BONE MARROW TRANSPLANTATION MANUAL

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INTRODUCTION

Bone marrow transplantation (HPSC/BMT) is a relatively new medical procedure being used to treat diseases once thought incurable.

Since its first successful use in 1968, HPSC/BMT has been used to treat patients diagnosed with leukemia, Aplastic Anemia, lymphomas such as Hodgkin's disease, multiple myeloma, Immune deficiency disorders and some others solid tumors.

Since 1991, thousands of patients underwent Stem Cell all over the world. Stem Cell transplant now save thousands of lives each year.

THE TRANSPLANT TEAM

The Hematopoitic Stem cell team

The group of specialists involved in the care of adult patients who are undergoing a transplant procedure is often referred to as the "transplant team." Each individual works together to provide the best chance for a successful transplant. The bone marrow transplant team consists of:

Physicians
physicians who specialize in oncology, hematology, immunology and bone marrow transplantation.

Transplant nurse coordinator
a nurse who organizes all aspects of care provided to your child before and after the transplant. The nurse coordinator will provide patient education and coordinate the diagnostic testing and follow-up care.

Social workers
will provide support to your family and help them deal with many issues that may arise including lodging and transportation, finance needs before and after the transplant. They will work closely with you and your family.

Physical therapists
professionals who will help you become strong and active post transplantation.

Other team members
Several other team members will evaluate you before transplantation and will provide follow-up care, as needed. These include, but are not limited to, the following:

- Pharmacists.
- Respiratory therapists.
- Lab technicians.
- Infectious disease specialists.
- Dermatologists.
- Gastroenterologists.
- Psychologists.

General information

What is bone marrow?

Bone marrow is a spongy tissue found inside bones. Bone marrow contains blood stem cells- special cells that generate most of the body's blood cells. And it is responsible for the development and storage of about 95 % of the body's blood cells.

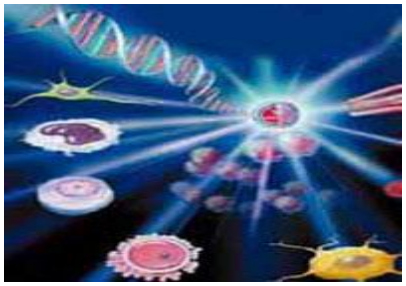
The three main types of blood cells produced in the bone marrow include.

White blood cells: which fight infections and aid the immune system.
Red blood cells: which carry oxygen to and remove waste products from organs and tissues?
Platelets: which help with blood clotting.

Each of these cells carries a life- maintaining function, the bone marrow is a vital part of the human body.

Stem Cells

What are the stem cells?



Stem cells are regarded as the building blocks or master cells of the blood and immune system. Stem cells are very clever and can develop into many different types of cell and tissues within the body. They can be seen as assort of repair system for the body. And rebuilding the destructed bone Marrow post high dose of chemotherapy and radiation therapy.

What happens if the bone marrow stops working?

If your bone marrow stops working, your body won't produce enough healthy stem cells. And that means you may not have enough healthy white blood cells, red blood cells or platelets. Putting you at risk of life-threatening infections, anemia and bleeding.

What are the reasons for stem cell transplant?

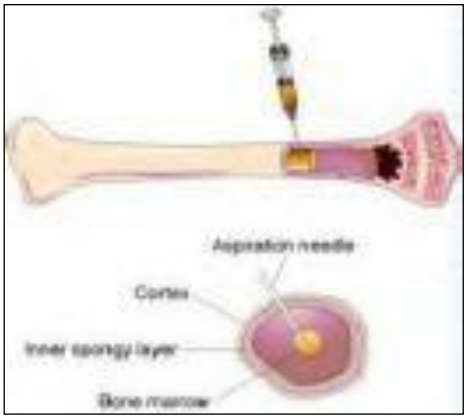
Stem cell transplants are used to treat people whose stem cells have been damaged by disease or treatment of a disease. Stem cell transplants can benefit from a variety of both malignant and nonmalignant diseases. For instance, in aplastic anemia, a nonmalignant condition, your bone marrow stops making enough new blood cells. A stem cell transplant destroys the dysfunctional marrow, and

healthy stem cells are infused. If all goes well, the new stem cells migrate to the marrow and begin working normally.

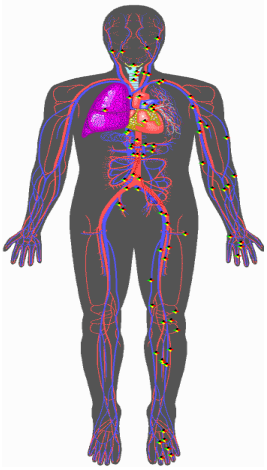
Sources of Stem Cells for Transplants

There are 3 possible sources of stem cells in the body to use for transplantation.

1- Bone marrow



2- Circulating (peripheral) blood



3- Umbilical cord blood

What is HLA Typing?

To be a suitable donor, the genetic make-up of the donor's white blood cells must closely match the patients, or serious complications can arise. If the donor's white blood cells are not a good genetic match, they will perceive the patient's organs and tissues as foreign material that should be destroyed.

This condition is known as Graft-versus-host disease (GVHD) and can be life threatening. Alternatively, the patient's immune system may destroy the donor's stem cell.

This is called graft rejection. An HLA matched sibling – one who shares most or all the same antigens as the patients – is usually the best donors.

Who can be a donor?

An HLA matched sibling

The stem cells are taken from matched brother, sister or parents
Stem cells from cord blood
The stem cells are taken from the cord blood immediately at the baby's birth

A matched unrelated donor

The genetically matched marrow or stem cells are from an unrelated donor. Unrelated donors are found through the national bone marrow registries.

Patient to him /herself

What are some diseases that may benefit from bone marrow transplantation?

The following diseases are the ones that most commonly benefit from bone marrow transplantation

- Leukemia's
- Severe a plastic anemia
- Lymphomas
- Multiple Myeloma
- Immune deficiency disorders
- Solid-tumor cancers, such as breast or ovarian

However, patients experience diseases differently, and bone marrow transplantation may not be appropriate for everyone who suffers from these diseases.

What are we transplanting?

The name of what is being transplanted has changed over the years. The cell that is being transplanted is the stem cell that is made in the bone marrow. Names you will hear include

- Bone marrow transplant
- Marrow transplant
- Peripheral blood stem cell transplant
- Stem cell transplant
- Hematopoietic progenitor cell transplant

Types of transplants

There are several types of transplants. You may hear other patients discussing a process different from yours. This chapter will then go into detail about the type of transplant you are considering.

1. Allogeneic related stem cell transplant.

   Stem cell sources will be from another person's family member. (Brother, Sister or one of the parents)

2. Allogeneic unrelated stem cell transplant

Goals

a) Deliver highest dose of chemotherapy and radiation to eliminate disease.
b) New cells replace patients' immune systems

Autologus stem cell transplant

The donor is the patient him/herself. Stem cells are taken from the patient either by bone marrow harvest or peripheral blood stem cells Via apheresis and then given back to the patient after intensive treatment.

THE STEPS OF THE TRANSPLANT

What are the Steps of Allogeneic Transplant?

The process of transplant can be divided into steps. Each step has its own purpose and challenges. It is as follows:

Planning Ahead

This step begins when the patient first thinks about transplant as a treatment option.

Preparation

Pre transplant evaluation

Pre-transplant evaluation is extensive and must be done to determine whether you are eligible for this difficult procedure. Cardiac, renal, pulmonary, and hepatic (liver) tests will be done to determine how your major organs are functioning. Test results must meet certain criteria for you to be eligible. Your doctor will do Comprehensive serologic (blood) testing to make sure you have no active infections and to determine your past exposure to certain viral infections. Bone marrow aspiration biopsy is done before the transplant to determine the response of the disease to treatment given. A dental exam is performed to make sure you have no active cavities or infections. This should include a full set of mouth X- Rays. The dentist should make dental repairs before your transplant.

What is involved in?

Pre - transplant work- up

During your pre -transplant work - up a team of physicians will carefully evaluate your medical history to make sure that the procedure is appropriate for you. They will decide whether an Autologous or Allogeneic transplant will be performed and what conditioning will be used. They will consider toxicities and weigh the benefits against the potential risks. You will need to sign a consent form stating that you are authorizing this procedure. Signing the informed consents tells the doctors that you have been given enough information to make an informed decision about the transplant and understand what the transplant involves, if there is anything about the procedure that you do not understand, you should ask questions. Do not sign the form until you are satisfied that you know what will happen.

ADMISSION FOR TRANSPLANT

Treatment in the inpatient unit

Location

The adult stem cell transplant unit is located in the Special unit at your hospital

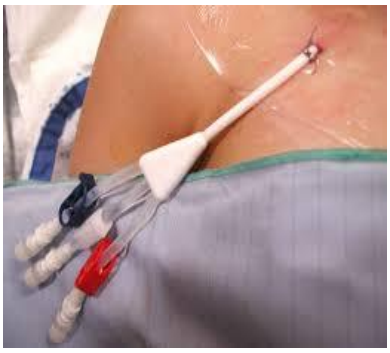
Admission to the inpatient unit

If your admission to the inpatient unit is scheduled in advance you will be notified of the time and date to go to the hospital. The stem cell coordinating team will stay in contact with you after your evaluation or work up is completed and will plan for your admission to the hospital. At that time the patient needs to wait for an available hospital room.

Patient rooms

The rooms have air filtered by specialized filters. They are all equipped with TV, Video/DVD players; movies are supplied for your interest. The rooms all have a telephone line for incoming and outgoing calls. Internet connections can be arranged if you wish to bring your own computer. Each room has an exercise machine for daily activity to promote recovery and well-being.

Central Venous Line Placement



A Central line catheter is a soft silicone (Plastic) tube inserted into a large vein in your chest. It is used to give you fluid, food, medicine and blood products. It is also used to obtain most blood samples without having to draw blood from your arm. There are many types of catheters available. The most common type used is triple lumen catheter. The insertion of the central line catheter is a minor surgical procedure. It is done in the angiography section, under local anesthesia and takes about one hour. With local anesthesia, the doctor will numb the chest and neck area. He will make two small incisions (cuts): one is in the upper chest near to the neck, and the second is lower on the chest. Between these two incisions, the doctor will make a tunnel just under your skin. The catheter is inserted in the lower incision on your chest and is pulled through the tunnel. It is then inserted through the vein by your neck. A small Dacron cuff holds the catheter in place in the skin tunnel. This cuff is also a barrier, which helps prevent bacteria from traveling up the catheter tunnel into your bloodstream. Your shoulder and chest area may be sore for a few days. A mild pain reliever will be prescribed.

A Day in the Life of a Transplant

You may wonder what the normal routine day is like for a patient on inpatient unit. What procedures are often done? What tests are usually run? What routine activities will be a part of every life on the unit? The inpatient nurse will explain this question in more detail, but in the meantime, here is what you can expect:

Routine blood tests

Early morning before 4:00 Am., the nurses will draw daily routine blood tests from your central line. We will disturb you as little as possible.

Vital signs
Your temperature, pulse, respiration and blood pressure will be taken every four hours. Sometimes they are taken more often if we need to monitor you more closely.

Physical Examinations
The nurses and physicians will, at different times, need to listen to your heart, lungs and abdomen with the stethoscope. The nurse will look at your mouth daily and more frequently during the period you are likely to experience mucositis, an inflammation of the mouth

Daily weight
A daily morning weight check is important to monitor the amount of fluid in your body. You may need to have your weight checked twice per day.

Bathing
Daily baths or showers are required to be taken to help cleanse the body of bacteria. This may help lower the chance of infection. Your nurse will work with you to fit your bath or shower into your schedule.

Central line care
The central line dressing will be changed daily right after your bath to guard against bacterial growth.

Exercise
We encourage you to arrange with the nurse a time to take a walk and exercise in the halls. Your doctor may order physical therapists to work with you to help you keep your activity level up.

Nutrition
Dietitians will talk to you about your food likes and dislikes. Patients who are not able to eat are given total parenteral nutrition (TPN), which goes through your central line and which you will not taste.

Medications & IV Fluids
Many medications will be given through your central line such as antibiotics, anti-nausea medication, or medication to prevent graft- versus-host disease. Fluids will be given if you cannot drink enough to meet your body's need.

Chest X-rays
Chest X-rays are done at least weekly to check your lungs.

Rounds

Every morning your doctor and other members of the health care team will do a round, that is a group discussion with each patient. This is to check on your progress and make changes in your therapy if needed. This is a good Time to ask any questions you may have and to discuss your plan of care.

Transfusion

Blood and platelet transfusion will be given to you as needed until you are able to make your own blood cells. Your blood counts will be checked every day.

TRANSPLANT CONDITIONING REGIMENS

What is the BMT conditioning regimen?

Conditioning

Conditioning consists of high dose chemotherapy with or without total body irradiation. Conditioning can be received in the outpatient clinic or in the hospital. Your doctor and nurse will discuss your treatment plan with you. The purpose of conditioning therapy is to remove cancer cells, or to remove the remaining immune system so that the new marrow can grow.

Chemotherapy

All chemotherapies and radiation have some effects on normal cells as well as on diseased cells. The specifics of the chemotherapy prescribed for you will be explained when your therapy program is planned. Side effects often experienced include nausea, vomiting, diarrhea, dry mouth, fatigue, hair loss and skin changes. Some of the side effects of chemotherapy happen right after away and can be managed with other drugs.

Nausea and vomiting are a major concern for patients. Several drug therapies are available to relieve nausea and keep you comfortable.

Diarrhea: can happen with chemotherapy and is treated with fluid and electrolyte replacement.

The hair loss is temporary, and your hair should start growing back a few months after the transplant.

Total body irradiation (TBI)

This radiation therapy utilizes high-energy x- rays for your cancer treatment. Total body irradiation (TBI) is radiation given to the entire body. TBI is given twice a day in small radiation fractions at 5 – 6 hours apart over 3 days. The time taken for each treatment varies from 20 – 40 minutes. The treatment length is dependent on your body size and prescribed radiation dosage. However, once determined the amount of time you spend on treatment will be the same.

What is TBI Treatment like?

There is no pain or discomfort during your treatment due to radiation. You will not have any unusual sensation while the radiation machine is on. You do not become “radioactive” A family member spouse, significant other, or friend may accompany you to the radiation therapy department. However, it is necessary for you to be in a room by yourself during treatment. You may feel alone during your treatment. Monitors are outside so that your nurse and radiation technician always see and hear you. You will be given detailed instructions when your nurse teaches you about your radiation. Side effects can include nausea, dehydration, and skin sensitivity, diarrhea, hair loss, swelling of parotid glands in your neck and dry mouth.

Side Effects

Nausea: most often occurs 1- 2 hours after a dose of TBI. You will start on medication to keep nausea from being too much of a problem. The day before TBI begins, your team nurse will review the medications you should take before each TBI treatment

Dehydration: can cause dehydration much like you were exposed to the sun for too long. Other side effects such as diarrhea and nausea add to this problem. Some of your hydration may be given IV during each day of TBI to help prevent dehydration.

Skin sensitivity: TBI acts as a heat source even though you will not feel this right away. You will notice your skin may appear flushed, or darker following radiation therapy.
Your skin following treatment will be more sensitive, especially to sunlight. Precautions are taken to avoid skin burns during treatment. Loose fitting clothing should be worn to avoid skin burns. All jewelry will be removed during treatments. If you wear eyeglasses, the radiation technician will have you remove them during treatment. Contacts should not be worn. The nurse or physician will assess your skin frequently. Avoid using lotion and deodorant prior to TBI.

Alopecia: temporary hair loss will occur gradually over about two weeks following treatment.

Pariotitis: the parotid glands are located near and in front of your ears. Pariotitis is swilling of the parotid gland. Pariotitis is not a common side effect but has been seen in TBI patients Symptoms will occur from 4 – 24 hours after TBI. Ice packs and Tylenol help to relieve the discomfort from the swelling. Pariotitis will be resolved in 24 - 72 hours following treatment.

Mucositis: glands that secrete mucous and fast-growing cells that line the mouth and throat are altered by TBI and /or chemotherapy and cause dryness, swelling and painful Mouth and throat. Most patients will get mucositis with any marrow transplant regimen. Mucositis is treated with salt – water rinses and pain medication. If pain continues, narcotics will be used.

Effects of chemotherapy and radiation on blood counts

The amount of chemotherapy and radiation used in conditioning cause the bone marrow to stop producing cells for a time. Your blood counts will be low during this period. After your blood counts are drawn, your doctor will determine your transfusion needs when your stem cells begin to engraft, your blood counts should start to rise. The actual time for recovery of cells will vary from person to person.

THE TRANSPLANT

Transplant

The transplant takes place a day or two after the chemotherapy and / or radiation treatment. The goal is to infuse stem cells from which all types of blood cells grow. These cells can be collected from bone marrow, from circulating blood, or from umbilical cord blood after baby's birth. Stem cells are infused through your central venous line in much the same way that any blood transfusion is given. It takes place in your room at the inpatient unit.

The bone marrow donor

Donors will receive their own educational materials when they arrive at the center. The bone marrow donor is the person who makes an allogeneic transplant possible. He or she is the person who most closely matches the genetic type of patient. The donor may be an immediate family member, often a brother or sister. In some cases, the donor and patient are not related but still closely matched in tissue type.

Marrow harvesting

The actual marrow harvesting is performed in surgery where marrow is taken from the hipbones. Marrow is obtained through needles inserted through the skin into the hipbones. Most donors go home from the hospital after marrow harvest unless an overnight stay is medically necessary

The stem cell donor

Stem cells are produced in the bone marrow and circulate in the bloodstream. The stem cells that circulate in the bloodstream are called peripheral blood stem cells, or PBSC. Normally small numbers of stem cells circulate in the bloodstream. In addition to obtaining stem cells by harvesting them from the bone marrow, it is possible to obtain them by collecting them from the bloodstream. However, before that can be done it is necessary to stimulate the movement of stem cells into the bloodstream. This is called mobilization.

Stem cell mobilization

Mobilization of stem cells is achieved by giving the donor special proteins called growth factors. It takes a few days for the body to respond to the mobilization therapy. When blood tests show that the cell count is high enough, collection can begin. Occasionally, stem cell donors undergo more than one cycle of mobilization to collect enough stem cells for transplantation.

Collecting stem cells

Stem cells are collected in the apheresis unit in the blood bank. Before beginning collection, the donor might need to have a catheter (tube) placed into a large vein. The location of the catheter may take place several days before or right before the collection. The collection of PBSC's takes about three hours. During the procedure, the donor relaxes in a chair or bed and watch television. The donor's blood is withdrawn through the catheter and circulated through a machine which separates out the stem cells and collects them. The remaining blood cells are returned to the donor via the catheter. The procedure is painless. When the procedure is over the donor can resume normal activities.

Infusion of donated cells into the patient

Marrow or stem cells are infused into the patient as soon as they are available from the donor, usually within a few hours after harvesting. There may be more than one bag of cells. In some cases, bone marrows are processed before infusion. For example, if the blood type between the patient and donor does not match, red blood cells can be removed from the marrow before infusion. Another example is the removal of T-cells from the marrow. The aim of removing the T- cells is to reduce the risk of the patient getting acute and chronic GVHD after transplant

The nurse attaches IV tubing to the bag of cells and connects the tubing to the patient's central catheter. Each bag of cells is infused one after the other. From time to time during the infusion, the nurse will check the patient's vital signs (blood pressure, pulse, respiration, and temperature). The length of the infusion depends on the volume, or amount of stem cells to be given. Typically, it takes 30 minutes to 2 hours to complete the infusion. Some patients will receive stem cells in more than one day because of the donor collection process.

THE ENGRAFTMENT

Before Engraftment

From 10 to 28 days after transplant, a sign that the new stem cells are growing (engrafting) and beginning to produce blood cells is expected. Often the first sign of engraftment is a rising white blood cell count.

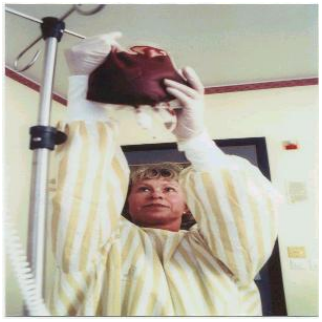
While looking at the first signs of engraftment, you require careful monitoring by nursing and medical staff. The goal is to support you until you are producing blood cells again, to provide prompt treatment if complications occur, and to prevent infections. Most patients experience the uncertainty of waiting for an engraftment as stressful. Feeling defenseless and vulnerable are common experiences. Associated with daily monitoring, medical procedures, and treatment is a feeling of loss of personal control. Coping at this time can be a challenge.

Engraftment

Engraftment is the process where transplanted stem cells migrate to the bone marrow cavities and begin to produce new white blood cells, red blood cells and platelets. The process takes one to three weeks for white blood cells to produce and 10 days to four weeks for red blood cells and platelets to produce. During engraftment, the flowing treatments are performed:

- **Medications**
  Growth factor medications may be given to help engraftment. Antibiotics are given to prevent infections.

- **Transfusions**



  Since the body is not yet able to produce blood cells, transfusions of red blood cells and platelets will be given as needed.

- **Nutrition**
  Adequate nutrition is important but may be difficult due to nausea and loss of appetite. Our nurses, dietitians and pharmacists collaborate in addressing nutritional needs.

- **Monitoring**
  because patients are vulnerable to side effects and infections during the waiting period, your status will be monitored frequently through measurement of blood levels, vital signs, weight and fluid status. Patients and staff will both be alert to early signs of complications.

- **Activity**
  staying active through walking in the halls or riding the stationary bike can help reduce fatigue, improve appetite and lower infection risks.

- **Self-Care**
  Instruction about hygiene practices to lower the risk of infection will be provided. Hygiene practices include bathing daily, using only electric razors and using special toothbrushes and mouthwash.

Side effects and complications

Possible side effects and complications include:

- **Short-term side effects**, often resulting from chemotherapy, radiation or medications, include:
  - Nausea, vomiting, diarrhea, loss of appetite
  - Hair loss
  - Mouth sores
  - Skin reactions
  - Fatigue

- **Potentially serious complications** related primarily to low blood counts including:
  - Infections
  - Bleeding

  You and the staff will carefully monitor for signs of all types of infection and bleeding. There are many treatments available that can help with these complications, but they are most effective if the complication is caught early.

- **Organ complications,** including problems developing in the following organ systems caused by chemotherapy, radiation, or medications:
  - Liver, including veno-occlusive disease (VOD), hepatitis, and infections
  - Kidneys, including kidney failure
  - Lungs, including inflammation and congestion
  - Heart, including reduced pumping ability

  As with other complications, the staff will help you be alert for signs of these organ complications so treatment may begin as soon as possible.

- **Graft failure:**
  Graft failure is a potential complication. Graft failure may occur because of infection, recurrent disease or if the stem cell count of the donated marrow was insufficient to cause engraftment.

  Graft failure may be treated with an additional marrow transplant if a source is available.

- **Graft-versus-host disease:**
  Graft-versus-host disease (GVHD) can be a serious and life-threatening complication of a bone marrow transplant. GVHD occurs when the donor's immune system reacts against the recipient's tissue. The new cells do not recognize the tissues and organs of the recipient's body. The most common sites for GVHD are the GI tract, liver, skin and lungs.

  GVHD is graded from I to IV and can be acute (occurs suddenly) or chronic (occurs over a period). You will be monitored closely for signs and symptoms of GVHD. Diarrhea, fever, rash, skin changes, abdominal pain, respiratory complications and decreased liver function may be present with GVHD.

Medications will be given prior to transplant to reduce the risk of this complication

- **Endocrine effects**
  Infertility is common in both male and female individuals. Secondary amenorrhea affects most women after stem cell transplant.

RECOVERY

Recovery

What is recovering?

Recovery is the long-term process of regaining blood cell production and immune function as well as strength, energy, and appetite following a stem cell transplant. The recovery process may last for months, even years, until your body has reached its highest possible level of functioning.

When will I be discharged from the hospital?

Your physicians will determine your readiness for discharge based on your blood counts, your nutritional status, and your overall level of health. Most patients are discharged in the 3rd or 4th week after the transplant.

Is there follow-up medical care after I leave the hospital?

Initially, you will be seen at least weekly in the Stem Cell Transplant Clinic, located on the 3rd floor of the cancer center. These weekly visits will continue until post-transplant complications are resolved, which could be a few weeks to several months. At that point, your care may be transferred to your physician in the outpatient. During each clinic visit, your blood levels and medication status will be reviewed, and you will be evaluated for any new symptoms of side effects or complications. The physician and nurse will be glad to answer questions at any time. The staff of stem cell transplant will schedule your clinic appointments.

How will I care for myself at home?

Stem cell transplant patients continue to be at risk for infection and complications for months or longer after transplant. You will play a very important role in the recovery process by following the self-care guidelines you will be given by the stem cell team.

Infection precautions

You will be given specific information about precautions you should take and symptoms that may be cause for concern. Most patients are encouraged to avoid crowds, gardening, pets, and contact with people who are ill. Since your skin is the first line of defense against infection, careful skin care is also essential.

Home environment

Your home will need to be thoroughly cleaned before your return, and you will be encouraged not to perform housecleaning functions for some time. You will also be given guidelines about handling pets and plants in the home.

Nutrition

Good nutrition plays an important role in your recovery. Our dietitians will give you information about foods likely to be appealing to your appetite as well as helpful in your recovery.

Physical activity

Throughout your transplant, it is important to get enough exercise to build your strength. When you return home, you will be encouraged to continue with some type of daily activity. The staff will help you find the types and amount of activity which supports your recovery.

Visitors

For at least the first few weeks at home, your immune system will still be fragile, and you will tire easily. For these reasons, it is best to limit the number of visitors and to be sure that all visitors are in good health. The staff of the Stem Cell Transplant Program will give you specific information about these and other ways you can protect and care for yourself during the recovery process.

Resuming Life

It is natural for you to have many questions about how and when you will be able to resume your life. Most patients wonder about when they will be able to return to work, to resume sexual activity to drive. You will most likely have questions also about your long-term medical and physical status.
The answers to each of these questions will be different for each person. The staff will be available to you throughout this process to anticipate concerns, to provide suggestions and support and to answer questions.

Acknowledgements

Information in this document is reproduced with kind permission of the Bone Marrow Transplant Unit, King Faisal Hospital & Research Centre-Riyadh, Saudi Arabia. The sources below were referenced during the writing of this document:

National Marrow donor Program (NMDP)
World Marrow Donor Association (WMDA)
European Bone Marrow Transplant (EBMT) textbook for nurses