over the vagina?

This is mostly due to bacterial or fungal infection, reduced female hormones secretion or GVHD.

How to manage when a female transplanted patient has sexual dysfunction, vaginal dryness and narrowing, difficult and painful sexual intercourse?

These are mostly due to previous chemoirradiation or GVHD. These can be alleviated by hormonal replacement therapy or adequate lubricant (K-Y jelly) during sexual intercourse.

Why do female transplant patients need hormonal therapy?

Young female transplant patients are susceptible to pre-mature menopause due to reduced female hormones secretion. As a result, they are at higher risk of osteoporosis and cardiovascular disease. They are recommended to have hormonal replacement therapy.

How long can the cryopreserved semen of the male transplanted patients be kept?

This is subject to the policy of assisted pregnancy, and it can be kept for up to ten years.

Are there ways for the transplanted patient to have baby?

Consult gynecologist or obstetrician.

Which therapy causes the transplanted patient to be infertile?

Theoretically either chemotherapy or radiotherapy of a large dosage will lead to loss of child-bearing ability.

When should transplanted patients resume sexual life?

Sexual life can be resumed when the neutrophil count is higher than $2 \times 10^9/L$ and platelet count higher than $50 \times 10^9/L$. Both patients and their partners should have no genital infection and their personal hygiene should be maintained at all times. They should always practice contraception to prevent unwanted pregnancy.

What is GVHD?

This is an alloimmune reaction of the donors' engrafted lymphoid cells against the recipients' tissues. It can be divided arbitrarily into acute (the first 100 days post-HSCT) and chronic (100 days after transplant) GVHD.

Who may develop GVHD?

GVHD occurs mostly in patients who receive transplants from matched siblings or unrelated donors.

What would the patients feel during acute GVHD and how to manage?

Acute GVHD affects primarily skin, liver and gastrointestinal tract. Skin GVHD is manifested as rash over the palms, soles and trunk and in severe cases as blisters or even desquamation of skin.

Liver GVHD may be asymptomatic and some patients may develop jaundice and mild abdominal aching.

Gut GVHD is manifested mostly as diarrhoea and abdominal pain and in severe cases as abdominal distension, intestinal obstruction and profuse rectal bleeding.

Daily monitoring of skin and stool conditions is needed and patients should inform doctors immediately should these happen.

How does chronic GVHD manifest itself and how to manage?

The areas affected are quite diverse such as skin, gastro-intestinal, eyes, reproductive organs, liver, lungs and immune system.

1. Skin:

Feel itchy or burning sensation. Patients may have skin redness then darkening and hardening with pain. They may have dry skin and joint stiffness. Avoid direct sunlight and apply sun screen with screening factor of 15 or above. Avoid over-hot shower and keep skin moist. Perform tolerable exercise daily to prevent joint stiffness.

2. Gastro-intestinal:

May have nausea, vomiting, diarrhoea, difficult in swallowing, dryness of mouth, taste change and white-coated oral mucosa. Try small and frequent feeds with moist, soft and non-irritating food. Maintain regular oral assessment and keep oral and dental hygiene. Continue "Buctidol" gargling when the neutrophil count is less than $1 \times 10^9/L$. Avoid using mouthwash with alcohol base. If diarrhoea persists, perineal hygiene is of utmost importance.

3. Eyes:

Include itchiness, grittiness, burning sensation, sensitive to light and eye dryness. Try instilling artificial tears for soothing effect. Avoid contact with cosmetics over the eyes and wear sunglasses when going out.

4. Reproductive organs:

Females may have inflammation over the vagina and lack of vaginal secretion leading to painful intercourse. Hence try water-based lubricant e.g. KY jelly. As for males, they may have abrasion over the penis, please inform health care professional for early treatment.

5. Liver:

Please follow medical advice for special diet, avoid drinking alcohol and have regular liver function testing.

6. Lungs:

The impact usually occurs at a later stage. Need to prevent and control early infection. Please perform daily tolerable exercise and regular lung function test.

7. Immune system:

Patients are susceptible to infection due to chronic GVHD and the use of immunosuppression. Patients should follow the infection control guidelines. Self-vaccination outside the BMT program should be strictly prohibited.

How to prevent GVHD?

Most patients will have to take cyclosporine and mycophenolate mofetil (MMF). Some patients will also need to take tacrolimus (FK506), thalidomide, azathioprine, and steroid (Prednisolone).

What are the side effects of these medications and are there any points to note to?

Drug	Route	Side Effect	Points to note to
Cyclosporin (Neoral)	Oral IV	Tremor, headache, gastrointestinal upset, liver and renal dysfunction, skin rash	<ul style="list-style-type: none">• Take drug regularly and at the right time• Do not stop or change dosage by yourself• Can take drug with milk products or orange juice to reduce the taste of the drug. Don't use grapefruit juice• Take drug immediately after opening the package• Don't crash the drug• Don't take drug on day of follow up for the need to check drug level. Bring drug along and have it after blood taking
Mycophenolate Mofetil (MMF)	Oral IV	Musculoskeletal pain, rash, gastro-intestinal upset, chest pain or arrhythmia	<ul style="list-style-type: none">• Take drug regularly and at the right time• Do not stop or change dosage by yourself
Tacrolimus (FK506)	Oral IV	Fever, headache, limb oedema, gastrointestinal upset, liver dysfunction	<ul style="list-style-type: none">• Take drug regularly and at the right time• Do not stop or change dosage by yourself• Take drug with empty stomach (1 hour before meal or 2-3 hrs after meal)
Thalidomide	Oral	Constipation, drowsiness, limbs numbness, rash, dizziness, fever, increase heart rate, oral mucositis	<ul style="list-style-type: none">• Take drug regularly and at the right time• Do not stop or change dosage by yourself• Avoid use during pregnancy
Azathioprine	Oral IV	Fever, tremor, musculoskeletal pain, liver dysfunction, arthralgia, alopecia, gastro-intestinal upset, haematopoiesis, oral mucositis	<ul style="list-style-type: none">• Take drug regularly and at the right time• Do not stop or change dosage by yourself• Avoid the use in pregnancy• No breastfeeding
Prednisolone/ Methyl- prednisolone	Oral IV	Moon face, hypertrichosis, muscle weakness, generalized oedema, weight gain, gastrointestinal upset, mood change	<ul style="list-style-type: none">• Take drug regularly and at the right time• Do not stop or change dosage by yourself• Decrease dosage slowly if on high dose therapy for a long time• Inform doctor before seeing dentist or have emergency operation

Note: IV - Intravenous