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# Bone Marrow Transplant

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Side effects of cancer and treatment vary from patient to patient. There are certain things you can do to help prevent, and treat some of the symptoms you may experience. This is meant to be a guide to assist you with understanding the treatment you are receiving, and managing the side effects that may occur. Ask the doctor or nurse if you have questions.

## History of Bone Marrow Transplantation

Bone marrow transplantation is a specialized transplant that is used to treat certain types of cancer and bone marrow disorders. This procedure was first performed in the 1950s, however the first successful bone marrow transplants didn't occur until 1968. In 1970, fewer than 100 bone marrow transplants were done at fewer than 10 centers. In 1988 the number of bone marrow transplants increased to 10,000 and were performed at more than 100 centers. (1) Today, thousands of bone marrow transplants are done annually at more than 250 centers worldwide. (2) Bone marrow transplant is becoming standard therapy in the treatment of many types of diseases.

Hoag Cancer Center's High-Dose Chemotherapy Program began in 1989. This was the first adult Autologous Bone Marrow Transplantation (ABMT) program in Orange County. (3)

## Overview of Bone Marrow Transplantation

The goal of bone marrow transplant is to provide a well functioning bone marrow. The ability of bone marrow to function properly can be altered by diseases such as leukemia, as well as by treatment such as high-dose chemotherapy and or radiation. In summary, bone marrow transplantation is used for replacement or rescue.

To better understand these rationales for transplantation it is important to understand what bone marrow is, and about other types of blood cells.

Blood is composed of many different types of cells, each with a specific function. These blood cells include white blood cells (WBCs),red blood cells (RBCs), and platelets. Most blood cells are formed in the bone marrow and released into the blood stream.

White blood cells help the immune system fight infection, red blood cells carry oxygen, and transport it to tissues throughout the body. Platelets help to control bleeding.

When cells are collected or "harvested for bone marrow transplant, it is stem cells that are being collected. Stem cells are the "mother cells" from which all blood cells evolve.

The greatest concentration of stem cells is in the bone marrow, however stem cells can also be found in the circulating or "peripheral" blood.

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When stem cells are infused into a person's circulating blood, they go into the interior of certain bones where they eventually mature into red blood cells, white blood cells, or platelets.

### Types of Bone Marrow Transplants

There are three different types of bone marrow transplant, all types allow for very high doses of chemotherapy and or radiation to be given to destroy the malignant cancer cells that would otherwise not be possible due to the destructive effects on the bone marrow. When high doses of chemotherapy and / or radiation are given the bone marrow stops making white blood cells, red blood cells and platelets. Without receiving stem cells after receiving these high dose treatments, the blood counts would not recover for several months or possibly not at all. By receiving a "bone marrow transplant" or stem cells, the blood counts should return to a safe level in four to six weeks. High dose therapy (chemotherapy with /or without radiation therapy) combined with conventional chemotherapy may be a curative method of therapy for some types of diseases.

Bone Marrow Transplants are named according to the donor source.

**Allogeneic Transplant:** this is a transplant which uses the bone marrow of a related or unrelated donor whose tissue closely matches the patient's tissue. To determine the tissue match a special test is done called HLA (human leukocyte antigen) testing. This is a blood test performed to determine if the "antigens" or markers on the white blood cells of the donor match those on the patient's white blood cells.

**Syngeneic Transplant:** this is a transplant, which uses the bone marrow of the patient's identical twin. A patient with an identical twin has a ready-made donor with perfectly matched bone marrow.

These two types of transplant are used when it is not possible to use your own bone marrow for transplant. This would be the case when it is necessary to replace the marrow due to disease.

Replacement is used when disease affects the functioning of the marrow.

Currently Allogeneic or Syngeneic Transplants are not available at Hoag Hospital. Hoag's Bone Marrow Transplant program utilizes the third type of transplant, which is Autologous Bone Marrow Transplantation. This is a transplant using the patient's own stem cells. Autologous Transplants are used in patient's with diseases such as leukemia, lymphoma, melanoma, breast cancer, testicular cancer and other solid tumors.

### Peripheral Blood Stem Cell vs. Bone Marrow Transplant

As mentioned previously the greatest concentration of stem cells is in the marrow, however stem cells can also be found in the circulating or "peripheral" blood. In some cases bone marrow is harvested for reinfusion after high dose therapy (an autologous bone marrow transplant or ABMT), in other cases peripheral blood stem cells are harvested (a peripheral blood stem cell PBSC transplant or "rescue").

The cure rate for the disease being treated is not affected for patients used either of these procedures, however patients transplanted with peripheral blood stem cells will begin producing white blood cells sooner, which decreases the amount of time they are at risk for developing a serious infection. (4)

The following section addresses the process of High Dose Therapy, in general. Specific chemotherapy and/or radiation protocols are addressed later in this issue.

### Preparing for the Transplant

#### Insurance Prior Authorization

Bone Marrow Transplant and Autologous Bone Marrow Transplant has been described as both intensive investigational therapy and standard curative treatment. (1) Both descriptions are accurate. Given the wide variety of diagnoses and types of bone marrow transplants, this form of treatment may be standard for one condition and investigational for another.

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The costs for Bone Marrow Transplant can vary from, the type of the treatment regimen, length of hospitalization, and other factors. The cost of Autologous Transplant has decreased over the past several years due to the ability to perform much of the transplant on an outpatient basis and the advances made in growth factors that decrease the time to engraftment. The cost generally ranges from \$100,000 to \$200,000.

It is necessary to find out in advance if the patient's insurance company covers the procedure. The process of obtaining insurance prior authorization is initiated by the doctor's office. This process is typically initiated during or just after the patient completes their induction chemotherapy. At that time a letter composed by the doctor is sent to the insurance company, this letter details the proposed therapy, rationale for the therapy, and the patient's medical history and current status. It can take from one to four weeks for a decision to be returned by the insurance company. It is critical that this response, whether it is an approval or a denial is in writing. If it is approved then the patient is ready to proceed with the procedure.

If the procedure is denied, there is most always an appeal procedure. Whether or not there is an appeal procedure, the doctor will ask the insurer again for coverage, often it is sent to an outside party for their opinion. Many times insurers will change their minds on this, especially if there is a second reviewer brought in. Sometimes entry of an attorney at this stage may lead to a reversal of the rejection without the need for litigation. The doctor can often direct patients to an attorney who has expertise in this area.

If all efforts have been exhausted and the insurer persists in denying the procedure, the patient has the option of paying for the Bone Marrow Transplant themselves. In these situations the hospital will work with patients in developing payment options.

Allogeneic and autologous bone marrow transplants are covered under Medicare for specific diagnoses only.

Every effort will be made by the doctor and nurses to seek approval for the procedure in a timely manner. It is helpful that the patient not contact the insurance company unless directed to do so by the doctor.

### **Induction Therapy**

Prior to undergoing a transplant a patient must first undergo induction therapy, which normally consists of chemotherapy for one to six months, (depending on the specific treatment plan for your diagnosis). Induction therapy is given to determine that the specific disease is sensitive (or responds) to chemotherapy, and in some cases to reduce the amount of tumor burden prior to undergoing the transplant.

### **Stem Cell Collection**

#### **Bone Marrow Harvest:**

Stem Cells collected from the bone marrow is obtained in the operating room, where the patient is given a general anesthetic. Multiple samples of the bone marrow are collected at the site of the posterior and iliac crests (this is back of the hip bone just above the buttocks). A large bore needle attached to a syringe is used by the doctor to draw up marrow in multiple aspirations. After the marrow is collected it is filtered (or strained), analyzed to determine that an adequate number of stem cells were collected, then cryopreserved until it is reinfused. During the filtering process the red blood cells collected are separated from the stem cells, these red cells are then given back (reinfused) to the patient.

This bone marrow harvest procedure usually takes between one and two hours and requires the patient to be hospitalized for one to two days. After the procedure the patient will complain of pain at the collection site, that is usually relieved with mild pain medications. The site will remain sore for the next several days.

### **Peripheral Stem Cell Harvest**

#### **Mobilization Therapy:**

This is therapy given prior to peripheral stem cell collection, patients receive chemotherapy for one to two days, and the chemotherapy agents are typically given at higher than standard doses. (The agents used are specific to the diagnosis and treatment plan). Prior to and following the chemotherapy the patient will receive large amount of intravenous hydration to protect the kidneys and help to eliminate the chemotherapy from the body. On the second or third day following chemotherapy the patient will receive cytokines to further stimulate the production of stem

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cells. Cytokines are also known as growth factors, such as GM-CSF and G-CSF. Patients receive GM-CSF and G-CSF before and during the period of time when peripheral stem cells are being collected (harvested).

It is expected that between 6 and 8 days after the mobilization chemotherapy is given that blood cells will markedly decrease, the white blood cells typically fall below 1000/ul, and at that time prophylactic (preventive) antibiotics are initiated. There is also an expected decrease in red blood cells and platelets for which red cell and platelet transfusions are often required. During this time it is not uncommon to feel fatigued, and it is advised to follow the general guidelines for chemotherapy as listed in the issue **Helpful Hints: CHEMOTHERAPY**, ask the nurse for a copy of these instructions.

Upon rebound from chemotherapy mobilization, peripheral stem cells are increased. This increase in peripheral stem cells correlates with the white blood count. This rebound will typically occur 12 to 14 days after the chemotherapy is given, it is at this time when stem cell collection is initiated. The process used to collect stem cells from the blood stream is similar to the process used to collect platelets from platelet donors, it is called apheresis (which means cell separation). A day or two prior to starting the stem cell harvest it is necessary to place a temporary pheresis catheter, this is a external catheter that is placed under a local anesthetic. The catheter is placed into a large vein called the subclavian, and enters into the body just below the collarbone. It remains in place until the stem cell harvest is complete, and at that time it is removed.

Patients are connected to an "apheresis" machine for the stem cell harvest. A tube is connected to each of the lumens of the pheresis catheter, through one of the lumens blood is extracted through the machine where it collects the stem cells. The remaining cells are returned to the patient through the other lumen of the catheter. The peripheral stem cell harvest (PSCH) is painless. Some patients occasionally experience lightheadedness, coldness and numbness around the lips, or cramping in the hands during the harvest. This is due to a temporary decrease in calcium; it is sometimes necessary to give the patient a calcium replacement in the form of Tums tablets. It is often helpful for the patient to drink a large glass of milk each day prior to the procedure.

Typically; several four to five hour sessions are required to collect sufficient stem cells from the blood stream for the transplant. The amount of stem cells to be collected is based on the patients body weight. If the patient is undergoing tandem transplantation, enough stem cells for each transplant will be collected. After each apheresis session, the stem cells are analyzed and frozen using a process called cryopreservation. The entire process is usually performed on an outpatient basis.

Sometimes PSCHs are used in addition to bone marrow harvests to augment the stem cells from the bone marrow harvest.

After stem cell collection is complete there is typically a one to two week break in treatment prior to beginning the high dose chemotherapy and / or radiation therapy. During this time the patient will undergo a series of tests (some of these tests may be performed prior to the stem cell harvest). These are routine tests required for all patients undergoing high dose therapy with stem cell rescue to assess organ function such as heart, lung, liver and kidney functions to assure these organs can tolerate the treatment, as well identify the response to induction chemotherapy. The type of testing may vary for each patient based on his or her specific diagnosis.

### **Pre-Treatment Testing**

Typically patients will require an **echocardiogram** and **EKG**. An echocardiogram is a diagnostic study to evaluate for any abnormalities of the heart wall, valves and blood vessels. It is non-invasive and does not use xray. There is no preparation or restrictions required for either an echocardiogram or an EKG.

**Pulmonary Function Testing**, is a series of breathing tests and an arterial blood test (ABG). It is required that the patient avoid any caffeine intake 24 hours prior to the testing, and if they are routinely taking any inhalers such as Provental these types of medications are to be held prior to the examination. It is recommended that patients wear light comfortable clothing and avoid eating a heavy meal prior clothing to the test.

**Brain MRI**, this test is required for each patient undergoing a bone marrow transplant. It must be done within four weeks of initiation of the treatment to assure there are no brain metastasis. Brain MRI (Magnetic Resonance Imaging) does not use xray and is non-invasive. It is one of the most useful scans in diagnostic techniques in imaging the brain. Prior to the scan a contrast called Gadolinium is injected into a vein (this is liquid, which enhances images of the or-

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gans and/or blood vessels). The patient may be asked to avoid eating and drinking for several hours prior to the MRI. The examination is painless, however for some patients who are claustrophobic this test may be uncomfortable; in these situations sedation can be provided. During the MRI the patient will hear a knocking sound from within the MRI system.

Depending upon the patient's specific diagnosis, CT and /or Bone Scans may also be done.

### **Laboratory Testing**

Patients must also have a series of blood tests done. It is helpful to eat prior to the blood tests to prevent feeling queasy or faint as the volume of blood taken will be about 1 to 2 cups. These blood tests are done to check the immune system, and organ function.

### **Blood Donor Program**

During both the chemotherapy mobilization and High Dose Therapy patients require red blood cell and platelet transfusions. It is helpful if compatible family members and friends can donate both red blood cells and platelets whenever possible. "Compatible" donors refer not only to a compatible blood typing, but also refers to CMV status. CMV (Cytomegalovirus) refers to a type of virus that many people are exposed to and is relatively harmless in persons whose immune system is not compromised. However, in patients who are immunocompromised, such as patients who are undergoing high dose therapy, it can cause serious complications. For individuals who have never been exposed to the virus it is important to use only blood products from donors that are CMV negative. Patients and donors are both tested for CMV. If a patient is CMV negative then they will only receive products that are CMV negative, if they are CMV positive it is not necessary to screen for CMV negative donors.

It is helpful if patients can identify a friend or family member to be their donor coordinator. This is a person who will be the contact for Blood Donor Services. This person will be especially helpful when the patient is in the hospital after the high dose treatment and the need for transfusions is the greatest. It is not feasible for the patients to be their own coordinator. For family members and friends who wish to donate blood for patients, instruct them to contact Hoag's Blood Donor Services at (949) 760-5621.

### **General Donor Information:**

It takes on the average 48 to 96 hours to process blood products once it is collected.

Red Blood cells can be stored for approximately 42 days, and platelets for 5 days.

You will be given a copy of the information flyer "IF YOU NEED BLOOD" for further information regarding blood transfusions.

### **Dental Care**

It is recommended that patients are examined by their dentist prior to high dose therapy, in order to prevent possible infection in the mouth during the treatment. This is especially important for those patients who will be receiving Total Body Irradiation. Patients may have to have dental work done based on the dentist's and oncologist's recommendations.

### **Preparing for Treatment and Hospitalization**

Most High Dose Therapy protocols can be administered as an out-patient, however there are certain protocols that require the patient to be hospitalized during the entire procedure. If the therapy can be performed as an out-patient then the patient will need to make arrangements for an adult to stay with them during this time (usually 8 to 10 days).

Alcohol interferes with the liver's ability to function. The liver is responsible for processing the chemotherapy in the body. Therefore, it is important that patients report their drinking habits to the doctor, and it is necessary to avoid any alcohol for at least two weeks or more before the high dose treatment.

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If patients have acrylic or artificial nails, they must be removed prior to the treatment, also nail polish must be removed prior to admission to the hospital.

When patients are admitted to the hospital there are restrictions on items that may or may not be brought into the transplant room. Patients may bring their own clothing, it is helpful to have clothing that buttons or fastens in the front for easy access to the Hickman catheter. Patients may bring videocassettes (there are VCR's in the rooms), tapes, radios, most computers, books, posters, and photographs. DO NOT bring plants, flowers, food, cosmetics, toothbrushes, perfumes, lotions, deodorants, or straight razors. It is best to leave money, jewelry, and other valuables at home.

It is helpful for patients to see the Oncology unit and transplant rooms prior to admission, a tour of the unit may be arranged by one of the nurses in our office.

### **Hickman Catheter**

Patients undergoing high dose therapy will require a Central venous catheter. These type of catheters allow patients to receive chemotherapy without repeated IV insertions. They allow patients to go home and receive chemotherapy, IV fluids, blood products and even have their blood drawn. The most common type of catheter used in high dose therapy is a **Hickman catheter**. A thin flexible tube is inserted into one of the central veins, the tube is then tunneled through surface skin tissue between the neck and shoulder to another separate incision, usually on the chest wall. The exit site for the catheter is easy to see and care for, and patients must change their dressing regularly to prevent infection. In addition, daily heparin flushes are required to prevent blockage of the tube. Home nursing services will be arranged to teach you how to care for your catheter and provide the supplies you would need.

### **Dietary Instruction (See Appendix A :Pathogen Free Diet)**

Specific dietary instructions are given to patients by a Dietician from Hoag Hospital. Arrangements are made to meet with each patient prior to starting their high dose treatment, this usually occurs when patients are undergoing their stem cell harvest. The patient should start the pathogen free diet at the time the high dose therapy is initiated.

### **High Dose Chemotherapy (See Appendix B: Commonly Used Drugs In Chemotherapy)**

The type of chemotherapy a patient is given is specific for the disease and transplant protocol (protocols are listed later in this issue).

Prior to and during the chemotherapy patients receive large amounts of intravenous fluids to prevent damage to the kidneys and bladder. These fluids help flush the chemotherapy through the body. This requires patients to carry a "pack" with intravenous fluids continuously during the chemotherapy. Patients also receive diuretics to help balance the amount of fluids going in the body to the amount the body eliminates. This helps prevent the body from becoming fluid overloaded. It is necessary for patients to strictly monitor their intake and output during the entire process. Daily weight will also be obtained.

Most chemotherapy protocols include several different chemotherapy agents which are administered either daily for several days or as a continuous infusion over several days. For patients receiving chemotherapy on an outpatient basis, they are required to come into the office daily for 4 or more hours each day. The days from the start of the chemotherapy to the day prior to the stem cell reinfusion are referred to as negative days counting backwards until day 0, which is stem cell reinfusion day.

Laboratory studies are done on a daily basis to monitor the white blood counts, red blood counts, platelets, electrolytes, kidney, and liver function.

The goal of the chemotherapy is for the drug to reach as many cancer cells as possible. However, chemotherapy also will affect non cancerous cells. When given in high doses, the side effects from the chemotherapy will be more profound than when given in standard doses. Some of the side effects with high dose chemotherapy will vary and have different intensities based upon what drugs the patient is receiving, and from patient to patient. Fortunately, most side effects are reversible. Most all of the chemotherapy used during the autologous bone marrow transplant will have the following side effects:

- **Bone Marrow Depression:** decreased red blood cells, white blood cells and platelets. The white blood cells typically start falling 2-4 days after chemotherapy is initiated, and will usually fall below 300u/l within 24-48 hours after the completion of chemotherapy. Preventive antibiotic therapy is initiated the day following the completion of chemotherapy.
- **Fatigue:** this symptom will vary in intensity based upon the chemotherapy drugs given. Most patients experience notable fatigue within 3-5 days of initiation of the chemotherapy. This fatigue persists throughout the transplant.
- **Hair Loss:** with most chemotherapy protocols total hair loss is to be expected, this may or may not include other body hair such as eyelashes, eyebrows, facial hair, pubic hair, hair on the arms and legs.
- **Diarrhea:** this symptom may occur as early as 48 hours after the initiation of chemotherapy, or as late as 7 to 10 days after chemotherapy is completed. This symptom varies in intensity with the type of chemotherapy drugs used.
- **Nausea and Vomiting:** Nausea is a frequent side effect of high dose chemotherapy. Antinausea medications are administered routinely in attempt to prevent and minimize the nausea.

Decadron: is a steroid given to prevent nausea, during the chemotherapy patients receive intravenous decadron daily.

Aloxi: Patients will receive Aloxi daily as an intravenous injection.

PCA Antinausea Infusion: This is an intravenous combination of four antinausea medications; decadron, ativan, benadryl, and reglan. It is delivered as a continuous infusion intravenously, and the portable pump allows the patient to administer "bolus" doses as needed for increased nausea or vomiting.

- **Changes in oral mucosa:** these side effects include dry mouth, and taste bud changes. These changes can last up to several weeks to months after chemotherapy. As with standard chemotherapy, sores to the mouth, tongue and throat can occur and with greater intensity. Diligent mouth care can help to minimize these effects. (Please refer to Helpful Hints: CHEMOTHERAPY for specific mouth care instructions)
- **Changes in electrolytes:** As the chemotherapy is eliminated from the body, there are often changes in some of the electrolytes. These values will be monitored daily and may require additional replacement of potassium and magnesium. It is also sometimes necessary for patients to take sodium bicarbonate tablets during or after the chemotherapy.

### Total Body Irradiation (TBI)

Radiation therapy is the use of high energy radiation in the treatment of cancer. When it is used as part of a bone marrow transplant it is combined with chemotherapy.

Total Body Irradiation or TBI is used in specific bone marrow transplant protocols. All parts of the body are treated with radiation to kill the cancer cells. Radiation therapy destroys both cancer cells and normal cells. Patient's receiving TBI will have destruction of the bone marrow cells.

For patients receiving TBI it is necessary to do planning and simulations prior to starting the therapy. Patient meet with the Radiation Oncologist several times to plan and prepare for their treatment. This planning process starts as early as a month prior to the therapy.

For autologous bone marrow transplants that include TBI, these protocols must be carried out as an inpatient. Patients receive high dose chemotherapy for 2-3 days prior to starting the TBI, the usual plan of treatment for TBI is twice a day for four days.

Each treatment lasts about twenty minutes. During the TBI the patients lungs will be partially protected by lead shields, and markings will be made on the chest and back area. It is necessary for the patient to lie still during the TBI

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and they will be repositioned several times during the procedure. It is not uncommon for the patient to become light-headed and dizzy upon changing positions. Patients may experience the following side effects from the TBI:

- **Hair Loss: total body.**
- **Changes to oral mucosa: patients are more prone to mouth sores, sore throat, swollen neck glands, and mouth dryness from the TBI. These symptoms tend to be more profound than with chemotherapy alone.**
- **Nausea and Vomiting**
- **Fever**
- **Skin Color Changes and Sensitivities: these are usually temporary.**
- **Bone Marrow Depression**
- **Sterility/ Infertility**

### **Washout**

Washout is the period immediately following the completion of the chemotherapy and / or chemoradiation therapy. This period of time is dependent upon the protocol a patient receives. During this time the patient receives large amounts of intravenous fluids to help flush the chemotherapy from the body. It is critical that the chemotherapy has been eliminated from the body prior to reinfusing the stem cells. During this time period the patient may experience more nausea, and fatigue as the chemotherapy is excreted from the body.

### **Stem Cell Reinfusion (Transplant Day 0)**

The stem cell reinfusion is fairly anticlimactic; it is similar to a regular blood transfusion. This procedure can be done on an inpatient or outpatient basis.

The stem cells are brought to the room in frozen bags. (The number of bags a patient receives is dependent upon the number of pheresis procedures, there are fewer bags for bone marrow vs. peripheral stem cells.) Each bag is placed in a warm water bath and quickly thawed. It is then reinfused into the patient through their Hickman catheter. During the procedure the patient's vital signs and pulse oximetry (measuring the level of oxygen in the tissue), are monitored. Each bag is administered rapidly over 5- 10 minutes. The total reinfusion time ranges from 30 to 45 minutes.

Side effects related to the stem cell reinfusions are rare, but patients may experience shortness of breath and may require oxygen for a short period of time. It is also possible for the blood pressure to drop, and patients may experience flushing, hives, nausea, vomiting and/or headache. Some of these side effects may be related to the preservative DMSO, which is placed with the stem cells when they are frozen. The DMSO has a distinct smell and sometimes the patient can taste it. Some patients note a garlic smell, that may be more apparent to those around the patient than the patient. This odor can last for several days. It is normal and expected for the patient to have dark bloody urine immediately after the reinfusion, this is from the break down (lysis) of the red blood cells. This symptom will resolve after the patient urinates several times.

Patients are premedicated prior to the reinfusion with medications to help prevent or minimize any reactions. These medications may cause the patient to become drowsy during the reinfusion.

If patients receive treatment on an outpatient basis, often they are admitted to the hospital after the reinfusion.

### **Recovery Period (Day 0 to Day 14)**

During this time, most patients are usually in the hospital, however in some cases patients have been able to complete the entire procedure as an outpatient. Although, this requires a high level of support from the patient's family. Days following the stem cell reinfusion are counted as positive days, starting with Day +1.

The following side effects most commonly occur during the week or two after stem cell reinfusion. These side effects are related to the high dose chemotherapy and/ or radiation therapy not the stem cell reinfusion.

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## Low Blood Counts

The chemotherapy and /or TBI a patient receives cause a decrease in the white blood cells, which will drop below 100u/l. There are several types of WBCs. Mature neutrophils is the first in line of defense in fighting infection. During the recovery period of the bone marrow, the neutrophils will drop to nearly 0. ANC (Absolute neutrophil count) is used to identify persons at risk for developing serious infection. The risk of infection is significant when the ANC is less than 500, and high when the ANC is less than 100. The length of the neutropenia also influences the risk of infection. ANC is calculated by multiplying the White Blood Count by the percentage of bands (immature white blood cells) and segmented neutrophils. During the patients time of recovery the doctor will monitor the patients ANC to determine their risk of infection.

During this period of time patients are in protective isolation. The purpose of this is to keep the environment as clean as possible. Patients have a private room with special filters, and during the time of marked neutropenia the door remains closed. Visitors and hospital staff entering the room will be required to wear a gown, gloves and a mask. Once the WBC is high enough patients no longer need to be in isolation. The door to the room will be opened, and patients are allowed to leave the room with a mask. Patients remain on antibiotics during the recovery period, and must continue on the pathogen free diet. Growth Factors, GM-CSF and G-CSF are given daily to promote recovery of the white blood counts. White Blood Cells are the first cells to recover or engraft. Most patients will begin to engraft somewhere between Day+9 to Day+14.

During the period of neutropenia patients are monitored closely. It is not uncommon to develop fevers. Monitoring during this time includes monitoring vital signs (temperature, pulse, blood pressure, and respiratory rate), and blood counts at least once daily. It is not uncommon for patients to experience fevers. If patients do develop a fever blood cultures, urine, throat, often stool cultures, and chest x-rays are obtained to help identify if there is infection present. It often takes a few days to resolve the symptoms of fever, Tylenol, cool compresses, or a cooling blanket may be used if the fever makes the patient uncomfortable. Some patients may develop shaking chills (rigors) with the fever, medication can be given to help alleviate these symptoms. The antibiotics will be stopped once a patient has an adequate number of neutrophils.

Common sites of infection are the skin, mouth, throat, esophagus, intestinal tract and rectal area.

The chemotherapy and / or TBI also affect red blood cells. While waiting for the bone marrow to recover, most patients require RBC (red blood cell) transfusions. The hematocrit is the measurement of red blood cells. When the hematocrit is low, this is anemia, which causes patients to feel fatigued, and sometimes short of breath. This cell line takes longer to engraft than the WBCs, often up to several weeks after the stem cell reinfusion. Patient's requirements for RBC transfusions will vary from patient to patient.

The third type of cell that is decreased is platelets. When platelets are low patients are at risk for developing bleeding. Platelet counts can drop below 10,000. During this period patients may require platelet transfusions. When platelets are low patients are instructed to take precautions to prevent bleeding. Platelets are the last cell line to recover, they can take as long as 4 weeks or more to engraft.

### NORMAL VALUES FOR BLOOD COUNTS

WBC:	4.8 - 10.8 k/uL
Neutrophil:	1.0 - 7.0 K/uL
Lymphocyte:	1.5 - 4.0 K/uL
Monocyte:	0.2 - 0.9 K/uL
Eosinophil:	0 - 0.7 K/uL
Basophil:	0 - 0.2 K/uL
RBC:	4.6 - 6.2 Mil/uL
HGB:	14.0 - 18.0 g/dL
HCT:	42.0 - 52.0 %
PLT:	150 - 400 k/uL

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## Gastrointestinal Side Effects

The mouth, throat, esophagus and gastrointestinal system can be affected by the chemotherapy and/or TBI. The tissues in the mouth can become dry, irritated and more painful. Some treatment regimens especially those that include TBI, are more likely to produce irritation or ulcers than others. Pain medications will be administered to help the discomfort. Most patients will experience appetite loss and often heartburn. Irritation of the stomach and intestine may lead to ongoing nausea, vomiting, and diarrhea. Diarrhea may be severe and prolonged. Some patients may require intravenous feedings in the form of TPN (total parental nutrition) to provide nutrition until they can eat food again. Most patients undergoing bone marrow transplants require intravenous hydration throughout the hospitalization.

## Skin Changes

Some patients may develop skin changes such as rashes due to medications and / or TBI. These are temporary and will resolve. With some treatment regimens patients skin pigmentation will darken, this darkening also can affect the fingernails and toenails. Pigmentation changes are also temporary.

## Preparing For Discharge

The patient and family may experience both excitement and apprehension anticipating the discharge to home. Discharge from the hospital generally occurs when the WBC count is 1000u/L or greater, the patient is able to tolerate food and fluids orally, nausea and vomiting are controlled, diarrhea is controlled, no fever, and there is adequate support for the patient within the home. The patient may still require growth factors, RBC, platelet transfusions, and sometimes antibiotics for several days. When a patient is discharged to home they will still feel fatigued, and will still have dietary restrictions that are advanced as the white blood count continues to rise. Patient's sense of taste and saliva production will gradually return over the next few months. It is best to try and stimulate your appetite by eating small frequent meals. It is not uncommon for patients and family members to feel frustration at the gradual nature of recovery, which is much slower than experienced with standard chemotherapy. It is necessary to return to the doctor's office several times per week for the first several weeks, the frequency of the follow-up decreases as the patient continues to recover. It is important for both the patient and their family members to understand that the patient will need to rely on the assistance from others for several weeks. Focusing on reasonable goals and being patient are critical to a successful recovery.

Exercise is important, although patients may feel that they don't have the energy, a lack of exercise will actually cause this to be more profound. Patients should start slowly and gradually increase their activity. Starting exercise in the hospital may actually decrease the amount of hospitalization time. Starting with gentle stretching and strengthening exercises, use of a stationary bike, short walks, etc. will promote the patient's energy level.

It is important for the patient to report to the doctor any symptoms they experience, the following are some general guidelines.

**Fever:** Any fever of 100.5 or greater, along with any chilling (associated with fever or not), or any signs or symptoms of infection must be reported to the doctor. Signs of infection include cough, diarrhea, urinary symptoms, redness or tenderness at the site of the Hickman catheter.

Patients remain at risk for infection for the next several months, despite the increase of white blood cells. When patients are first discharged from the hospital it is important to stay away from large crowds such as malls or large restaurants. Avoiding people with obvious cold or flu symptoms is also important for the first several weeks.

**Skin Changes:** If a patient notices lesions such as pimples, blistering, small red spots or bruising, it is important to notify the doctor. These may be signs of bleeding or herpes zoster. Patients normally remain on a medication to prevent herpes zoster during the recovery period.

Sexual activity is not recommended until the patient's platelet count is greater than 50,000. The use of a condom is recommended for several months, along with a lubricant to reduce the likelihood of trauma or irritation to the delicate tissue. This will also help with vaginal dryness which female patients may experience from the treatment.

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Hygiene continues to be important when patients are discharged from the hospital. Continuing good oral hygiene and inspecting the oral mucosa for any lesions. For females replace make-up articles such as lipstick, creams, lotions, etc. with hypoallergenic products. Look for products that do not contain alcohol (perfumes or scents). Mascara is not recommended for the first several months. It is also not recommended that patients have artificial nails placed during the first several months following the transplant. Contact wearers should avoid wearing them for the first month or so due to drying of the eyes.

All patients should avoid exposure to the sun, especially those who underwent TBI. Wearing a #15 sunscreen is recommended.

Patients should avoid using a straight razor until their platelet count has reached 50,000 or greater.

Pets are permitted in the home as long as the patient is not providing direct care i.e. changing the cat litter box, grooming etc. Exposure to birds is not recommended for six months.

Notify the doctor before taking any medications he has not prescribed for you. It is important to not take aspirin, use Tylenol instead. Alcohol is to be avoided until the doctor instructs the patient that it is ok, it can damage your bone marrow.

Emotional well being is an important factor in a patient's recovery. Many patients describe a decreased ability to concentrate, especially during the hospitalization. Fluctuating emotions are not uncommon, this is due to the extreme fatigue, changes in lifestyle, fear, apprehension and often medications a patient is receiving. These are normal for a patient to experience throughout the process. Sometimes it is helpful to discuss what you are feeling with either another patient who has been through the same treatment or even a psychologist. The doctor or nurse can arrange for patients to meet with a psychologist or another patient. Bone Marrow Transplant can be a stressful as well as a hopeful time for patients and their families. It is normal to experience a wide range of emotions, how a patient deals with them is as important as the other aspects of their care.

### **Potential Long Term Effects and Infrequent Complications**

As with any treatment there are potential complications. The following are toxicities, which can occur, some of these are temporary and reversible.

#### **Central Nervous System Toxicities**

Confusion, altered thinking is an occasional, temporary side effect of some of the high dose therapy. Occasionally with certain high dose chemotherapy regimens a patient may experience hearing loss or tinnitus (ringing in the ears). The tinnitus is usually temporary and reversible once the chemotherapy is excreted from the body. Hearing loss can be a more long term, and in some cases a permanent side effect.

#### **Bladder Irritation (Hemorrhagic Cystitis)**

Bladder irritation, sometimes evidenced by bloody or painful urination, can occur following the high dose chemotherapy. Administering a drug called Mesna and providing intravenous hydration is commonly used to prevent this effect.

#### **Lung, Liver, and Heart**

Temporary organ damage can occur following high dose chemotherapy and / or TBI. It is usually mild and completely reversible. Liver damage occurs in approximately half of patients following high dose treatment. Symptoms can include abnormal blood levels of liver enzymes and bilirubin (a pigment produced during the break up of red blood cells), jaundice (yellow discoloration of the eyes and skin), and fluid retention. "Resting" the liver, counteracting some of the symptoms and avoiding medications that aggravate the condition is the most common treatment until the liver heals itself.

Breathing problems can occur following some types of high dose therapy. In most cases, injury to the lungs is mild and temporary, but some patients do experience breathing problems long term.

Mild, temporary heartbeat irregularities (arrhythmia) or rapid heartbeat can occur following some high dose therapy. Severe or long-term heart problems are rare.

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## Reproductive Organs

Damage to the reproductive organs from high dose chemotherapy and / or TBI is common, and can result in long term infertility. The patient's age, sex, stage of sexual maturity, and dose of therapy administered affect the likelihood of infertility. Few patients who receive TBI regain fertility post bone marrow transplant.

Despite the frequency of infertility post bone marrow transplant, many healthy children have been born to former bone marrow transplant patients. There are options such as sperm banking available to patients with fertility issues. The doctor can discuss with each patient what options they may have.

## Specific High Dose Protocols

The following protocols are the standard protocols for a specific disease. Modifications are sometimes made based upon the individual case. The doctor will discuss your particular protocol with you.

### Breast Cancer

Breast cancer protocols are divided into two separate categories because of the prognostic differences. The categories are patients with distant metastatic disease, or patients treated in the adjuvant setting (those patients who are at a high risk for developing metastatic disease)

#### Metastatic Breast Cancer

Since 1990, 49 patients with distant metastatic breast cancer have been treated in Hoag Cancer Centers High Dose Chemotherapy Program. (5) Patients on this protocol are treated with tandem (back to back or sequential) high dose chemotherapy with peripheral stem cell rescue.

The treatment regimen or protocol is as follows:

#### Mobilization Chemotherapy:

Patients undergo mobilization of peripheral blood stem cells with Taxol, Cytosan, G-CSF, and GM-CSF.

Prior to peripheral blood stem cell collection, patients receive Cytosan at a dose of 4gm per square meter (square meter is calculated by the patients height and weight), with Mesna plus Taxol 200mg per square meter per day. To facilitate the harvesting of peripheral blood stem cells, patients receive GM-CSF 250mcq per square meter subcutaneously daily on days 3-14 following mobilization chemotherapy alternating with G-CSF intravenously or subcutaneously on days 3-14.

Peripheral blood stem cell harvesting is performed by apheresis technique for adequate amounts of peripheral blood stem cells for cryopreservation.

#### Sequential (Tandem) High-Dose Chemotherapy:

Patients receive sequential high-dose chemotherapy regimens with stem cell support using chemotherapy agents that are "non-cross resistant" schedules of chemotherapy.

Patients may receive high-dose chemotherapy on an outpatient or inpatient basis. Patients receiving their high-dose chemotherapy on an outpatient basis will be monitored at least once daily by the physician. Patients can maintain therapy as an outpatient throughout the high-dose chemotherapy infusion as long as the physician deems the patient sufficiently stable for outpatient management.

The first high-dose chemotherapy consists of: Mitoxantrone 60mg per square meter over 72 hours as a continuous infusion on days -6, -5, -4, and thiotepa 300mg per square meter per day as a 2-hour infusion on days, -6, -5, -4 (MiTepa). A 72-rest period will take place commencing with completion of the 72 hour (MiTepa) infusion, and ending with the infusion of the autologous peripheral blood stem cells. Patients are then hospitalized during the period of pancytopenia (low blood counts) until marrow re-engraftment occurs.

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Six to eight weeks from the start of the first high-dose chemotherapy, patients will commence the second sequential high-dose chemotherapy regimen which consists of: Carboplatin 1800mg per square meter for 96 hours as a continuous infusion on days -7,-6,-5,-4, ifosfamide 12gm per square meter over 96 hours as a continuous infusion with 120 hours of Mesna days -7,-6,-5,-4,-3 and etoposide at a dose of 2000mg per square meter over 96 hours continuous infusion on days -7,-6,-5, and -4 (ICE). A 72-rest period will take place commencing with completion of the 96 hour (ICE) infusion, and ending with the infusion of the autologous peripheral blood stem cells. Patients are then again hospitalized during the period of pancytopenia until marrow re-engraftment occurs.

#### **Post High-Dose Chemotherapy:**

Post hospital discharge follow-up as dictated by serial blood counts and blood chemistries. The patient will then undergo radiation to the chest wall and axillary lymph nodes as appropriate. Subsequently, the patient will be placed on ongoing adjuvant hormonal therapy. Patients are followed up to a minimum of 5 years status post treatment with tracking of response rate, relapse, and over-all survival data.

#### **Adjuvant Breast Cancer**

Since 1990, 33 patients have been treated in Hoag Cancer Centers High Dose Chemotherapy Program in an adjuvant setting. (5) Patients on this protocol are treated with single high dose chemotherapy with peripheral stem cell rescue.

The treatment regimen or protocol is as follows:

#### **Mobilization Chemotherapy:**

Patients undergo mobilization of peripheral blood stem cells with Taxol, Cytosan, G-CSF, and GM-CSF.

Prior to peripheral blood stem cell collection, patients receive Cytosan at a dose of 4gm per square meter (square meter is calculated by the patients height and weight), with Mesna plus Taxol 200mg per square meter per day. To facilitate the harvesting of peripheral blood stem cells, patients receive GM-CSF 250mcq per square meter subcutaneously daily on days 3-14 following mobilization chemotherapy alternating with G-CSF intravenously or subcutaneously on days 3-14.

Peripheral blood stem cell harvesting is performed by apheresis technique for adequate amounts of peripheral blood stem cells for cryopreservation.

#### **High-Dose Chemotherapy:**

The patient may receive high-dose chemotherapy on an outpatient basis or on an inpatient basis. Patients receiving their high-dose chemotherapy on an outpatient basis will be monitored at least once daily by the physician. Patients can maintain therapy as an outpatient throughout the high-dose chemotherapy infusion as long as the physician deems the patient sufficiently stable for outpatient management.

High-Dose chemotherapy consists of: Carboplatin 1800mg per square meter for 96 hours as a continuous infusion on days -7,-6,-5,-4, Ifosfamide 12gm per square meter over 96 hours as a continuous infusion with 120 hours of Mesna days -7,-6,-5,-4,-3 and Etoposide at a dose of 2000mg per square meter over 96 hours continuous infusion on days -7,-6,-5, and -4 (ICE). A 72-hour rest period will take place commencing with completion of the 96-hour (ICE) infusion, and ending with the infusion of the autologous peripheral blood stem cells. Patients are then hospitalized during the period of pancytopenia (low blood counts) until marrow re-engraftment occurs.

#### **Post High-Dose Chemotherapy:**

Post hospital discharge follow-up as dictated by serial blood counts and blood chemistries. The patient will then undergo radiation to the chest wall and axillary lymph nodes as appropriate. Subsequently, the patient will be placed on ongoing adjuvant hormonal therapy. Patients are followed up to a minimum of 5 years status post treatment with tracking of response rate, relapse, and over-all survival data.

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## Non-Hodgkin's Lymphoma

Since 1990, 27 patients have been treated in Hoag Cancer Centers High Dose Chemotherapy Program. (5) Patients on this protocol are treated with single high dose chemotherapy with peripheral stem cell rescue.

The treatment regimen or protocol is as follows:

### Mobilization Chemotherapy:

Patients may receive their mobilization therapy on an outpatient basis. Prior to peripheral blood stem cell collection, patients receive Cytoxan at a dose of 4gm per square meter with Mesna plus Taxol 200mg per square meter per day. To facilitate the harvesting of peripheral blood cells, patients receive GM-CSF 250mcq per square meter subcutaneously daily on days 3-14 following the mobilization chemotherapy alternating every 12 hours with G-CSF 5mcq/kg intravenously on days 3-14.

Peripheral blood stem cell harvesting is performed by apheresis technique for adequate amounts of peripheral blood stem cells for cryopreservation.

### High-Dose Chemotherapy:

The patient may receive high-dose chemotherapy on an outpatient basis or on an inpatient basis. Patients receiving their high-dose chemotherapy on an outpatient basis will be monitored at least once daily by the physician. Patients can maintain therapy as an outpatient throughout the high-dose chemotherapy infusion as long as the physician deems the patient sufficiently stable for outpatient management.

High-Dose chemotherapy consists of: Carboplatin 1800mg per square meter for 96 hours as a continuous infusion on days -7, -6, -5, -4, Ifosfamide 12gm per square meter over 96 hours as a continuous infusion with 120 hours of Mesna days -7, -6, -5, -4, -3 and Etoposide at a dose of 2000mg per square meter over 96 hours continuous infusion on days -7, -6, -5, and -4 (ICE). A 72-hour rest period will take place commencing with completion of the 96-hour (ICE) infusion, and ending with the infusion of the autologous peripheral blood stem cells. Patients are then hospitalized during the period of pancytopenia (low blood counts) until marrow re-engraftment occurs.

### Post High-Dose Chemotherapy:

Post hospital discharge follow-up as dictated by serial blood counts and blood chemistries. Upon hematological recovery following high-dose chemotherapy, the patient will then undergo adjuvant radiation therapy to consolidate a complete response. Subsequently, any patient with CD20-positive antigen non-hodgkins lymphoma will receive Rituxan therapy weekly for 4 consecutive weeks, then every 6 months for 2 years. Patients are followed up to a minimum of 5 years status post treatment with tracking of response rate, relapse, and over-all survival data.

## Hodgkin's Lymphoma

Since 1990, 6 patients have been treated in Hoag Cancer Centers High Dose Chemotherapy Program. (5) Patients on this protocol are treated with single high dose chemotherapy and TBI with peripheral stem cell rescue.

The treatment regimen or protocol is as follows:

### Mobilization Chemotherapy:

Patients may receive their mobilization therapy on an outpatient basis. Prior to peripheral blood stem cell collection, patients receive Cytoxan at a dose of 4gm per square meter with Mesna per day, plus, Taxol 200mg per square meter per day. To facilitate the harvesting of peripheral blood cells, patients receive GM-CSF 250mcq per square meter subcutaneously daily on days 3-14 following the mobilization chemotherapy alternating every 12 hours with G-CSF 5mcq/kg intravenously on days 3-14.

Peripheral blood stem cell harvesting is performed by apheresis technique for adequate amounts of peripheral blood stem cells for cryopreservation

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### **High-Dose Chemotherapy and TBI:**

Patients receive high-dose chemotherapy and TBI regimen with stem cell support on an inpatient basis. The patient's high-dose therapy regimen which consists of: Cytoxan 60mg per kilogram as a 2 hour infusion on days -6, -5, with Mesna 25mg per kilogram IV bolus 30 minutes before, and 3 hours, 6 hours, and 9 hours following Cytoxan and for an additional day for a total of 12 doses. VP-16 200mg per square meter as a 90-minute infusion every 12 hours for a total of 4 doses on days -6, -5. This is followed by five days of twice daily total body irradiation, on days -4, -3, -2, -1, 0. The reinfusion of the autologous peripheral stem cells following the last dose of total body irradiation. Patients require hospitalization throughout the second high-dose therapy regimen, discharge occurring when marrow re-engraftment occurs.

### **Post High-Dose Chemotherapy:**

Post hospital discharge follow-up as dictated by serial blood counts and blood chemistries. Patients are followed up to a minimum of 5 years status post treatment with tracking of response rate, relapse, and over-all survival data.

### **Multiple Myeloma**

Since 1990, 7 patients have been treated in Hoag Cancer Centers High Dose Chemotherapy Program. (5) Patients on this protocol are treated with single high dose chemotherapy and TBI with peripheral stem cell rescue.

The treatment regimen or protocol is as follows:

### **Mobilization Chemotherapy:**

Patients may receive their mobilization therapy on an outpatient basis. Prior to peripheral blood stem cell collection, patients receive Cytoxan at a dose of 4gm per square meter with Mesna per day. To facilitate the harvesting of peripheral blood cells, patients receive GM-CSF 250mcq per square meter subcutaneously daily on days 3-14 following the mobilization chemotherapy alternating every 12 hours with G-CSF 5mcq/kg intravenously on days 3-14.

Peripheral blood stem cell harvesting is performed by apheresis technique for adequate amounts of peripheral blood stem cells for cryopreservation.

### **Tandem (Sequential) High-Dose Chemotherapy and TBI:**

Patients receive tandem high dose chemotherapy/ high dose chemotherapy and TBI regimens with stem cell support. The patient may receive high-dose chemotherapy on an outpatient basis or on an inpatient basis. Patients receiving their high-dose chemotherapy on an outpatient basis will be monitored at least once daily by the physician. Patients can maintain therapy as an out-patient throughout the high-dose chemotherapy infusion as long as the physician deems the patient sufficiently stable for outpatient management.

The first high-dose chemotherapy regimen consists of: Melphalan 100mg per square meter as a 2-hour infusion on days -4, -3. A 72-hour rest period will take place commencing with completion of the second dose of Melphalan infusion, and ending with the infusion of the autologous peripheral blood stem cells. Patients may then be hospitalized during the period of pancytopenia (low blood counts) until marrow re-engraftment occurs.

Six to eight weeks from the start of the first high-dose chemotherapy, patients will commence the second high-dose therapy regimen which consists of: Melphalan 100mg per square meter as a 2-hour infusion on days -6, -5. This is followed by five days of twice daily total body irradiation, on days -4, -3, -2, -1, 0. The reinfusion of the autologous peripheral stem cells following the last dose of total body irradiation. Patients require hospitalization throughout the second high-dose therapy regimen, discharge occurring when marrow re-engraftment occurs.

### **Post High-Dose Chemotherapy:**

Post hospital discharge follow-up as dictated by serial blood counts and blood chemistries. Upon hematological recovery following the second high-dose therapy, the patient will be placed on ongoing adjuvant immunotherapy with, interferon (IFN) maintenance subcutaneously three times per week for a total of two years. Patients are followed up to a minimum of 5 years status post treatment with tracking of response rate, relapse, and over-all survival data.

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## Solid Tumors

Since 1990, 27 patients with solid tumors have been treated in Hoag Cancer Centers High Dose Chemotherapy Program. (5) This group of patients include patients with melanoma, testicular cancer, lung cancers, sarcomas, bladder cancer and medulloblastoma. Patients on this protocol are treated with single high dose chemotherapy with peripheral stem cell rescue. See Appendix B: Timeline

The treatment regimen or protocol is as follows:

### Mobilization Chemotherapy:

Patients may receive their mobilization therapy on an outpatient basis. Prior to peripheral blood stem cell collection, patients receive Cytoxan at a dose of 4gm per square meter with Mesna plus Taxol 200mg per square meter per day. To facilitate the harvesting of peripheral blood cells, patients receive GM-CSF 250mcq per square meter subcutaneously daily on days 3-14 following the mobilization chemotherapy alternating every 12 hours with G-CSF 5mcq/kg intravenously on days 3-14.

Peripheral blood stem cell harvesting is performed by apheresis technique for adequate amounts of peripheral blood stem cells for cryopreservation.

### High-Dose Chemotherapy:

The patient may receive high-dose chemotherapy on an outpatient basis or on an inpatient basis. Patients receiving their high-dose chemotherapy on an outpatient basis will be monitored at least once daily by the physician. Patients can maintain therapy as an outpatient throughout the high-dose chemotherapy infusion as long as the physician deems the patient sufficiently stable for outpatient management.

High-Dose chemotherapy consists of: Carboplatin 1800mg per square meter for 96 hours as a continuous infusion on days -7, -6, -5, -4, Ifosfamide 12gm per square meter over 96 hours as a continuous infusion with 120 hours of Mesna days -7, -6, -5, -4, -3 and Etoposide at a dose of 2000mg per square meter over 96 hours continuous infusion on days -7, -6, -5, and -4 (ICE). A 72-rest period will take place commencing with completion of the 96-hour (ICE) infusion, and ending with the infusion of the autologous peripheral blood stem cells. Patients are then hospitalized during the period of pancytopenia (low blood counts) until marrow re-engraftment occurs.

### Post High-Dose Chemotherapy:

Post hospital discharge follow-up as dictated by serial blood counts and blood chemistries. Patients are followed up to a minimum of 5 years status post treatment with tracking of response rate, relapse, and over-all survival data.

## Leukemia

Since 1990, 6 patients have been treated in Hoag Cancer Centers High Dose Chemotherapy Program. (5) Patients on this protocol are treated with single high dose chemotherapy with peripheral stem cell rescue. The treatment regimen or protocol is as follows:

### Mobilization Chemotherapy:

Patients may receive their mobilization therapy on an outpatient basis. Prior to peripheral blood stem cell collection, patients receive Cytoxan at a dose of 4gm per square meter with Mesna plus Taxol 200mg per square meter per day. To facilitate the harvesting of peripheral blood cells, patients receive GM-CSF 250mcq per square meter subcutaneously daily on days 3-14 following the mobilization chemotherapy alternating every 12 hours with G-CSF 5mcq/kg intravenously on days 3-14.

Peripheral blood stem cell harvesting is performed by apheresis technique for adequate amounts of peripheral blood stem cells for cryopreservation.

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### **High-Dose Chemotherapy :**

The patient may receive high-dose chemotherapy on an outpatient basis or on an inpatient basis. Patients receiving their high-dose chemotherapy on an outpatient basis will be monitored at least once daily by the physician. Patients can maintain therapy as an outpatient throughout the high-dose chemotherapy infusion as long as the physician deems the patient sufficiently stable for outpatient management.

High-Dose chemotherapy consists of: Bulsulfan 16mg/kg over four days, and Cytoxan (plus Mesna) 15mg/kg over 3 days. A 72-hour rest period will take place commencing with completion of the chemotherapy, and ending with the infusion of the autologous peripheral blood stem cells. Patients are then hospitalized during the period of pancytopenia (low blood counts) until marrow re-engraftment occurs.

### **Post High-Dose Chemotherapy:**

Post hospital discharge follow-up as dictated by serial blood counts and blood chemistries. Patients are followed up to a minimum of 5 years status post treatment with tracking of response rate, relapse, and over-all survival data.

### **Ovarian Cancer**

Since 1990, 8 patients have been treated in Hoag Cancer Centers High Dose Chemotherapy Program. (5) Patients on this protocol are treated with tandem high dose chemotherapy with peripheral stem cell rescue.

The treatment regimen or protocol is as follows:

### **Mobilization Chemotherapy:**

Patients undergo mobilization of peripheral blood stem cells with Taxol, Cytoxan, G-CSF, and GM-CSF.

Prior to peripheral blood stem cell collection, patients receive Cytoxan at a dose of 4gm per square meter (square meter is calculated by the patients height and weight), with Mesna plus Taxol 200mg per square meter per day. To facilitate the harvesting of peripheral blood stem cells, patients receive GM-CSF 250mcq per square meter subcutaneously daily on days 3-14 following mobilization chemotherapy alternating with G-CSF intravenously or subcutaneously on days 3-14.

Peripheral blood stem cell harvesting is performed by apheresis technique for adequate amounts of peripheral blood stem cells for cryopreservation.

### **High-Dose Chemotherapy:**

The patient may receive high-dose chemotherapy on an outpatient basis or on an inpatient basis. Patients receiving their high-dose chemotherapy on an out-patient basis will be monitored at least once daily by the physician. Patients can maintain therapy as an out-patient throughout the high-dose chemotherapy infusion as long as the physician deems the patient sufficiently stable for outpatient management.

The first high-dose chemotherapy consists of: Cytoxan 60mg/kg on days -6, and day -5, Taxol 150mg per square meter on day -4 and Mesna days -6, -5, and -4. A 72-hour rest period will take place commencing with completion of the chemotherapy, and ending with the infusion of the autologous peripheral blood stem cells. Patients are then hospitalized during the period of pancytopenia (low blood counts) until marrow re-engraftment occurs.

Six to eight weeks from the start of the first high-dose chemotherapy, patients will commence the second sequential high-dose chemotherapy regimen which consists of: Thiotepa 100mg/m<sup>2</sup> per square meter on days -7, -6, and -5, and Taxol 150mg/m<sup>2</sup> per square meter on day -4. A 72-hour rest period will take place commencing with completion of the chemotherapy, and ending with the infusion of the autologous peripheral blood stem cells. Patients are then again hospitalized during the period of pancytopenia until marrow re-engraftment occurs.

### **Post High-Dose Chemotherapy:**

Post hospital discharge follow-up as dictated by serial blood counts and blood chemistries. Patients are followed up to a minimum of 5 years status post treatment with tracking of response rate, relapse, and over-all survival data.

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## New Developments in Bone Marrow Transplant

### Stem Cell Factor (Stemgen)

Stemgen is the newest growth factor to be developed and was recently given approval for use by the Food and Drug Administration. Stemgen works in combination with other blood cell growth factors to generate mature, functional cells, it is the major regulator of stem cells. It has been demonstrated in clinical trials that if used in combination with G-CSF, Stemgen can reduce the number of collection (or harvest procedures) required to collect the needed amount of stem cells for patients preparing to receive high dose chemotherapy. (6)

### CD34+ "Positive Selection" and Stem Cell Purging

Another fairly new development in bone marrow transplant is selecting only those cells necessary for engraftment, leaving all other cells behind. "Positive selection" using antibody techniques that select for cells that are positive for the CD34 antigen, a protein found to be present in the stem cell population. It is thought that malignant cells are not CD34+.

The process of "positive selection" occurs after the stem cells are harvested. The collected stem cells are then purged for CD34+ cell using a specialized column with antibody beads. The benefit of purged cells is removing any malignant cells that may be present in patients with disease in the bone marrow. It also reduces the amount of DMSO required to preserve the cells, so the patient experiences less or no effect from the DMSO upon reinfusion of the stem cells. Currently Hoag is utilizing CD34+ "positive selection" in selected patients.

The information in this issue is meant to assist you as you undergo a bone marrow transplant. There is a multitude of information, and the process is long and often stressful. Hopefully this information will be helpful in helping you understand the process as you go through it. It is important to remember that not all regimens are alike and that each individual will have their unique tolerances to the treatment.

You are encouraged to ask the doctor or nurse any questions that you may have.

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**Appendix A:**  
**Pathogen-Free Diet**

"Non-Authentic" Pathogen Free Diet

Hoag Hospital does not have the facilities to serve completely Sterile

Or Pathogen Free Diet. The patient will receive a Regular Diet WITH THE FOLLOWING MODIFICATION:

NO FRESH FRUIT AND VEGETABLES ARE ALLOWED.

ALL FRUIT AND VEGETABLE JUICES ARE TO BE SERVED IN CANS.

SPICES, OTHER THAN SALT AND SUGAR, ARE NOT TO BE ADDED TO FOODS AFTER COOKING.

MICROWAVE FOOD WHEN AT ALL POSSIBLE.

This will eliminate some of the pathogens but is not pathogen free.

The dishes, utensils, and tray used in the hospital will not be sterile.

**Appendix B:  
Commonly Used Chemotherapy Drugs in  
High Dose Chemotherapy**

Drug Name	Common Side Effects	Other Less Common Effects
<b>Cytosan (Cyclophosphamide)</b>	Nausea/Vomiting Hair Loss Mouth Sores Infertility Diarrhea Bone Marrow Depression	Allergic Reaction Irregular or fast heart beat Reversible lung disorders Hemorrhagic Cystitis
<b>Taxol (Paclitaxel)</b>	Bone Marrow Depression Hair Loss Mouth Sores Diarrhea Peripheral Neuropathy	Fluid retention Skin rash Allergic Reaction
<b>Carboplatin (Paraplatin)</b>	Nausea/ Vomiting Mouth Sores Bone Marrow Depression	Temporary Liver Disorder Reversible Kidney Disorder Hearing Impairment Rash Peripheral Neuropathy
<b>Etoposide (Vp-16)</b>	Nausea/ Vomiting Diarrhea Mouth Sores Hair Loss Bone Marrow Depression	Low Blood Pressure Reversible Liver Disorder Lung changes Confusion
<b>Ifosfamide (Ifex)</b>	Nausea/Vomiting Hair Loss Mouth Sores Bone Marrow Depression	Bladder Irritation Reversible kidney disorder Confusion Irregular or fast heart beat
<b>Mitoxantrone (Novantrone)</b>	Mouth Sores Irregular Heart Beat Hair Loss Bone Marrow Depression	Nausea/ Vomiting Discoloration of skin, urine, and nail beds Reversible liver disorder
<b>Thiotepa (Thioplex)</b>	Nausea/Vomiting Hair Loss Rash Mouth Sores Bone Marrow Depression	Allergic Reaction Infertility Reversible liver disorder
<b>Melphalan (Alkeran)</b>	Mouth Sores Bone Marrow Depression Nausea/ Vomiting Diarrhea	Allergic Reaction Rash
<b>Bulsufan (Myleran)</b>	Nausea/Vomiting Hair Loss Mouth Sores Bone Marrow Depression Diarrhea Reversible liver disorder Infertility	Skin changes (dark pigmentation) Cataracts Reversible lung disorder Seizures
<b>Mesna (Bladder Protectant)</b>	Bad taste in mouth	Headache Low Blood Pressure Allergic Reaction



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