



*Bone Marrow Transplant
Network NSW*

ALLOGENEIC STEM CELL TRANSPLANT

A PATIENT'S GUIDE

A Collaborative Effort on behalf of the BMT Network NSW

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FOREWORD

This book has been written to provide background information for people who are being assessed for treatment with a transplant from a healthy bone marrow donor.

We recognise that there is a wide range of information needs amongst patients and that some patients want to know more than others. Chapter 1 is written as a stand alone chapter covering the basics of the BMT process. For those who want to know more, more detailed information about the process introduced in chapter 1 is available in the subsequent chapters.

The chapters in this book cover many important aspects of the process of a bone marrow transplant, from identifying a donor, through how a transplant happens and what occurs afterwards, the various complications and side effects, and how a transplant can affect the lives of people long-term. The book has been written in lay language, attempting as much as possible to avoid technical jargon. Nevertheless, it is impossible to completely by-pass the need to introduce a variety of medical and scientific concepts, which have direct relevance to bone marrow transplantation. Some of these inevitably may prove to be distressing or disturbing to some people thinking about having a transplant, and it is suggested that these issues be talked through with the doctors looking after your care.

The material covered in this book is by necessity general in nature, and does not in any way always directly refer to each patient or treatment hospital. The circumstances applying to each person being considered for a transplant naturally vary widely, depending on age, the underlying blood disease being treated, what stage the disease is at, and what treatment has been given previously. All these factors will have an important influence on how the transplant is done, what the risks are, and what the chances of success are likely to be. These issues are not covered in any detail in this book, and each person must go through these possible risks and benefits with the transplant doctor who will be responsible for their care. Each person deciding to have a transplant should be entitled to ask for a copy of the treatment protocol that will be used to guide therapy during the course of their hospital stay and beyond.

CHAPTER 1

The basics of bone marrow transplants

A bone marrow transplant (BMT) is a fairly new treatment for diseases that until recently could not be cured. Since it was first used with good results in 1968, this treatment has been used for patients with immune system diseases and blood diseases such as leukaemia, lymphoma and multiple myeloma.

In Australia each year, around 1,000 children and adults have a BMT. More than 300 people have a BMT each year in New South Wales.

What is bone marrow?

Bone marrow is the soft, spongy part in the centre of your bones where blood cells are produced. The bone marrow makes stem cells, which are early-stage cells that produce other cells. Each tissue in the body contains stem cells that renew and replace that tissue when needed due to damage or wear and tear. Stem cells generate all blood cells in the human body, including red cells, white cells and platelets.

What is a BMT?

A BMT is a treatment option for some people who have life-threatening blood or immune system diseases.

It allows doctors to use high doses of chemotherapy and radiotherapy to increase the chance of a cure. A BMT replaces bone marrow stem cells in people whose bone marrow has been destroyed by large doses of chemotherapy or radiotherapy.

The healthy stem cells are put into your body intravenously, and then find their way into your bones to become healthy marrow. The transplant of healthy stem cells rescues you from your chemotherapy, and/or radiotherapy by enabling your bone marrow to start making new red and white blood cells and platelets.

While BMTs save thousands of lives each year, some people needing a BMT can't have one because the right donor cannot be found. For some of these people, stem cells from umbilical cord blood may be used instead.

Types of BMT

Allogeneic transplant

This type of transplant uses stem cells donated by another person (a donor) and is the focus of this book. It is called a syngeneic transplant if the donor is an identical twin.

The two types of allogeneic transplants are:

- Myeloablative or full allo: the aim is to destroy the patient's marrow and kill the cancer cells.
- Non-myeloablative ("mini" allo): the aim is to suppress the patient's marrow and allow the donor cells to grow and attack the cancer cells. This is the graft-versus-tumour effect.

There are two ways to collect or harvest the donor's stem cells:

- A peripheral blood stem cell harvest: this is used for most adult transplants and collects stem cells from the donor's circulating blood.
- A bone marrow harvest: this collects stem cells from the donor's bone marrow, usually from the hip bones.

The donor's stem cells must match the genetic make-up of your own cells as closely as possible. Blood tests, called tissue typing, are done to work out if the donor's cells match.

The most suitable donor is usually a brother or sister whose bone marrow is a close match. There is a 25-35% chance that a patient will have a family member whose stem cells match. But if no matching relative can be found, an unrelated donor may be found in the Australasian/International Bone Marrow Donor Registry. A mismatched or autologous BMT may also be considered.

Autologous transplant

An autologous transplant uses your own stem cells. This type of transplant can be done if the disease is in remission or if the illness does not involve the bone marrow (eg, Hodgkin's disease, non-Hodgkin's lymphoma).

For an autologous BMT, stem cells are taken from the patient's blood before the transplant, stored and then given back after high-dose chemotherapy or radiotherapy.

This book does not describe autologous BMT in detail. For more information about autologous transplants, see the BMT Network NSW publication, *Autologous Bone Marrow Transplant: A Patient's Guide*.

Preparing for a BMT

The BMT team

An expert team of doctors, nurses and other support staff will care for you. The team can quickly identify and treat any problems or side effects. A good BMT program will also give patients and their families emotional and psychological support before, during and after the transplant.

For a BMT to work well, you must be healthy enough to cope with the procedure. When deciding if you should have a BMT, your doctor will consider your age, general physical condition and the type and stage of your disease.

The work up

Before a BMT, a number of tests are carried out to ensure you are healthy enough for the treatment. You will also have tests of heart, lung and kidney function before and after the BMT so your doctor can check whether these organs are still working as well after the transplant. The pre-BMT tests (also called the work up) are usually done before you are in hospital, but may be done after you are admitted.

You will need to have a dental check-up and all necessary work done before the BMT. If you or your dentist is unsure, please check with your BMT team before any work is started.

Making informed decisions

Long-term implications

It is important to think about some of the possible long-term effects, such as infertility, and discuss them with your transplant doctor before starting a BMT. See page ?? for more information.

Gathering information

When you are considering a BMT, you will be given a lot of information about the process. Some people do in-depth research and think through every detail, while others just want enough information for the next day or stage. Some people only want to know enough to be informed, and choose not to read or listen to anything negative so they can stay motivated and focused.

A BMT is a serious and complicated procedure so it is vital you are informed and that you clearly understand what the BMT means for you. This requires good communication with your BMT doctor and the rest of the team.

At your first visits to the doctor, you will receive a lot of information about the proposed BMT, its side effects and possible complications. To help you absorb this information, it can help to take notes during the consultation or tape-record the discussion. Many people like to have a relative or friend go with them, to take part in the discussion, take notes or just listen.

If you don't understand what you've been told, don't be afraid to ask questions or to ask for the information to be repeated as often as you need. Questions are a good sign that you are working in partnership with your medical team. It is very important to be involved in your care and to express your concerns before, during and after a BMT. Your role is crucial, particularly in telling the team about how you are feeling and any symptoms you are having.

In the days before the BMT, you will need to sign a number of consent forms for the treatment or clinical trial.

Finally, remember that not everyone will want to go ahead with a BMT. After thinking about all the possible risks and benefits, some people decide it is not for them. In this case, you need to tell your doctors, and talk to them about other treatments. Your doctor will still give you the best other treatment options available.

How is a BMT done?

Collecting bone marrow stem cells

The stem cells are collected from the donor's blood or bone marrow. If the donor is related to you, the stem cells will usually be collected from the blood. Cells from unrelated donors are harvested from either the peripheral blood or the bone marrow, under general anaesthetic, depending on what your doctor believes is best for you and/or donor preference.

The central line

If you don't already have one, a central venous catheter will be inserted under the skin of your chest into a vein. It is also called a central line or Hickman catheter depending on the type of line.

A central line is a long, hollow tube that usually has two or three passages (called lumens) to allow for a number of uses. It is made of silicone or hard plastic. Your central line will stay in place during the BMT and may be used to collect blood samples and to give you all the medications and fluids you need.

Your central line will usually be inserted into a large vein that runs beneath your collar bone with the tip sitting near to the entry into your heart. The rest of the central line remains outside your body for easy access. A clamp keeps the tube closed when it is not being used. The central line may be put in when you are in the operating theatre, in the x-ray department or on the ward.

Add diagram showing central line in place

Conditioning treatment

You will have several days of chemotherapy and/or radiotherapy, which destroy bone marrow and cancerous cells and make room for the healthy stem cells. This is called the conditioning or preparative regimen.

You may also hear the phrase 'countdown to transplant', because this treatment is expressed in your medical notes in terms of the number of days until the transplant. For example, day -5 (minus 5) means that you are five days away from the transplant day, which is called day 0. The type and number of days of chemotherapy and/or radiotherapy vary according to the disease being treated and the protocol or preferred treatment plan of the hospital where the BMT is being done.

For a myeloablative BMT, the dose of chemotherapy and/or radiotherapy given to patients during conditioning is much stronger than doses given to patients with the same disease who are not having a BMT. You may become weak, irritable and nauseous. Anti-nausea medications will help during this period. Don't be alarmed if your blood results go down at this time, as this is what the chemotherapy or radiotherapy is supposed to do – that is, empty your bone marrow before your transplant.

The transplant

The transplant will take place a day or two after the chemotherapy and/or radiotherapy. The transplant is not a surgical procedure. It takes place in your hospital room, not an operating room.

You may be given medication before the transplant to prevent a reaction to the transplanted cells. This is more likely to occur when the match between the donor marrow and the patient is not exact or the blood groups are different.

The healthy bone marrow stem cells are infused through your central line, in much the same way that any blood product is given. Many patients describe the actual transplant as an anticlimax, as it all over so quickly – usually between 30 minutes and an hour.

You will be checked frequently for signs of fever, chills, hives and chest pains while the bone marrow is being infused. When the transplant is completed, the days and weeks of waiting begin.

The bone marrow begins to grow (engraftment)

Engraftment means new cell growth. It takes place after your bone marrow transplant when there is a sustained rise in new blood cell production. As a general guide, engraftment is said to have happened once the white blood cell count rises above 0.5×10^9 /L and the platelet count to above 20×10^3 /L without transfusion.

The 2-4 weeks after the transplant are the most critical. The high-dose chemotherapy and/or radiotherapy given to you during conditioning destroyed your bone marrow, crippling your immune or defence system, leaving your body with no natural defences against infection.

As you wait for the transplanted bone marrow to migrate to the cavities of the large bones, engraft and begin producing normal blood cells, you will be very susceptible to infection and excessive bleeding. You will be given multiple antibiotics and blood transfusions to help prevent and fight infection. You will also have transfusions of platelets to prevent bleeding and additional medications to prevent and control graft-versus-host disease (GVHD), which happens when the white blood cells from the donor marrow attack the cells of the patient's body. (For detailed information of GVHD, see page?)

While many infections start from within the body, your BMT team will take a number of precautions to minimise your exposure to viruses and bacteria in your environment. These will vary from centre to centre. Visitors and hospital personnel will wash their hands with antiseptic soap and may wear protective gowns, gloves and/or masks while in your room.

Any visitors or relatives will be asked not to visit if they are unwell eg, if they have a sore throat, runny nose, a cold /flu or upset stomach. Fresh fruits, vegetables, plants and cut flowers, which often carry fungi and bacteria that pose a risk of infection, may not be allowed in your room.

When leaving the room, you may wear a mask, gown and gloves as a barrier against bacteria and virus, and also to remind others that you are susceptible to infection.

Blood samples will be taken daily to monitor engraftment and organ function. When the transplanted bone marrow engrafts and begins producing normal blood cells, you will gradually be taken off the antibiotics, and blood and platelet transfusions will generally no longer be required.

Once the bone marrow is producing a sufficient number of healthy red blood cells, white blood cells and platelets, you will be discharged from the hospital, provided no other complications have developed. BMT patients typically spend 4-8 weeks in hospital.

How you may feel physically during the transplant

A BMT is a physically, emotionally and psychologically taxing procedure for you and your family. Seek as much help as you need to cope – toughing it out on your own is not usually the best way to cope with the transplant experience.

At times, you may feel very sick and weak during the transplant. Walking, sitting up in bed for long periods of time, reading books, talking on the phone, visiting with friends or even watching TV may require more energy than you have.

Complications can develop after a bone marrow transplant such as infection, bleeding, GVHD or liver disease, which can create additional discomfort (see page?). Pain is usually controlled with medication, which may include the use of intravenous morphine or other narcotic drugs. In addition, mouth and throat sores can develop that make eating and swallowing uncomfortable and difficult. Temporary mental confusion sometimes occurs and can be frightening for the patient who may not realise it is only temporary. The medical and nursing staff will help you and your carers deal with these problems.

Dealing with emotional and psychological concerns

Being diagnosed with a life-threatening illness can be a traumatic experience. It is common to feel overwhelmed by the amount of information you receive and the need for urgent treatment. Each person feels differently and responds differently. People will find some aspects of the treatment process more stressful than others.

It is important you know that BMT is a team effort and that you are the central and most important person in this team. Understanding your treatment plan and clear communication are essential elements in maintaining your emotional and psychological well-being. People often say it is the unexpected symptom, complication and treatment that upsets or frightens them the most. A BMT already involves a degree of uncertainty. Poor communication can add unnecessary stress to this situation. **Don't hesitate to clarify any aspect of the process.**

People will vary in the amount of information they want about the transplant. Some will want to speak to others who have been through a bone marrow transplant. Some will want to be well researched on all aspects of the transplant process. Others will only need to have minimal facts about their proposed treatment. Whichever category you fall into, it will be important for you to have all the information **you** need about your treatment before the transplant.

You may find that you feel isolated with little control over your day-to-day activity because of the precautions taken to guard against infection while your immune system is not working properly. You will be in a single room and the number of visitors you can have at one time is restricted.

Make your room your own space with your personal effects. Try to stay as independent as you can and talk to your nurses about how you can participate in your care. Lack of privacy is another common issue for people having a BMT – talk to your nurse about allocating times when you will be as undisturbed as possible.

Waiting for the transplanted stem cells to engraft, for blood counts to return to safe levels or for side effects to disappear can be very frustrating and lead to increased stress. Try to remain positive and be realistic in your goals. BMT is an individual process that cannot be predicted all of the time.

You may find that personal relationships with family and friends come under pressure during BMT. This is not uncommon. Relationships within families will change, and it is important to recognise what these changes will be. Talk to the BMT social worker if you need help.

Each family member or close friend will cope with your BMT in their own way and this may, at times, lead to misunderstandings or conflict. Just because a family member or friend is not visiting does not mean they don't care – they may just be taking some time out as their way of coping.

Psychological discomfort, like physical discomfort, is a normal symptom of the BMT experience. Social workers and psychologists/psychiatrists are also part of your BMT team, so call on them when you need help. There is no right or wrong way to manage all the challenges and stresses that BMT throws at you. There is only the method that works for you.

Going home

Recovering from a BMT continues for some months after you leave hospital. For the first few weeks you may be too weak to do much more than sleep, sit up and walk a bit around the house. You will need to visit the hospital or clinic regularly so your BMT team can monitor your progress and administer any medications and/or blood products needed.

It will take at least six months before you will be ready to return to work or your normal daily activities. You'll need lots of patience and determination to cope during this period. Some people find that reaching their 'new normal' takes longer than others.

Your new marrow is still in its infancy and is not yet able to protect you from some bacteria and viruses encountered in everyday life. The medications you will need to control GVHD only add to this. So it is important to protect yourself from potential sources of infection. Enjoy the outdoors, dine alfresco, keep sick friends and relatives away, see movies and do the shopping at quiet times. You can get back to a normal life; you just have to take a little extra care.

Life after BMT

Life after transplant can be both exhilarating and stressful. On the one hand, it is exciting to be alive after being so close to death, and many people find their quality of life has improved after transplant.

But there is always the worry that a relapse will occur. Also, innocent statements or events can sometimes conjure up unpleasant memories of the transplant experience long after recovery. It can take a long time to come to grips with these difficulties. Tell your BMT team about **any** difficulties you experience.

Shaded box

Frequently asked questions

What is a bone marrow transplant (BMT)?

A BMT is a standard treatment option for some people who have life-threatening blood or immune system diseases. It is the process of replacing unhealthy bone marrow cells (stem cells) with healthy bone marrow cells. The healthy bone marrow cells are re-infused intravenously after very strong chemotherapy and/or radiotherapy, which kills your unhealthy bone marrow cells. The re-infusion of healthy bone marrow cells essentially rescues you from your chemotherapy and/or radiation by enabling your bone marrow to start producing new red and white blood cells and platelets.

What is the difference between a BMT and a peripheral blood stem cell transplant?

Both transplants aim to do the same thing – replace bone marrow stem cells in a person who has had their bone marrow destroyed by large doses of chemotherapy and or radiotherapy.

Bone marrow is the spongy substance found in the hollow of bones of the hips, legs and arms. It contains stem cells (also called CD34s), which produce all circulating blood cells: red blood cells, white blood cells and platelets.

When the stem cells are collected from circulating blood, the transplant is called a peripheral blood stem cell transplant. A transplant with stem cells collected from the marrow, usually from the hip bone area, is called a bone marrow transplant.

Are there different types of BMT?

Yes, there are two different types of BMT. This book focuses on allogeneic bone marrow transplant, which involves finding a donor whose tissue type closely matches yours. The donor can be related or unrelated. Related donors are usually a brother or sister. If no matching relative is found, your transplant doctor will ask the Australian Bone Marrow Donor registry to start a search (see Finding a donor, page ?). An autologous BMT uses your own blood stem cells, but this type of transplant is not discussed in this book.

If I have a common blood group, will I have a common tissue type?

No, not necessarily. There is no link between your blood type and your tissue type. Tissue type is determined by different sets of genetic proteins called human leukocyte-associated antigens (HLA), which are found on the surface of most cells. A person's tissue type is identified by a blood test called tissue typing. Therefore, your donor can still be a bone marrow match for you but have a different blood group.

Will I need an operation to have a BMT?

No, the stem cells will simply be re-infused through your central line in the same way you receive transfusions such as platelets or red blood cells (packed cells).

What is engraftment and when will it happen?

Engraftment means new cell growth, and takes place after your bone marrow transplant when there is a sustained rise in new blood cell production. This generally occurs within 2-4 weeks after your transplant. The first obvious sign may be a rise in your white blood cell count above 0.5. This tells us that your new bone marrow cells are starting to produce new blood cells. Until this time, you are at high risk of infection and need to avoid possible sources of infection.

What are the possible side effects of a BMT?

The two main risks from the transplant process are an increase risk of infection and bleeding due to high doses of chemotherapy and/or radiation. Short-term effects may include nausea, vomiting, fatigue, mouth ulcers, weight loss, hair loss and skin reactions. Long-term effects include infertility, cataracts and possible complications in the liver, kidneys, lungs, joints and/or heart.

Allogeneic transplants carry the risk of GVHD. This occurs when the white blood cells from the donor marrow (the graft) identify the cells of the patient's body (the host) as foreign and attack it. This can be mild in the form of skin rashes on the hands and feet, to very severe affecting liver, gut and/or lung function. (For detailed information about possible BMT complications, see page??)

What are my chances of having a successful BMT?

This is very difficult to answer as so many individual issues come into play. The outcome of your transplant is highly influenced by your original disease, the stage of your disease and your general condition at the time of the transplant. There are many other variables, including how you have responded to treatment and the closeness of the match of your donor. The best person to discuss your possible transplant outcome is your transplant doctor. He/she can discuss your individual factors that may influence your chances of success.

Resources

Leukaemia Foundation

Tel: 9969 1762

Free call: 1800 620 420

Fax: 9969 8542

Website: www.leukaemia.com

The Leukaemia Foundation has a team of trained patient support staff, who are available for patient care, family counselling, friendly advice, practical help or just simply understanding and personal empathy when it's needed most.

Services offered to people living with leukaemia and related disorders, and their carers include: **Information, education and support**

- a telephone service, which includes counselling, information and education about diseases, treatments and their effects
- information booklets, courses and group workshops for people living with these illnesses

- talks to schools, community groups and work places.

Practical and financial support

- accommodation and other housing arrangements close to hospitals; offering a home away from home for you and your family during treatment
- transport services in some areas
- financial support offered in special circumstances, ranging from paying for an airfare for treatment or a utility bill.

CanTeen

NSW 9382 1563

Illawarra 4227 6481

Hunter 4957 6614

Website: www.canteen.com.au

CanTeen provides support for young people aged between 12 and 24 who either have cancer, or are the siblings or children of someone who has cancer.

Cansupport

Tel: 9926 7246

Website: www.nsh.nsw.gov.au/services/cansupport/

Cansupport offers a wide range of support services for people with cancer and their families, including:

- volunteer visitors who have had a range of different cancers and visit people in hospital
- telephone support
- information and support meetings
- relaxation sessions.

The Cancer Council NSW

Tel: 9334 1900

Cancer Helpline 13 11 20

Website: www.cancercouncil.com.au

The Cancer Council NSW is a charity that provides information and support to people with cancer and their carers. It runs a Cancer Helpline, a free and confidential telephone information and support service. The Helpline, which is staffed by oncology nurses:

- can answer questions on how to cope with treatment and side effects
- send you written information
- put you in touch with services in your own area
- offers emotional support.

The Helpline is staffed during business hours, or leave a message after hours and the nurses will return your call. Only local call costs from anywhere in NSW.

As well as English, the Helpline offers cancer information and advice in:

Cantonese 1300 300 935

Mandarin 1300 300 935

Arabic 1300 301 625

Greek 1300 301 449

Italian 1300 301 431

Centrelink

Appointments: 13 1021

Centrelink multilingual tel: 13 1202

TTY toll free 1800 810 586

Disability, sickness and carers: 13 2717

Family Assistance Office: 13 6150

Youth and student services: 13 2490

NSW Department of Housing

Tel: 131571

Website: www.housing.nsw.gov.au

- mortgage assistance scheme
- rent assistance

Look Good Feel Better

Tel: 1800 650 960

Web site: www.lgfb.org.au

Free workshops for women having chemotherapy or radiotherapy for cancer, which teach beauty techniques to maintain self-image during cancer treatment.

Web resources

Australia

BMT Network NSW

www.nswbmt.com.au

Arrow Foundation

www.arrow.org.au

Cancer Council NSW

www.cancercouncil.com.au

Leukaemia Foundation

www.leukaemia.com

Look Good Feel Better

www.lgfb.org.au

Cancer Council Australia

www.cancer.org.au

Australian Bone Marrow Registry

www.abmdr.org.au

International

Association of Cancer Online Resources

www.acor.org

American Cancer Society

www.cancer.org

BMT resources/self help websites

www.bmtinfonet.org

www.marrow.org

www.nbmtlink.org

www.bmtnews.org

www.leukaemia-research.org.uk/

www.leukaemia.com/

www.cancerbacup.org.uk

www.leukemia-lymphoma.org

CHAPTER 2

All about blood cells

Blood is made up of many different kinds of cells, each with a specific function. Most blood cells are formed in the bone marrow and are released into the bloodstream at various stages of maturity. The function of each of the blood cells and their normal ranges are shown in Table 1.

Table 1. Blood cell functions and blood tests

Cell type	Function	Blood tests	Normal range
Red blood cells, also called RBCs or erythrocytes	Contain a protein called haemoglobin, which carries oxygen from the lungs to all parts of the body and gives blood its red colour. Also pick up carbon dioxide, and take it to the lungs to be breathed out.	Red blood cell count or RBC Haemoglobin or Hb: oxygen-carrying capacity	Males 4.5-6.0 Females 3.8-5.4 Males 131-180 Females 115-160
Platelets	Initiate blood clotting to stop bleeding	Platelet count	150-400
White blood cells, also called WBCs or leukocytes	Fight infection and protect the body against foreign organisms, including bacteria, viruses, parasites and fungi	White blood cell count or WBC Leukocyte differential count: proportions of the five main types of white blood cell	4.0-11.0 Neutrophils 60-70% Monocytes 3-8% Eosinophils 2-4% Basophils 0.5-1% Lymphocytes 20-25%
Types of white blood cells Neutrophils, also called neut or N	Ingest and destroy bacteria – first line of defence against infection	Absolute neutrophil count or ANC	2.0-8.0
Monocytes, also called mono	Ingest and destroy bacteria and fungi, and clean up cellular debris left behind after infection	Monocytes	0.1-0.8
Lymphocytes	Fight viral infections and help destroy other parasites, bacteria and fungi	Lymphocytes	1.0-4.0

Blood cell production

The body constantly makes new blood cells. In healthy adults, about 100 billion red cells and 400 million white cells are made each hour. The life span of mature blood cells is only a few days or months.

Almost all (95%) of the body's blood cells are made in the bone marrow; the rest are made in the spleen. While most blood cells made in the bone marrow are discharged directly into the bloodstream, one type of lymphocyte, T cells, first travel to the thymus gland (thus, the name T cells) where they develop further before being released into the bloodstream.

Stages of maturity

All mature blood cells come from very early stage cells in the bone marrow called pluripotent stem cells. This type of cell is able to make copies of itself. Pluripotent stem cells also make lymphoid and myeloid stem cells, which evolve into the different types of blood cells.

Illustration NOTE

(Diagram showing sequence of cell maturation – see <http://press2.nci.nih.gov/sciencebehind/immune/immune08.htm> for an example of style, although it doesn't include red cells because it is only describing the immune system)

Like pluripotent stem cells, the myeloid and lymphoid stem cells can make copies of themselves as well as make early-stage blood cells. However, they are not able to make as many copies of themselves as pluripotent stem cells do, and they make fewer different types of offspring. The offspring of lymphoid stem cells can only turn into lymphocytes (T cells or B cells). The offspring of myeloid stem cells can only turn into red blood cells, platelets, or white blood cells other than lymphocytes.

The offspring of myeloid and lymphoid stem cells that can only turn into one type of mature cell are called committed progenitor cells. Cells that are almost mature are called precursor cells.

Regulating stem cells

In healthy people, the number of each type of stem cell and their offspring stays within very narrow limits. Certain proteins in the body, such as interleukins and colony-stimulating factors, play a key role in determining the amount of stem cells in the body and how active they are at any time. These factors also control the maturation of precursor cells.

If this control system breaks down, too many or too few stem cells will be present in the bone marrow and/or certain precursor cells will proliferate and fail to properly mature. In patients with leukaemia, for example, one or more types of blood cells (usually white blood cells) fail to mature properly. They stall at one stage of development and self-replicate uncontrollably. Because they are immature, they are unable to function normally.

CHAPTER 3

Searching for a donor

The most suitable donor for a stem cell transplant is a fully matched (tissue typed) family member, but only about one person in three has such a donor. If a suitable donor is not found in the immediate family, a wider family search and/or unrelated donor search may be needed.

Tissue or HLA typing

Tissue typing or HLA typing is done to check how closely your cells match the potential donor's cells. HLA (human leukocyte antigen) markers are found on almost all the cells in your body. They are one of the main ways your immune system can tell the difference between your own cells and foreign cells, such as bacteria, which should be attacked. The closer the match in HLA types, the better the chance of a successful transplant.

If the HLA markers on the donor's cells are too different from yours, your immune system will see them as foreign and attack them. This is called rejection. Likewise, the donor's immune cells (the graft), which are put into your body along with the stem cells, can also attack vital organs of your body (the host) if the HLA markers are too different. This is called graft-versus-host disease (GVHD).

The closer the donor and recipient match, the less likely it is that rejection or severe GVHD will occur.

Understanding HLA types

Everybody has two sets of HLA markers (or haplotypes). We inherit one set from each parent. Because your parents each have two sets, there are four possible combinations of their HLA markers in their children. This means you have a one in four chance of having the same HLA markers as your brother or sister. HLA matching is not related to similar appearance or personality between family members, or their blood group or sex.

Your donor can still be a bone marrow match for you but have a different blood group.

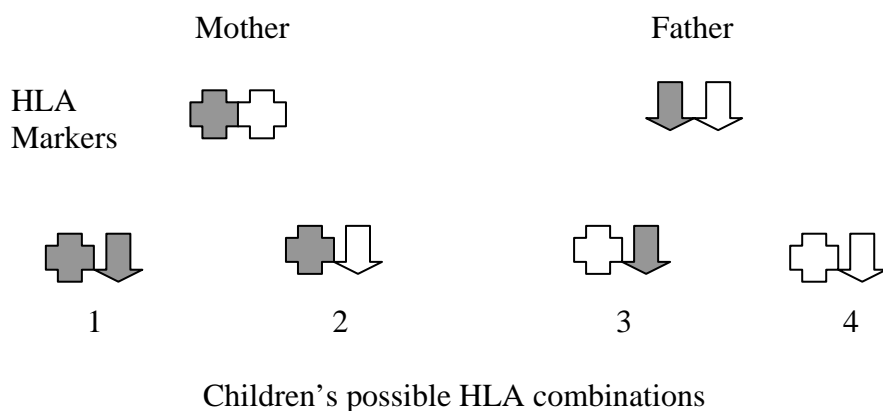


Figure 1. How we get our HLA type. There are four possible combinations of the parents' HLA marker sets, so siblings have a one in four chance of being an HLA match.

An HLA type consists of two main groups:

- class I antigens (HLA A, B, C)
- class II antigens (HLA DR, DQ, DP).

The most important HLA antigens for matching you and your donor are: two A antigens, two B antigens and two DR antigens. These are reported as a series of numbers, as shown below.

Patient A3, 32; B7, 37; DRB1*0101, 1501

Donor A3, 32; B7, 37; DRB1*0101, 1501

Figure 2. Example of fully matched patient and donor HLA typing results.

How is HLA typing done?

A 40-60mL sample of blood is needed for HLA typing. The white cells are taken from the blood and typing is done two ways:

- serological testing: where the white cells are used
- DNA testing: where DNA from the white cells is used.

When DNA testing is done, confidentiality is maintained. The DNA is only used for tissue typing and ethically approved research purposes, and remains the property of the tissue-typing laboratory.

Basic tissue typing takes about two weeks. Further high-resolution (more detailed) tissue typing of the patient and any potential matched donor samples may take another 2-4 weeks.

The laboratory will send your HLA typing results and those of possible donors to your doctor. The hospital's BMT co-ordinator or your doctor will tell you and your family the results. Your doctor will be available to discuss the results.

Searching for a related donor

Your doctor will ask the hospital's BMT co-ordinator to start a family search. The co-ordinator will arrange for HLA typing of family members, starting with the people who are the most likely match, usually siblings. Typing of family members needs to be done systematically. Family members who want to be tested should contact your BMT co-ordinator.

Immediate family

Any member of your family who would like more information about being a donor should contact either your doctor or your BMT co-ordinator **before** they have the initial blood test.

To help with the search, the co-ordinator needs:

- you or your representative to ask immediate family members if they are willing to be tested
- contact details for all members of your immediate family only – that is, parents, siblings and children.

Extended family

An extended family search may be considered if a match is not found in your immediate family and you have at least one haplotype that is commonly found in the general population.

An extended family search is done systematically, testing the side of the family from which you inherited the least common HLA set. The aim is to look for a person who has inherited the less common HLA set from one of your ancestors and who has inherited the more common set from the parent who is not your blood relative. The Australian Bone Marrow Registry (ABDMR) will conduct the extended family search.

If an extended family search is to be done, you will need to talk to your family and provide your BMT co-ordinator with the following:

- a family tree showing each person's relationship to you, sex, age and number of children of family members willing and available for tissue typing
- a designated contact person in the family to liaise with the ABDMR search co-ordinator
- contact details for all family members who are willing and available for tissue typing.

Typing friends

The best chance of finding a matched donor is in the immediate family (siblings), with a lower chance in the extended family. The chance of an unrelated person (friend) having the same tissue type as you is remote.

Friends who wish to be tissue typed as potential donors must be willing to donate blood and must also be willing to join the bone marrow registry and donate stem cells for any person if required.

Searching for an unrelated donor

Unrelated bone marrow donor registries and cord blood registries have been developed to help the 60-70% of patients who are unable to find a suitably matched related donor.

More than 8 million donors from around 35 countries are listed on Bone Marrow Donors Worldwide, an international database managed by The Netherlands. Of these, more than 155,000 are cord blood units.

Bone marrow donor registries

Bone marrow donor registries list volunteers willing to anonymously donate stem cells for anyone worldwide who needs a stem cell transplant. Donors have had preliminary tissue typing and the results are recorded on a database.

Cord blood registries

Blood from newborn babies' umbilical cord and placenta is a rich source of stem cells suitable for transplantation in some patients, especially young children. Registries record details of stored cord blood units donated by mothers on the birth of their babies.

Mismatched donors

Sometimes it is not possible to find a completely matched donor so a mismatched donor will be used. Your doctor will discuss this with you. Terms you may hear include 5/6 match (ie, five out of six HLA antigens are the same) or one-antigen mismatch. The example below shows a 5/6 match between a patient and donor HLA types. The second A marker is not the same, so five out of the six HLA markers match.

Patient A 3, 32; B 7, 37; DR 1, 15
Donor A 3, 17; B 7, 37; DR 1, 15

How are registries searched?

If your doctor thinks you would benefit from a transplant using an unrelated donor, a registry search is started. This is done by a team, which includes the transplant unit staff, tissue-typing laboratory staff and ABMDR co-ordinators. Patients do not have direct access to the registries.

The steps for a search are:

- ABMDR search request forms are completed with the details of the patient's tissue type, age, sex, ethnicity and disease. These are forwarded to the ABMDR national office.
- The ABMDR national office enters the patient's tissue type into the database and a computer program compares the patient's tissue type with those of all donors on the Australian registry every day. A list of potentially matched donors is usually available the next day.
- If a potential donor is not found on the ABMDR, an international search of bone marrow donor or cord blood registries may be started after discussion with your doctor.
- The Bone Marrow Donors Worldwide website is searched, to provide a list of potential donors worldwide.
- Any potential donors will be identified, and their tissue type confirmed. High-resolution DNA sub-typing will also be done if not already known. Samples are sent to the ABMDR tissue-typing laboratories for testing.
- The patient's tissue type is also confirmed and high-resolution DNA sub-typing begins.
- Donors are volunteers and may change their minds about donating at any time until the patient is admitted for the transplant.

How long does it take to identify a donor?

The time it takes to find a well-matched donor or cord blood unit varies greatly, and it is important you understand the process:

- If your donor is a direct family member, you will usually know whether you have a suitable match within 2-3 weeks of testing.
- The identification of an extended family donor may also be known quite quickly, but it will take longer if your family is widespread or international.
- The initial identification of a potential donor from a registry may be quick if the donor has previously had high-resolution DNA typing. (These tests take up to four weeks.)

- All results must be confirmed with repeat testing, whether the donor is a family member or not. This is known as confirmatory testing.
- Confirmation of an appropriate donor can take several months if the donor is from an international registry. If the donor is from the ABMDR or a family member, the process usually takes 2-3 weeks.
- Blood samples are also tested for infectious diseases.
- Sometimes more than one donor is identified.

If a suitable donor is found, what happens next?

Once a suitable donor is found, the transplant team will determine the urgency of the transplant depending on your disease and how well you are. If the transplant is urgent, the search co-ordinator will ask for a work up of the compatible donor. This is a series of medical tests to check whether the donor is healthy enough.

If an unrelated donor is identified, but a transplant is not needed straight away, the donor can be reserved for the matched patient for up to nine months. After that time, the donor is released, but their ID, registry and tissue type are recorded in the patient's file for easy recall when a transplant is needed.

The ABMDR does not encourage contact between donors and patients, but it is acceptable for a letter to be given to your BMT co-ordinator to be sent to the donor. No personal details (name, date of birth or address) may be disclosed.

After 12 months, you can decide to ask the ABMDR to release your personal details to the donor, by signing a consent form. It is then up to the donor to initiate contact. This is a personal decision, which can carry both positives and negatives.

Key points

- About one in three people have a fully matched (tissue typed) donor in their immediate family, which is the preferred source of donor stem cells.
- Tissue typing or HLA typing is done to check how closely the potential donor's cells match your own.
- The closer the match in HLA types between you and your donor, the better the chance of a successful transplant.
- HLA matching is not related to similar appearance or personality between family members, or their blood group or sex.
- If any member of your family is considering being a bone marrow donor, they should contact your doctor or your BMT co-ordinator **before** they have the initial blood test.
- An extended family search may be considered if a match is not found in your immediate family and you have at least one haplotype that is common in the general population.
- If no match is found in your immediate or extended family, international bone marrow and cord blood donor registries may be searched for an unrelated donor.
- It can take weeks or months to find a well-matched donor.
- Once a donor is found, the transplant team will determine the urgency for the transplant depending on your disease and how well you are.

CHAPTER 4

Donating bone marrow stem cells

There are two ways of collecting stem cells from donors for a transplant:

- **peripheral blood stem cell (PBSC) harvest:** where donor stem cells are collected from the circulating blood using a process called leukapheresis (see below)
- **bone marrow harvest:** where bone marrow is collected from bone while the donor is under general anaesthetic.

Most transplants from related donors use PBSC, while transplants from unrelated donors use either PBSC or bone marrow harvest depending on a number of factors, including the patient's disease and donor preference.

Collecting peripheral blood stem cells

Many donors prefer this method because they don't need an anaesthetic and won't have pain after it is done. They need to be injected with a drug called granulocyte colony stimulating factor (G-CSF) for a few days before the procedure, which may have some temporary side effects.

Pre-treatment with G-CSF

The transplant team will prescribe G-CSF. The donor takes it home, and has it injected under the skin once or twice a day for about four days before stem cells are collected on the fifth, and occasionally the sixth day. Some donors choose to inject themselves, but others have someone else – a relative, a nurse or their local doctor – inject the drug.

G-CSF is a synthetic copy of a naturally occurring bone marrow hormone. The hormone is not usually detectable in the body, but the immune system makes it in response to infection. Its natural action is to stimulate the growth of bone marrow stem cells, which can become white cells to fight infection. It also causes the release of stem cells from the marrow into the blood. When enough G-CSF is given, large numbers of stem cells are released into the blood, which can be collected for the transplant.

Side effects

Most donors experience some side effects from G-CSF. These are mostly flu-like symptoms, such as aches and pains, fatigue and generally feeling a "bit off." The symptoms usually are mild and controlled by paracetamol, but occasionally donors can feel more unwell and need stronger painkillers.

Severe side effects are rare but there have been rare reports of a ruptured spleen in donors, as G-CSF enlarges the spleen (a large organ under the left side of the rib cage). However, many thousands of normal donors have been treated with G-CSF without any serious short- or long-term side effects.

Harvesting the cells – leukapheresis

On the day of collection, the donor is attached to a machine that collects or ‘harvests’ stem cells from the blood. The collection process, which is called leukapheresis, is usually done at the transplant centre if the donor is related, but always at another collection centre if the donor is unrelated, on an outpatient basis over 3-6 hours.

The donor is awake throughout the procedure. At the beginning, a needle is put into a large vein in the crook of each elbow, and connected by tubes to the apheresis machine. This is basically a big centrifuge, which spins the blood and separates it into white blood cells, red cells and plasma.

The blood is withdrawn from one arm of the donor, passed through the machine, and the portion of the white blood cells that includes the stem cells are collected – a bit like skimming cream off milk. The rest of the blood is then returned to the donor through the other arm. About 12L of blood is processed through the machine.

The donor usually notices no side effects, but occasionally changes in the calcium level in the blood, caused by the anticoagulant solution (citrate) used to stop the blood clotting in the machine, may cause a tingling feeling. Calcium treatment will reverse this. More rarely, donors can feel faint during the procedure because of low blood pressure. The collection will be stopped if this happens.

Some donors don’t have accessible veins in their arms and may need to have the needle put into a large vein in the groin. The insertion of this needle is less pleasant and has a greater risk of bruising, so is only used if there is no alternative.

Most donors can go home within a few hours of the collection. The side effects of G-CSF usually go away within a few days of the drug being stopped.

Most donor leukapheresis procedures collect enough stem cells for a successful transplant. The cells are collected in a bag, usually in a volume of 150-200mL, and the stem cells are counted in the laboratory. About one in three donors will need to have a second collection the next day, after another dose or two of G-CSF.

Bone marrow harvest

A bone marrow harvest is done in a hospital operating room, usually under general anaesthesia. It is a low-risk procedure, but the donor will feel sore afterwards. While the donor is under anaesthesia, a needle is put inside the rear hipbone (the iliac crest), which contains a lot of bone marrow.

The bone marrow is a thick, red liquid and is extracted with needles and syringes. Several skin punctures on each hip and multiple bone punctures are usually needed to extract the required amount of bone marrow. No surgical cuts or stitches are involved – only skin punctures where the needle was inserted.

The amount of bone marrow harvested depends on the size of the patient. Usually 1L of marrow and blood is harvested. Although this may sound like a lot, it is only about 2% of a person’s bone marrow and the body replaces it in four weeks.

When the anaesthesia wears off, the donor will feel some discomfort at the harvest site, as if they have had a hard fall. It can usually be relieved with paracetamol. There may be some colourful bruising at the back of the hips in the week after the harvest.

Donors can usually go home after an overnight stay in hospital and can resume their normal activities in a few days. Regular blood donors will probably need to wait a while before giving blood, at least until they have their haemoglobin level checked after the harvest.

Sometimes the bone marrow may be treated to remove T cells (T cell depletion) to reduce the risk of graft-versus-host disease.

Key points

- Most transplants from related donors use stem cells collected from the circulating blood using a process called leukapheresis.
- Most transplants from unrelated donors use bone marrow cells, which are collected from bone while the donor is under general anaesthetic.
- Before the harvest donors will be injected with a drug called G-CSF, which stimulates bone marrow stem cells to grow and multiply.
- G-CSF often causes mild side effects, such as flu-like symptoms. The side effects of G-CSF usually go away within a few days of the drug being stopped. Severe side effects are rare.
- Leukapheresis is a relatively painless procedure. Almost all donors can go home within a few hours of it being done.
- Bone marrow harvest is done in a hospital operating room, usually under general anaesthesia. It is a low-risk procedure, but the donor will feel sore afterwards.

CHAPTER 5

Preparing for the BMT

The work up

Some routine medical tests will be done before you have the BMT, usually before you are admitted to hospital. These tests determine whether your body is fit enough to endure the physical stresses of a BMT. You may have some or all of the tests, depending on your disease type.

Your BMT doctor or transplant co-ordinator will give you more information about the tests, which are called the 'work up' and are summarised below.

Gated heart pool scan (GHPS or 'gate')

This is a test of your heart function, which is done in the hospital's nuclear medicine department. It is needed because some chemotherapy drugs can damage your heart. The scan will determine if this has happened to you. Also, during the BMT you may be given large volumes of fluid and it is important that your heart is working well enough to cope with these extra fluids.

Glomerular filtration rate (GFR)

This kidney function test measures how fast your kidneys filter and remove waste products. It is done in the hospital's nuclear medicine department or by using calculations based on a 24-hour urine collection. It checks whether your kidney function is good enough to cope with the large number of drugs and the volume of fluids needed for your BMT. If you have kidney damage, the dose of some drugs may need to be reduced. Generally, it needs to be done on a different day from the GHPS.

Lumbar puncture (LP)

Depending on your type of disease, you may have had lumbar punctures as part of your diagnosis and/or treatment. You will be informed if you need to have one as part of your workup. If you haven't had one previously, your doctor will discuss the procedure with you.

If you require a lumbar puncture, a needle is carefully inserted between the bones in your spine into the fluid that circulates around the spinal cord and your brain (cerebrospinal fluid or CSF). A small amount of CSF is taken out and tested for the blood disease you are being treated for. Some people need a dose of chemotherapy to be injected into the CSF at the same time as the sample is taken.

Chest X-ray

If you have not recently had a chest X-ray, you will have one to check for abnormalities in your lungs before the BMT.

Sinus X-ray

If there is any suspicion that you have had a sinus infection, you will need an X-ray of this area. It is important to tell your doctor if you think or know you have a chronic sinus problem, as it will need to be fixed before the BMT.

Computerised Tomography (CT or CAT) or Positron Emission Tomography (PET) scan

Depending on your type of disease and when you had your last scan, you may need another one to ensure you have no active disease. If you haven't needed scans as part of your treatment plan, you probably won't need one before the BMT.

Blood tests and bone marrow biopsy

You will also have a number of blood tests, many of which you have had before, to establish a baseline before the BMT. You may also need to have a bone marrow biopsy, depending on when you had your last one, to ensure you are in remission.

Dental care

The mouth, or oral cavity, is one of the major sources of bacteria that can cause infections during BMT, so it is important to have a dental checkup and have any problems fixed before the BMT. If your dentist is unsure about the treatment, please ask him or her to contact your doctor.

If you can't afford the dental treatment, talk to your doctor, BMT co-ordinator or social worker, as they may be able to organise alternatives to a private dentist.

Eating well

If you are having trouble eating or are losing weight before your transplant, you should ask to see the haematology dietitian in your area.

Good nutrition before a BMT is important for:

- maintaining a healthy weight and improving protein and muscle stores
- providing essential nutrients for fighting infections and promoting wound healing and recovery
- boosting your energy levels and ability to cope with the treatment.

Fertility

The high doses of chemotherapy and/or the total body irradiation treatment (see Chapter 7) you have before your BMT will damage the cells needed for reproduction – the eggs or sperm.

In some people this damage is permanent, causing infertility, and in others only temporary, but unfortunately there is no way to predict this. A number of factors affect the likelihood of infertility, including age, gender, sexual maturity, the type of conditioning therapy used and your previous treatment.

This can be devastating news for people who have not had children or haven't completed their family. Fortunately, there are ways to store eggs, ovarian tissue or sperm for later use. If you want to store tissue, you will be referred to the fertility centre your BMT hospital uses.

It's important to think about these issues before deciding to go ahead with the BMT because reproductive tissue MUST be stored before the conditioning therapy.

Key points

- Some routine medical tests, called the 'work up', will be done before the BMT to determine whether your body is fit enough to cope with the physical stresses of the transplant.
- The mouth is one of the major sources of bacteria that can cause infections during BMT, so it is important to have a dental checkup and have any problems fixed before the transplant.
- Good nutrition is important. If you are having trouble eating or are losing weight before your BMT, talk to the haematology dietitian.
- If there is a chance you want to have children in the future, talk to your BMT specialist about options for storing eggs, ovarian tissue or sperm well before your admission to hospital for your BMT. Reproductive tissue **MUST** be stored before the conditioning treatment.

CHAPTER 6

Taking care of yourself before and during a BMT

Much of the information covered in this chapter may be relevant during and after the BMT. It is important to consider these issues before the transplant so you and your family can plan for the challenges you may face during transplant.

Being diagnosed with a life-threatening illness can be a traumatic experience. It is common to feel overwhelmed by the amount of information you receive and the need for urgent treatment or hospitalisation. Each person feels and responds differently. People will find some aspects of the treatment process more stressful than others.

Dealing with stress

Everyone has their own way of coping with emotional stress and physical discomfort. Psychological discomfort, like physical discomfort, is a normal 'symptom' of the BMT experience.

You don't have to cope alone. Social workers and psychologists/psychiatrists are part of your BMT team. It can help to establish a relationship with your social worker or psychologist/psychiatrist early in the process of diagnosis and treatment. You don't need to wait until things are really stressful before you ask to talk to someone.

For some people, just talking honestly with a social worker can be very helpful. Some people worry they may be judged as 'not coping' if they ask for help. There is no right or wrong way of managing all the challenges and stresses that BMT throws at you. There is only the method that works for you.

Communicating with your team

BMT is a team effort and you are the central and most important person in this team. Understanding your treatment plan and clear communication are essential elements in maintaining your emotional and psychological wellbeing. People often say it is the unexpected symptom, complication and treatment that upsets or frightens them the most. A BMT already involves a degree of uncertainty. Poor communication can add unnecessary stress to this situation.

Don't hesitate to clarify any aspect of the process. If something is not clear, no matter how insignificant it may seem, don't be afraid to ask about it. Ask for information to be repeated as often as you need. If you still have a niggling doubt, ask. Recognising and addressing any doubts can ease your anxiety and help you to understand the treatment plan.

People vary in how much information they need about the transplant. Some will want to speak to others who have had a BMT. Some will want to research every aspect of the transplant process. Others will only want minimal facts about the treatment.

Whichever category applies to you, it's important you have all the information **you** need before your transplant. There is no right or wrong amount of information. There is only the amount you need to meet your needs.

Focus on your goals

Some people feel as though they have no choice but to have a BMT – that the transplant is their best chance to enjoy as normal a life as possible.

But it's important to be clear about your reasons for having the transplant. What are the things in your life that make it worth fighting for? For many people this may be partners, children and other family. For others, it may be friends, work, travel, adventure and much more.

During the BMT, when you are having a hard day, it will be important to remember why you decided to have the transplant. It can help you see past the setbacks to what the future promises.

Impact on relationships

Role changes

Not surprisingly, BMT has a big impact on family relationships. Some people find that their main role changes. They may take time out from being the primary income earner or main carer of children. There can be other changes to the position and the roles that people have in a family.

The hospital stays and recovery can mean that your partner and others in your family take on some of your day-to-day roles. Similarly, the experience of being seriously ill and being away from home can change the relationships you have with your loved ones.

It is important that you and your family discuss the changes, and recognise that they are essential, even if they are difficult for some members of the family. It can help to talk to the social worker on your team about these issues.

Different ways of coping

The time before and during the transplant can be stressful, and can cause tension in relationships with loved ones, such as partners. People have different ways of coping when someone close to them is going through a transplant. Some people need to talk openly about feelings while others prefer to keep things to themselves, or to use stress management and problem-solving techniques. It is important to respect different ways of coping and communicating.

Try to keep the lines of communication open with family and friends throughout the transplant. Don't assume that friends or family don't care because they are not there – they may just need time out.

Sexuality

Previous treatment and the emotional stress that occurs in the lead up to BMT can have an undesired effect on body image and sexuality.

Some people may have had difficulties in sexual relationships before the BMT. Body changes from initial treatment can leave people feeling less confident about the way they look and can impair sexual functioning and libido.

Sex during the BMT process is not recommended because of the risk of infection and the potential to expose the partner to toxic drugs.

But sexuality means more than physical appearance or having sex – it is about you and your partner as individuals, who you are and what you feel. It is about your touch, your warmth – how you laugh and smile, how you care and your personality. These will not change before or during BMT.

If you are having problems, it can help to talk to a counsellor or sex therapist. Ask your social worker for more information.

Talking to children

It is difficult to know how to talk with your child about your transplant and about being in hospital for long periods. As a parent, you have the best understanding of your child and their strengths and needs. If you need help, the social worker or psychologist in your team can give you information about how to talk to your children and what to say.

Protecting children by not telling them about your disease or transplant can sometimes make things worse as children often imagine things that are worse than reality.

Try to explain your diagnosis and the transplant to your children in language they will understand. It is good to have honest communication with your child so that they can ask questions. Sometimes they will be worried about certain aspects of the transplant and may need reassurance.

Give them regular updates about your progress, and stay in touch with your children as best you can during the transplant process. This may be difficult at times, due to the nature of the transplant and concerns about infections. Relationships with children can be maintained by talking on the phone, making videos, letters or drawings etc.

Children vary in their responses to the transplant and its effects on you and the family. Here are some general examples of responses of children at different ages:

- **Babies and toddlers:** will feel some sense of loss and will often pick up on the concern of a parent or caregiver. They are likely to notice changes to routines, and may change their eating, sleeping or toileting habits.
- **Children under five:** may respond to the extended hospitalisation of a parent with periods of sadness, questioning or withdrawn behaviour.
- **Young children:** are often puzzled and confused by the experience of a parent going through transplant. The family is the centre of their world and they are likely to be very aware of the absence of a parent. They have little understanding of time. They generally do not have logical thinking and tend to connect things that are not related. For example, they may think that something they have done has made their dad sick.
- **Adolescents:** their ways of thinking are adult, but they are likely to be unsure of how to handle their emotions and may need adult help with coping. Some have to take on some of the roles of the parent and may resent this at times.

If you have children at school, it can be useful to tell the school and your child's main teacher about your situation so they can be supportive and be more understanding if your child's mood and ability to concentrate are affected. Talk to the school counsellor for more help.

For more information about talking to children, talk to your social worker. CanTeen has programs for teenagers dealing with their own cancers as well as those with parents or siblings with cancer – ask your social worker or nurse how to contact CanTeen. Other options include calling the NSW Cancer Council's Helpline, 13 11 20.

Family and friends

It can be hard for family and friends to know how to support you during a transplant. People want to help you through the transplant process but may be unsure of your needs. They will want to be useful and to visit and talk to you. They won't want to waste your energy, cause distress or be a nuisance.

Your family and friends are your support base and, just like your BMT team, you need to let them know what you need. Communicate clearly with them and get the help that you need. It can be useful to suggest practical ways to help and allocate these jobs to each family member or friend. You might find it useful to get one friend or family member to be the main contact and to organise people to do various jobs. There is no right or wrong way of enlisting their support – only the method that works best for you.

Tips for carers

It can be stressful and tiring to be the main carer and to see your loved one in discomfort. You may feel frustrated at not being able to ease their discomfort all the time. Sometimes they will seem dependent on you for their care and at other times they will feel quite unwell and may not want any visitors. It is a fine balance.

Offer your support and encouragement. Just be there with them – even if they don't feel like talking, they'll know that you care. Try to understand the feelings that they are expressing – both positive and negative. Allow them to talk about negative thoughts as the transplant process is difficult and such thoughts reflect the reality of their situation. If you are asked to leave, don't take it personally. They probably just want some rest and space.

If you find it emotionally or practically difficult to keep visiting, it can help to talk about your feelings with the team social worker.

It is vital to look after yourself if you want to properly care for your loved one throughout a BMT. Ensure you get regular breaks, and have your own support in place, including close family and friends. Support services for carers, such as the social worker or psychologist at the hospital, can help maintain your health and wellbeing. For more information on caring for someone through a BMT, see www.marlow.org.

Dealing with your emotions

Side quote:

“I used to be in control of my life. I used to be the captain of the ship, steering the boat down the river through life. I would decide how fast to move, which turn to make, where to stop, who would share my life. When I was diagnosed with cancer, it was as if someone reached down, picked me up off the ship and placed me on the riverbank. Now I watch from the riverbank as my life goes on. I do not feel in control of the ship. Someone else is directing my life.”

(A patient describing their perception of being diagnosed with cancer and then facing a BMT.)

Putting your life on hold

When diagnosed with a serious illness, all normal life experiences are put on hold. Arrangements have to be made for caring for family members, education, employment and social activities. Health care issues now dominate a life where previously they were scarcely considered. Any family who experiences this trauma will feel confused, disoriented and, at times, overwhelmed.

This change in normality can be very difficult. There is no easy way to accept the changes. You will work out your own way of managing. Support and reassurance from family, carers, close friends and the BMT team is vital. It can help to have a tour of the unit before admission, so you feel familiar with the surroundings and staff. Your social worker can recommend support services that may be able to help you during this time.

‘No one understands’

People who have not had a BMT usually find it hard to understand what you’re going through. You will experience strong emotions and psychological challenges, at times in isolation, and even those closest to you will be unaware of your turmoil. Always keep in mind that you can talk to your social worker about these issues.

It is important that you and your family have realistic expectations of each other, and respect and recognise each other’s experience and limitations. Family and friends will support you but can’t possibly understand every experience you will have. Nevertheless, they can still respect and recognise your experience even though they may not fully understand the complexity of the moment.

Be positive

A positive outlook and encouraging support from others will help you deal with the demands of treatment. But you and your carers may feel that others expect you to be strong and positive even when you don’t feel like it. This pressure to be positive can mask your true emotions and make it harder to understand each other’s reality.

Lighten your load. If this feels comfortable for you, take the opportunity to share your feelings and concerns with people you trust, whoever they may be. It helps many people to do this.

Make the most of the positive news, big or small. From a simple improvement in mouth ulcers to engraftment day, feeling good about it can help you get through the day and feel better about your overall progress.

Uncertainty – living in limbo

Living with uncertainty is a constant stress during BMT. Somehow people work out how to cope with such stress. Some people choose to tackle their worst fears immediately and look for honest rather than reassuring opinions from their team. Others prefer uncertainty than to face the fear of bad news.

It is not possible to know for sure how you will respond to your treatment, the symptoms you will experience, or how long it will take your body to recover.

You are doing well to manage at all. People are often surprised by their determination and their ability to tough it out. Your BMT team and community providers are able to support you in living with the daily uncertainty.

Spiritual beliefs

If you are a spiritual person, your beliefs may be more important than ever and provide you with comfort and inspiration during the BMT. Pastoral staff in the hospital can come and talk to you and your carers at any time – just ask your nurse or social worker to arrange it.

If you have other ways of expressing your spiritual beliefs and need privacy in hospital to do this, talk to your social worker about setting aside time for this important part of your day.

Changes in your body

A BMT often means changes to your body and appearance, such as temporary hair loss, having a Hickman catheter or nasogastric tube, or changes in weight. These changes may be upsetting but are related to your treatment drugs and are temporary.

Long-term changes to your body may also occur. These can be very individual and are best discussed with your BMT team.

Changes in your level of independence

One of the frustrating aspects of having a transplant is the lack of control –you no longer have control over your own body, and you have no control over the treatment you receive or the side effects that occur.

During a long hospital stay, you may have little control over your environment. For people who are used to being independent, it can be hard to adjust to needing help to do basic things such as showering, walking or going to the toilet.

During your transplant you may find yourself in a contradictory situation. You may have trouble walking without help, feel exhausted after your morning shower or even struggle to get out of bed, yet your BMT team assures you are right on track.

How can I be on track when I feel this bad? This is a common question among transplant patients. Talk to your BMT team if something seems inconsistent or unclear. You need to remain as independent as possible but be open to assistance when it is required. This can be important in helping to maintain your own sense of independence.

Creating privacy

Your concept of privacy may change after you spend time in hospital. Some people describe the hospital stay as like living in a fish bowl.

The need for privacy is unique to the individual and can vary day to day. Privacy can be very important on some days, particularly if you're feeling vulnerable. Nurses, specialists and cleaners can constantly interrupt you when you're trying to have a private phone conversation, having some personal time with people close to you, or even having a shower.

There are ways to create privacy, even in hospital. Discuss this issue with the nurse looking after you and set aside some time each day when you will not be disturbed. You can put a sign on your door during that time.

If you need time alone, with no visitors or phone calls, you can ask for your phone to be diverted to the front desk where the ward clerk can take messages, and let family and friends know that you want time alone.

Managing your 'space' in hospital

You will probably spend many long and perhaps trying days in your hospital room. Familiar surroundings can be reassuring, so personalise your room to make it feel more like 'your place' and help you feel connected to your life outside hospital. Personal possessions can help provide comfort and reassurance, particularly at night when sleep may be difficult and you're alone.

Ask the ward's Nursing Unit Manager if you can use a laptop computer to get Internet access. E-mails are a good way to keep in touch with family and friends from your hospital bed at a time that suits you.

Twenty-four hours in a hospital bed can seem like an eternity. The sameness of the routine can make the hours pass very slowly. Sometimes it seems as though nothing is happening. Night-time and being on your own can also make your thoughts seem more exaggerated.

Try these tips for breaking up the endless hours:

- Plan a schedule for your day and night so you have regular activities to keep you occupied, but be prepared to be flexible as the hospital routine may interfere at times.
- Roster your visitors to arrive at different times.
- Make an effort to consider ideas about how to make the time pass. Get some ideas from others. Explore these ideas with friends, family and staff, if necessary.

Tiredness and fatigue

Most people experience fatigue during the transplant and for a significant time after it. This is normal. The amount of fatigue and how long it lasts varies from person to person. It may last for months or several years after your transplant. For most people, it will ease gradually but slowly, which can be frustrating. Various factors affect this process, including whether or not you get GVHD.

Maintaining your physical condition throughout the treatment process can help you cope with fatigue and help your progress. Try to stay active in hospital. Simple activities can help to keep your body in good condition throughout all stages of transplant. Ask the hospital physiotherapist for more information.

Practical issues

Finances

For many people, treatment for their initial illness already has made it hard to work full time. The transplant process and long recovery period often makes this situation even more difficult, which may lead to financial problems.

For those moving to Sydney for treatment, the costs of living in the city and maintaining a second home can also be considerable.

It is important to explore your options to ease any financial burden, such as:

- **Work:** ask your employer what types of leave are available.
- **Superannuation:** if you are in a superannuation scheme, check if you can get access to some of your funds.
- **Government assistance:** you may be eligible to receive payments from Centrelink or from the NSW Government's Mortgage Assistance Scheme.
- **Banking:** if you have a mortgage, talk to your lender about restructuring the payments for a period.

The social workers at your home hospital or on the BMT team are experienced in these matters and can help you.

Accommodation

BMT is a specialised procedure, so many people have transplants far from their local hospital and may have to move to Sydney for long periods.

You will need accommodation close to the treatment hospital for yourself and your family. There may be accommodation available at the hospital.

Patients who are required to travel more than 200km from home for treatment may be eligible for assistance with travel and accommodation expenses through the Isolated Patients Travel Accommodation and Assistance Scheme (IPTAAS).

Talk to the hospital or BMT team social workers for more information about accommodation and IPTAAS.

Transport

Your family will visit you many times in hospital so it is a good idea to ask about the availability of parking and public transport at the hospital.

Also, after the transplant you will need close follow-up, and will visit hospital regularly. When you leave hospital, your immune system will be compromised for some time, so it's best not to travel by public transport initially, to avoid contact with large numbers of people. You will therefore need someone to bring you to your follow-up appointments. If this is not possible, see your social worker about community transport options.

Legal and financial advice

Think about seeing a solicitor and financial adviser before the transplant. It is important to consider your current situation and think about what relevant measures may need to be put in place, such as:

- making or updating your will
- drawing up an enduring Power of Attorney/enduring guardian
- bank account arrangements
- financial plans
- sickness benefits
- carer's pension.

If necessary, your social worker may be able to arrange appointments with a solicitor or centre link.

Key points

Ask for help

Some people think they'll be judged as 'not coping' if they ask for help. There is no right or wrong way of managing all the challenges and stresses that BMT throws at you. There is only the method that works for you.

Ask questions

If something is not clear, no matter how insignificant it seems, don't be afraid to ask about it. Ask for information to be repeated as often as you need. If you still have a nagging doubt, ask again.

Focus on your goals

During the BMT, when you are having hard days, it will be important to remember why you decided to have the transplant. It can help you see past the setbacks to what the future promises.

Be open about role changes

It is important that you and your family discuss changes in roles during a BMT, and recognise that they are essential and may be difficult.

Be honest with your kids

Protecting children by not telling them about your disease or transplant can make things worse as children often imagine things that are worse than reality. Try to explain your diagnosis and the transplant to your children in language they will understand.

Call in the cavalry

Your family and friends are your support base and, just like your BMT team, you need to let them know what you need. Communicate clearly with them and get the help that you need.

Caring for the carer

It is vital to look after yourself if you want to properly care for your loved one throughout a BMT. Ensure you get regular breaks, and have your own support in place, including close family and friends. Support services for carers, such as the social worker or psychologist at the hospital, can help maintain your health and wellbeing. For more information on caring for someone through a BMT, see www.marrow.org.

Celebrate good news

Make the most of the positive news, big or small. From a simple improvement in mouth ulcers to engraftment day, feeling good about it can help you get through the day and feel better about your overall progress.

Have time for yourself

There are ways to create privacy, even in hospital. Discuss this issue with the nurse looking after you and set aside some time each day when you will not be disturbed. If you want, put a sign on your door during that time.

Try to stay active

Maintaining your physical condition can help you cope with fatigue and help your progress. Try to stay active in hospital. Simple activities can help keep your body in good condition throughout all stages of transplant.

Get organised

Explore options to ease any financial burden, such as restructuring loan payments or applying for financial assistance. Get legal and financial advice before you go into hospital, so you can make sure the necessary paperwork has been done, such as Power of Attorney and updating your will.

CHAPTER 7

Conditioning therapy

As discussed in Chapter 1, conditioning or preparative therapy is a crucial part of the transplant process, which is done in the few days before the stem cell infusion. It usually involves giving very high doses of chemotherapy drugs, sometimes with whole body irradiation therapy.

The conditioning therapy usually has two important aims:

- **To kill cancer cells:** if you're having a BMT for cancer, these higher doses of chemotherapy may kill more cancer cells than the chemotherapy you have had before, and are likely to help cure you.
- **Suppress the immune system:** without conditioning therapy, the donor's transplanted stem cells would usually be rejected and the BMT would fail.

When your immune system is suppressed, both the donor's blood-forming stem cells and their critically important immune cells can become established in your body. The transplanted stem cells start producing red and white blood cells and platelets, and the immune cells (lymphocytes) rapidly take over the functions of your immune system. This process is called engraftment.

As will be explained in later chapters, the donor's immune cells can cause one of the major complications of allogeneic BMT, GVHD. But they also help cure the cancer through a graft-versus-tumour effect, where the donor's immune cells attack the cancer.

In certain types of cancer, particularly leukaemia and lymphoma, the graft-versus-tumour effect can kill more cancer cells than the high doses of drugs and radiation given during conditioning therapy.

Different types of cancer respond differently to the graft-versus-tumour effect and also to the variety of combinations of chemotherapy drugs and radiation used in conditioning therapy. So the choice of conditioning therapy can be complex, and may be tailored to the individual patient.

Types of conditioning therapy

There are two types of conditioning therapy: myeloablative and non-myeloablative.

Myeloablative therapy

Myeloablative means to destroy the marrow. It comes from the Greek words myelo (marrow) and ablate (destroy). Myeloablative therapy is the oldest form of conditioning therapy for BMT, and involves the use of extremely high doses of chemotherapy drugs and radiation to kill cancer cells.

Originally myeloablative treatment was developed to treat patients with leukaemia when all other forms of treatment had failed. It also destroys all the patient's normal bone marrow stem cells, which would be fatal without the transplant of normal stem cells.

Non-myeloablative therapy

Non-myeloablative conditioning protocols suppress your immune system and allow the donor's immune cells to engraft and attack your cancer cells (the graft-versus-tumour effect). The conditioning therapy itself does not kill all your cancer cells.

It is also sometimes called reduced intensity conditioning, or a “mini” transplant.

This treatment relies on the graft-versus-tumour effect to cure the cancer – that is, the donor's immune cells kill the cancer cells. Non-myeloablative conditioning therapy allows the donor's immune cells to engraft. This, in turn, results in the donor stem cells taking over bone marrow function. (In this respect, non-myeloablative transplants are ultimately myeloablative because the donor cells end up destroying the patient's bone marrow stem cells.)

Common conditioning protocols

While many drugs have been trialled for conditioning therapy over the past 30 years, most allogeneic BMTs done in Australia use a few, well-established treatment protocols. The details of the specific drugs and their side effects are covered later in this chapter.

Most myeloablative transplants use either cyclophosphamide with total body irradiation (CY/TBI) or busulphan and cyclophosphamide (Bu/CY).

Cyclophosphamide with total body irradiation (CY/TBI)

CY/TBI is the oldest type of conditioning therapy, dating back to the 1960s, when it was used to treat patients with late-stage leukaemia. It usually involves six days of treatment leading up to the transplant.

- Cyclophosphamide is usually given first, by a short intravenous infusion on two consecutive days. Lots of IV fluids are given at the same time to wash out the toxic breakdown products of the drug in the urine.
- Total body irradiation is given next. This means radiotherapy to all of the body so no cancer cells are missed. It is usually given in six treatment sessions over three days, most often early in the morning and then late in the afternoon. The radiotherapy is given in specialised radiation oncology departments using machines called linear accelerators, which produce X-rays for treating cancer.

Busulphan and cyclophosphamide (Bu/CY)

The Bu/CY protocol was developed about 10 years later and is now widely used. Unlike the CY/TBI protocol, Bu/CY does not use radiotherapy, but relies on the effects of two strong chemotherapy drugs: cyclophosphamide and busulphan, another strong drug.

- Busulphan is given by mouth, usually in the form of a suspension four times daily, for four successive days.
- After the busulphan treatment is finished, cyclophosphamide is given in two doses, just as in the Cy/TBI protocol.

Fludarabine-based protocols

Two non-myeloablative protocols are mainly used in Australia. Both rely on the powerful immunosuppressive action of a drug called fludarabine, which doesn't damage bone marrow stem cells as much as the drugs used in myeloablative

conditioning. Fludarabine is now often used with cyclophosphamide (Flu/CY protocol) or with melphalan (Flu/Mel protocol).

In both protocols, fludarabine is given by daily IV infusion for five successive days. The other drug is then given towards the end of the fludarabine course, or the day after in the case of melphalan (which is also given IV).

Compared with the traditional myeloablative forms of conditioning therapy described above, fludarabine-based protocols cause less nausea when given, and later produce fewer side effects, in particular less damage to the lining of the mouth and bowel.

Conditioning therapies in detail

Cyclophosphamide

This is a chemotherapy drug widely used in conditioning therapy for BMT. Cyclophosphamide is given as an intravenous infusion, usually over one or two hours. It is one of a class of anti-cancer drugs called alkylating agents, which act by damaging the DNA in cancer cells, making them unable to grow. Cyclophosphamide also has a strong suppressive effect on the immune system.

Common side effects

- nausea and vomiting
- metallic taste in the mouth during the infusion
- drop in the blood count, especially the white blood cells
- hair loss
- infertility.

Less common side effects

- bladder irritation. This is called haemorrhagic cystitis, and is caused by the breakdown products of cyclophosphamide in the urine irritating the lining of the bladder. This condition can start days to weeks after the drug is given. Symptoms include painful urination, the urge to urinate frequently, and blood and clots in the urine. To reduce the risk of this complication, large quantities of IV fluids are given after cyclophosphamide. Sometimes another drug called mesna is given as well.
- second cancers.

Busulphan

Like cyclophosphamide, busulphan is an alkylating agent. It is a strong stem cell poison and has strong anti-leukaemia activity. Busulphan is given as a suspension of crushed tablets, usually four times daily for four days (a total of 16 doses).

Common side effects

- nausea and vomiting
- damage to the lining of the mouth and intestines
- hair loss
- seizures during the days when the drug is being given. An anticonvulsant drug, such as clonazepam, is given during this time to prevent this complication.
- drop in the blood count.

Less common side effects

- lung damage, leading to a condition causing stiff lungs (pulmonary fibrosis)
- increased skin pigmentation
- second cancers.

Melphalan

Melphalan is also an alkylating agent, which is used in intravenous form for BMT, usually as a single dose.

Common side effects

- nausea and vomiting
- damage to the lining of the mouth and intestines
- hair loss
- drop in the blood count.

Less common side effects

- second cancers.

Fludarabine

Fludarabine belongs to a different class of drugs called nucleoside analogues, which resemble the building blocks of DNA. Fludarabine acts on only a few cancer cell types – mostly lymphatic cancer cells – but it is used in conditioning therapy because of its strong immune-suppressant properties. It is the most commonly used drug for non-myeloablative transplants.

Common side effects

- mild nausea
- mild drop in the blood count
- increased risk of infection due to impairment of the body's immune system, irrespective of whether the white blood cell count is normal or low.

Less common side effects

- nerve damage, resulting in confusion and coma
- second cancers.

Anti-thymocyte globulin (ATG)

ATG is an immunosuppressive drug sometimes used in conditioning therapy to boost the effects on the patient's immune system. ATG is prepared from the serum of animals, usually horses or rabbits, and immunised with human thymocytes, the precursors of T lymphocytes.

The serum contains antibodies against human T cells, which have a potent effect in killing remaining patient lymphocytes that might reject the bone marrow stem cell graft. ATG also can kill donor T cells that cause graft-versus-host disease. ATG is usually given over 3-5 days during conditioning therapy as an intravenous infusion over 4-6 hours.

Common side effects

- fever, chills, hives, and low blood pressure during the infusion. Sometimes the infusion may need to be slowed or stopped temporarily if the symptoms are severe. Drugs such as hydrocortisone (a steroid), paracetamol and antihistamines are usually given before the infusion to minimise the symptoms.
- increased risk of infection due to suppression of the immune system.

Less common side effects

- serum sickness, due to an allergic reaction to the foreign material in the animal serum. This can cause a fever, skin rash and loss of protein in the urine.

Total body irradiation (TBI)

TBI is a form of radiotherapy that is used along with chemotherapy for some people having a BMT. TBI has two actions: it kills the cancer cells and suppresses your immune system to allow the transplanted cells to engraft.

A machine called a linear accelerator gives the treatment. It allows radiation oncologists to give treatments tailored to each person. Certain radiation sensitive organs of your body, such as your lungs, may be shielded for part of the TBI.

During TBI you may be asked to sit, stand or lie, but in each position you will be kept still within a brace. You'll be alone in the room, but can talk to the radiation therapist who will watch you at all times.

Usually TBI is given twice daily for three days, but this may vary depending on your individual protocol. Each treatment will involve you being off the ward for about 30 minutes to one hour. In most cases you will be given lorazepam, a drug that both relaxes you and decreases nausea.

- Possible side effects nausea and vomiting
- hiccoughs
- skin redness
- mouth dryness due to decreased saliva production
- mouth ulcers
- swelling of saliva glands and thickened saliva
- dry eyes due to decreased tear formation
- diarrhoea
- bone marrow suppression
- lung damage.

Key points

- Conditioning therapy is given in the days leading up to the BMT and is an important part of the process.
- Myeloablative conditioning protocols use high doses of chemotherapy, and sometimes radiotherapy, to help cure you by killing your cancer cells and bone marrow cells. The treatment also suppresses your immune system so the donor's blood-forming stem cells and immune cells can become established or engrafted and start working in your body.
- Non-myeloablative conditioning protocols suppress your immune system and allow the donor's immune cells to engraft and attack your cancer cells (the graft-versus-tumour effect). The conditioning therapy itself does not kill your cancer cells.

CHAPTER 8

Dealing with side effects

Unfortunately the BMT process often has a number of unpleasant side effects. The most common side effects, and some ways to control or reduce them, are described in this chapter.

Nausea and vomiting

Many of the drug treatments given as part of your BMT can cause nausea and vomiting. Nausea is most commonly experienced during conditioning therapy, when strong anti-cancer drugs and radiation therapy are given. However, nausea and vomiting may result from other drugs, especially some antibiotics, or from damage to the lining of the intestines from drugs and radiation, or graft-versus host disease.

There are many drugs that control nausea and vomiting. Sometimes it takes a while to find the combination that works for you. The major anti-nausea drugs are ondansetron and tropisetron, which only help to control nausea caused by chemotherapy.

Other drugs used to prevent or control nausea include Maxolon, Stemetil, cyclizine and haloperidol. Your team will work out which ones are best for you to use.

If you feel squeamish or nauseated, tell the nurses immediately, because it's harder to get the nausea under control once you've started vomiting.

Diarrhoea

Just as for nausea and vomiting, many of the treatments used for the BMT can cause diarrhoea. GVHD of the gut can also cause severe diarrhoea.

You can lose a lot of fluid very rapidly from diarrhoea so it's important to tell the nurses about the severity of the diarrhoea, such as the number of times you have to go each day. Severe diarrhoea can cause dehydration and can severely affect kidney functioning. It may be accompanied by cramps and pain, particularly if it's due to GVHD.

A number of drugs control diarrhoea and, again, it may take some time to find the one that works for you. These drugs include loperamide and narcotic drugs such as codeine phosphate. Once the best medication is found, tell your team when your diarrhoea is easing up, so they can reduce the amount of medication or you might become constipated.

Mouth and throat problems

People having a BMT often experience a condition called mucositis, which leads to mouth and throat discomfort. It is caused by a number of factors, including chemotherapy, TBI, low white cell count and infections. You may have pain and discomfort from mouth and throat ulcers, dryness and changes in taste.

For many people, mucositis is the most distressing aspect of their BMT, so it is important that you keep your team accurately informed of how well your pain is

controlled. It is often accompanied by large quantities of thick saliva that is difficult to swallow due to pain and swelling in the mouth and throat.

Mucositis pain can be difficult to completely control, but these tips might help:

- Increasing the number of times you perform your mouthwashes may soothe your mouth pain.
- Suck on hard lollies to help remove the saliva.
- Use gentle suction to remove your saliva so that you don't have to worry about swallowing.

Pain

Most people who have a BMT have pain and in varying degrees. Common causes of pain include:

- Mucositis
- Severe GVHD

A number of methods of pain control are available and may be tried, but in most cases morphine or another narcotic medication is required. This can be given in tablet or liquid form, by injection under the skin or intravenously.

Initially, the analgesic drug may be given on request. Eventually, depending on your pain and preference, it will be given either intermittently on a regular basis (eg, every four hours) or by continuous IV infusion. Another option is for you to control the dose of pain control by pressing a button on a remote control device, which injects a preset dose intravenously. This is called patient controlled analgesia or PCA.

In most cases, the hospital's acute pain team will assess you for pain relief and make a recommendation. The team will review your requirements regularly until your pain resolves. The amount of morphine needed will vary. Some patients fear they will become addicted to morphine or another narcotic. This is unusual, as the pain team will monitor you closely and assess your analgesic requirements against your pain, as rated by you.

Pain associated with GVHD of the gut may often need to be controlled by morphine or another narcotic as well as an anti-spasmodic drug to control cramps.

Key points

- Nausea is a common side effect of medications used during a BMT. If you feel nauseated, tell the nurses immediately, because it's harder to get the nausea under control once you've started vomiting.
- There are many drugs that control nausea and vomiting, and sometimes it takes a while to find the combination that works for you.
- Many of BMT treatments – and GVHD of the gut – can cause diarrhoea. You can lose a lot of fluid very rapidly from diarrhoea so tell the nurses about the severity of the diarrhoea. Once the best medication is found, tell your team when your diarrhoea is easing up, so they can reduce the amount of medication or you might become constipated.
- People having a BMT often experience a condition called mucositis, which leads to mouth and throat pain and can be distressing. It can be difficult to completely control but there are ways to relieve the discomfort.

- Most BMT patients have pain. There are a number of ways to ease your pain. In most cases, the hospital's acute pain team will assess you for pain relief and make a recommendation.
- In most cases morphine or another narcotic medication is required for pain relief. Some patients worry they will become addicted to morphine or another narcotic. This is unusual.

CHAPTER 9

Nutrition and BMT

Eating well is important for good health. Food provides the fuel our body needs to grow and function. We need protein-rich foods to build and repair muscle and body tissues, and vitamins and minerals to keep our body systems functioning properly. Good nutrition is also important to help fight illness, infection and to cope with treatment side effects.

Nutrition assessment, education and support are vital parts of your medical care before and after the BMT. You will need extra energy and protein to cope with the physical demands of the transplant.

Also, your eating patterns will be affected because of the side effects of conditioning therapy and other treatment. These side effects, including lack of appetite, taste changes, nausea, vomiting, diarrhoea and mucositis, affect your ability to eat sufficient food for weeks or months after the transplant, increasing the risk of malnutrition. It is expected that you will not necessarily have the best nutrition during your transplant, but the BMT team will work with you to help maximise it.

Food can be a source of micro-organisms such as bacteria or fungi, especially if it is not handled correctly or hygienically prepared, so it is important to follow good food hygiene practices before and after the transplant, until your immune system has returned to normal.

Nutrition assessment

Wherever possible, the BMT dietitian should assess all patients in the week before the transplant or on admission to hospital. The dietitian will assess your:

- height and weight
- recent weight changes
- gastrointestinal symptoms, such as nausea and diarrhoea, which may affect how much food you can eat and absorb
- energy and protein requirements
- usual diet habits, which may be affected by other factors such as illness and medications, religion and alternative therapies.

The dietitian will arrange an individual nutrition care plan for you. The type and amount of food you eat in hospital will be monitored, and you may be asked to fill out daily food charts.

Nutrition support

All conditioning treatments significantly affect the lining of the gastrointestinal tract, from the mouth to the bowel. This is one of the main reasons people need nutrition support during a BMT.

Most people develop oral and oesophageal mucositis and gastrointestinal disturbances and discomfort 3-10 days after chemotherapy. The severity and the duration of these side effects can vary greatly between patients.

Your appetite and food intake may change from day to day. At times, you may find it difficult to eat enough food because of mouth problems or stomach upset. The dietitian can help you find ways to change your diet, such as eating soft or liquid food, or specialised nutritional high-energy/high-protein supplements.

Some people will need more intensive support for short periods, such as nasogastric tube feeding or intravenous feeding, which is called total parenteral nutrition or TPN. The medical team will discuss this with you if required.

GVHD, especially in the gastrointestinal tract, increases the threat of malnutrition and the need for nutrition support.

You may experience one or more of these side effects of treatment listed in this chapter. These suggestions may help you cope.

Appetite and weight loss

Treatment side effects – as well as anxiety, depression and fatigue – can contribute to decreased appetite and weight loss.

Tips

- Have small frequent meals and nourishing snacks.
- Eat foods you enjoy, even if higher in fat and sugar.
- Limit low-calorie foods and fluids.
- Try nutritional supplements as recommended by the dietitian.

Nausea and vomiting

These are common problems especially during the conditioning period. Mild symptoms may persist for several weeks.

Tips

- Try six small meals and snacks a day, rather than three main meals.
- Include high carbohydrate foods and fluids.
- Have cold foods and clear fluids.
- Limit high-fat foods.
- Avoid strong odours and cooking smells.
- Take anti-nausea medication as prescribed.

Diarrhoea

Chemotherapy, total body irradiation, GVHD, infections and some antibiotics can increase bowel activity and lead to diarrhoea.

Tips

- Drink plenty of fluids.
- Limit caffeine and spicy foods.
- Try a low-lactose diet as you may be temporarily lactose intolerant.
- Limit high-fibre foods such as legumes, whole grains and seeds.
- Take anti-diarrhoea medication as prescribed.

Sore mouth and swallowing difficulties

Depending on the type of treatment you have, you may develop mouth or throat pain around 7-10 days after conditioning therapy. Infection, GVHD and certain medications can also cause mouth discomfort and mucositis. This usually improves once the white blood cell count returns to normal.

Tips

- Avoid foods that sting your mouth such as spicy or salty foods, fruit juices and very hot or cold foods.
- Try soft, moist or pureed foods.
- Choose nourishing fluids, such as soups, milk drinks and commercial supplements.
- Keep your mouth fresh and clean and use mouthwashes as recommended.

Taste changes

Total parenteral nutrition and some medications, such as antibiotics and pain relief, may change the taste of food. This can last for several months after the transplant, and longer for those who have had total body irradiation.

Tips

- Increase the flavour of food by adding salt, garlic, cooked herbs and spices.
- Marinate meat, fish, poultry or tofu to add flavour.
- Add sugar or honey if food tastes metallic or salty.
- Add salt, lemon juice or vinegar if food tastes too sweet.

Other side effects

Heartburn, constipation, abdominal discomfort and fatigue are common side effects. The dietitian can advise you how to reduce these symptoms.

Food hygiene

You will be at increased risk of infections from food, so it is essential to maintain good personal and food hygiene practices.

You and your family can reduce the risk of food-borne infections at home and in hospital by following these simple guidelines.

1. **Clean** – wash hands and kitchen surfaces often
2. **Separate** – prevent cross-contamination of foods by separating raw and cooked foods
3. **Cook** – ensure food is cooked thoroughly and reheated properly
4. **Chill** – refrigerate all food promptly
5. **Avoid** – high-risk foods, such as:
 - foods close to or past their use-by date
 - foods from salad bars, smorgasbords and self-serve restaurants
 - takeaway foods
 - soft uncooked cheeses such as brie, ricotta, camembert and fetta
 - soft serve ice-cream, yoghurt and milkshakes
 - raw or undercooked meats, chicken, fish, seafood, eggs, tofu and sausages
 - deli meats, pates and dips
 - sprouted seeds, fresh herbs and raw mushrooms
 - unwashed raw vegetables and fruit.

You should follow these safe food hygiene practices for 3-12 months after discharge as recommended by your transplant doctor.

To minimise the risk of infection, some hospitals provide low-microbial/low-bacterial diets. The benefits of these restricted diets have not been scientifically proven but they may reduce the risk of harmful organisms from food and food handlers.

For more information on food hygiene, talk to the dietitian at your hospital.

Alternative dietary therapies

Some BMT patients, while following prescribed medical treatments, also like to explore alternative therapies. If you're considering an alternative dietary therapy, talk to your transplant doctor or dietitian first, because some alternative diets are nutritionally incomplete and unbalanced.

Despite research over many years, there is no evidence that special foods or diets can cure cancer. Diets that restrict food groups, such as meat and dairy, make it difficult to achieve adequate protein and energy intake and may lead to weight loss and increased tiredness.

Before changing your usual meal plan, consider if the new diet:

- provides adequate energy to maintain body weight
- is well balanced in vitamins, minerals and fibre
- is difficult to buy, expensive or takes a lot of time to prepare
- has any proven health benefits.

If you are in any doubt, talk to your dietitian or your doctor.

It's also important to talk to your doctor or dietitian before taking alternative products, such as herbs, high-dose vitamins, antioxidants and other 'health food' preparations.

These products may contain contaminants such as bacteria and fungi, which may interfere with your treatment or be toxic to organs such as the kidney and liver.

However, other alternative therapies such as meditation and relaxation may complement your treatment and help you feel better. Talk to your BMT team for more information.

Key points

- Eating well is vital for BMT patients because it helps:
 - you to cope better with treatment and side effects
 - damaged tissue to heal
 - your body to fight off infection.
- Nutrition support is a key part of your medical care before and after the BMT. It helps to ensure you eat enough of the right sort of food to cope with the physical demands of the transplant and the side effects.
- Treatment side effects can affect your eating patterns and can cause problems such as nausea, diarrhoea and mucositis. These side effects can make it difficult to eat enough food for weeks or months after the transplant, increasing the risk of malnutrition.
- Food hygiene is very important after a BMT to reduce the risk of infections from food. When preparing food, follow these guidelines:
 - Clean** – wash hands and kitchen surfaces often
 - Separate** – prevent cross-contamination of foods by separating raw and cooked foods
 - Cook** – ensure food is cooked thoroughly and reheated properly
 - Chill** – refrigerate all food promptly
 - Avoid** – high-risk foods.
- There is no evidence that special food or diets can cure cancer or stop it recurring. But if you're considering an alternative dietary therapy, talk to your transplant doctor or dietitian first.

CHAPTER 10

Complications

This chapter covers the most common complications that may occur after BMT. Everyone who has a BMT is an individual with their own medical history and, therefore, their own risk factors. You may get none of the following complications, or you may get one or more – there is no way of predicting your particular case.

After reading this chapter you may feel frightened and overwhelmed by the possible complications. You may want to ask more questions about these important issues, or ask to talk to someone who has experienced complications. It is important to keep in mind that their experience is unique to them and will not necessarily apply to you. Talk to your BMT team about your concerns.

How to read this chapter

This chapter is very long and detailed, and contains important information about complications.

Reading this chapter may be very confronting or scary, but it is important to remember that it is very unusual for one person to get all of the complications discussed.

Each person is different. Some people have one complication; others have none or some of the complications listed here. Unfortunately, there is no way to accurately predict what will happen to you.

You may decide to skim through this chapter initially and only read it in depth if and when you need to.

Whatever you decide, remember, it is unlikely that all the complications will happen to you, but the information is here if you need it.

Infection and living with a compromised immune system

Everything we do in our daily activities, from eating, breathing and contact with people and animals, is a potential source of infection. For people with a normal immune system, these everyday encounters are not a major problem. The body and its immune system work to prevent infections by recognising and destroying harmful organisms if they enter the body.

But for people who have had or are about to have a BMT, the normal function of the immune system is disrupted. Conditioning therapy before the BMT affects all cells in the body – both cancerous and normal cells. The rapidly dividing cells found in the mouth, gut, bone marrow and hair are affected the most. Conditioning therapy decreases the number of circulating blood cells, including the white cells and particularly the neutrophils, which are responsible for fighting infection.

The skin and mucous membranes lining the mouth and nose provide the body's first line of defence against infection and repel millions of potentially harmful organisms and foreign substances each day. Normally, if you cut yourself, white blood cells or leukocytes spring into action to fight the infectious organisms that enter the body. This process is disrupted during your BMT and in the months after it.

Proteins called antibodies – which all humans make in response to contact or infection with a variety of bacteria or viruses such as measles, cytomegalovirus (CMV) or chicken pox – are also depleted or destroyed. This means you may get these infections again. (For more detail on the function of white blood cells and the immune system, see Chapter 2)

Until your immune system returns to normal, you are extremely vulnerable to infections and in some cases these may be life threatening.

The first 2-4 weeks after the transplant is a critical time as the new bone marrow finds its way via the blood stream into the cavities of the large bones and begins producing new blood cells. This is also the time when you will be at most risk of infection.

Although the risk of infection steadily decreases once the transplanted marrow successfully engrafts, your immune system remains compromised (not at full strength) for 6-12 months after the transplant and longer for those with GVHD. This is due to the process of GVHD and the medication given to treat it, which prolongs the period of immune suppression.

Your role in preventing infection

Good hygiene is extremely important.

- Ensure **all** visitors, including staff, carefully wash their hands with antiseptic soap before touching you (hands are a primary carrier of infectious agents). If you are not sure if they have washed, **ask**.
- Shower or wash every day (including hair or scalp) using the antibacterial skin wash or liquid soap you have been given. Don't use cake soap.
- Use disposable wash cloths or change your washer daily.
- Examine your body daily and report anything you feel is not normal for you.
- If you need to shave, use only an electric razor. The razor should be cleaned thoroughly after each use, or if using a ward razor, the disposable blade should be discarded.
- Try to avoid constipation – tell your BMT team if you're having problems.
- Report any abnormalities when passing urine, such as burning, stinging or blood in the urine.
- Use a mouthwash at least four times a day. Good mouth care may not prevent ulcers, but it will reduce the risk of infection. It generally doesn't matter which mouthwash you use, as long as you have a regular routine.
- Use a soft toothbrush and avoid any extra trauma to the gums by only brushing your teeth.
- Limit the number of family and friends who visit you in hospital and keep visits to two people at a time. Apart from the risk of infection, visits can be very tiring. Tell family and friends not to come if they have any symptoms of cold, flu, diarrhoea or any other potentially infectious disease, or if they have had any recent vaccination. If they're not sure, they should check with staff before visiting you.
- Ask visitors not to bring flowers and plants (both live and dried) to you in hospital. They can harbour harmful bacteria or fungi, are generally not encouraged in the room while you are neutropenic.
- Eat sensibly and avoid foods that may be a potential source of infection. The dietitian will discuss the sorts of food you should eat and also those that you

should avoid until your immune system has returned to normal. (See Chapter 9 for more information about diet).

Bacterial infections

Bacteria are microscopic organisms that can cause infection anywhere in the body. They secrete toxins that can interfere with normal organ functions or cause problems when they multiply rapidly. Some pneumonias, for example, are caused by bacteria that fill up the spaces in the lungs where air is normally absorbed into the body.

Bacterial infections are most common in the 2-4 weeks after a BMT and affect more than half of BMT patients. These infections occur most often in the gastrointestinal tract (gut), on the skin (especially around a Hickman catheter or central line) and in the mouth. They also occasionally occur in the bladder and can cause pneumonia in the lungs.

Bacterial infections anywhere in the body can suddenly become extremely serious and can be fatal.

If you have an infection you may have some or all of the following symptoms:

- high fever
- high pulse rate
- low blood pressure
- fast breathing rate
- discoloured sputum
- pale appearance and clammy (sweaty) skin.

If you have an infection or sepsis (bacteria or their toxins in your bloodstream), you will be monitored closely for any changes. If you have pneumonia, you may need a machine to help you breathe – this may be able to be done on the ward, or you may require transfer to intensive care. Sometimes the decision to help you with your breathing is made early, before it is necessary, and this will be discussed fully with you. This may be done because your breathing rate is very fast making you extremely tired and your breathing is inefficient.

Life-threatening bacterial infections

Sometimes, complications can occur suddenly and progress quickly. These complications can lead to a septic shock, a life-threatening condition that occurs when an overwhelming infection leads to low blood pressure and low blood flow.

If septic shock occurs, large amounts of extra fluids or drugs are given to try to increase blood pressure. If this does not work, the patient may need to move to intensive care where their condition can be monitored even more closely and they can be given special drugs to maintain blood pressure.

This is important because a long period of low blood pressure can cause major damage to important body organs, particularly the kidneys. Organs in the lower part of the body can be damaged if they don't get enough oxygen because not enough blood is being pumped through them. You may also need help with breathing via a machine.

Dealing with an emergency

Unfortunately, in times of medical emergencies such as septic shock, treating your physical condition is the medical team's first priority and there may not be enough time to explain everything fully. So it is important that you and your carers discuss these issues, in advance, with your BMT team.

If you become seriously ill, it is stressful for you and your carers, and it difficult for everyone to think clearly. It is important to remember that such serious complications are relatively rare and that you and your carers will be involved as much as possible in discussing treatment options.

Prevention

You will be given oral antibiotics before and after your BMT to try to prevent common infections that come from your gut. These antibiotics may include ciprofloxacin and Flagyl (see drug appendix for more information). Fever is often the only obvious sign of infection, so your temperature will be monitored at least every four hours while you are neutropenic.

Treatment

If your temperature goes above 38°C, samples of blood, sputum, urine and stool will be taken to try to find the source of infection. An X-ray of the chest may be done. Treatment with antibiotics is started immediately without waiting to identify the source of infection. This may take a few days, but often no source of infection can be identified.

Some examples of antibiotics that are commonly used include gentamicin, vancomycin, cephalosporins and penicillins (see appendix for more information on specific drugs).

The antibiotics are given intravenously over a number of days depending on the severity and response of the infection. Your doctor may change the combination of drugs until the best for your particular infection is found.

Fungal infections

Fungal infections are common in the first three months after a BMT, particularly in people who have GVHD. Fungi may be a yeast (candida or thrush is the best known example) or a mould (such as those found on old bread). Some fungi live in our bodies without causing problems. However, the use of antibiotics before and after BMT to treat bacterial infections also destroys the beneficial bacteria in the body that keep fungi under control.

Prevention

Candida and aspergillus are the most common fungal infections after BMT.

Candida, which is the fungus that causes thrush, is very common. It normally lives inside the mouth, vagina or gut, but beneficial bacteria that also live in these areas keep it under control.

Aspergillus is a common type of fungus that grows on decaying vegetation, such as compost heaps and fallen leaves. It can also be found in air-conditioning systems and

at building sites. Aspergillus infections occur most often in the sinus passages or lungs and can cause pneumonia.

You will be given a drug called fluconazole orally or via your drip every day to prevent fungal infections (particularly candida infections). You will continue to take fluconazole after your discharge until about day+75.

If you have had an aspergillus infection in the past, you may be given amphotericin or itraconazole instead.

At some BMT centres, special air-filtering equipment is installed in hospital rooms to remove fungi and other potential infections from the air. Eliminating fresh plants, fruits and vegetables from your environment also reduces the risk of fungal infections.

Treatment

Fluconazole and amphotericin are used to treat candida infections.

Amphotericin and other antifungal drugs are given to treat aspergillus infections. Treatment may continue for a long time, until after discharge from hospital, as the infection is difficult to treat. (See drug appendix for information on these drugs.)

Viral infections

Viruses are tiny parasites that need other organisms (hosts), such as human cells, to survive and multiply. Viruses enter the host cell, change the genetic machinery of the cell and turn it into a factory that produces more of the virus. The virus eventually destroys or cripples the host cell and moves to nearby cells.

In healthy people, T cells and antibodies produced by B-cells protect against invading viruses. Because these cells are destroyed or depleted after your conditioning therapy, you will be more at risk of viral infections. Viral infections can be difficult to treat because they tend to recur repeatedly.

Viral infections after a BMT are caused by either exposure to a new virus or reactivation of an old virus that had been dormant in your body. They are most common in the first year after a BMT, but may occur as late as two years after BMT. The most common fungal infections in BMT patients are caused by the cytomegalovirus (CMV), herpes simplex virus (HSV) and varicella zoster virus (VZV).

Cytomegalovirus (CMV)

About half the general population is exposed to CMV during their lifetime. It is more common in people who live in cities. You may not even know that you have been infected because CMV gives you flu-like symptoms and causes no long-term effects, unless your immune system is compromised.

About a third of BMT patients develop a CMV infection, usually in the second or third month after the transplant. CMV infections can affect several different organs, including the liver, colon, eyes and lungs. The risk of CMV infection is higher in older patients and in people who have GVHD.

Prevention and Treatment

Before the BMT, you will have a blood test to see if CMV is in your body. If it is not, you are said to be CMV-negative and care is taken to prevent exposure to CMV before, during and after the BMT. If possible, a CMV-negative bone marrow donor is used. Whenever possible, only blood products that are CMV-negative are used, and special filters are used when transfusing blood products to stop blood-borne transmission.

If you are CMV-positive, you will be given the anti-viral drug, ganciclovir, into your drip twice a day for seven days before the BMT. This is changed to another antiviral drug called acyclovir from day+1 and continues three times a day until day+28. Acyclovir is used in place of ganciclovir after BMT because it doesn't suppress bone marrow function as much.

If you are CMV-negative and your donor is also CMV-negative, you won't need any preventive treatment.

You will have twice-weekly blood tests to check to see whether you are developing a new or reactivated CMV infection, which is treated with ganciclovir into the drip twice a day for 14 days.

Herpes simplex virus (HSV)

Herpes simplex infections are caused by two separate viruses: herpes 1 and herpes 2.

The herpes 1 virus causes cold sores in and around the mouth. About 70% of people are exposed to the herpes 1 virus, usually during childhood. The virus is highly contagious and is transmitted through contact with people who have active cold sores on their mouths.

Herpes 2, or genital herpes, is transmitted through sexual intercourse with an infected partner. Active infection causes blisters on the genital area.

Herpes infections often recur after the first episode. The virus can lie dormant in the body for many years, usually flaring up at times of stress or exposure to sun or wind. Some people who have the virus may not remember ever having had an active case of herpes, but the virus may still be in their body and will show up on a blood test.

Herpes infections usually occur in the first month after BMT and are mostly caused by the virus that is already present in your body. As well as the cold sores of a herpes 1 infection, BMT patients sometimes get skin lesions. In rare cases, a herpes 1 infection can occur in the brain.

Prevention and Treatment

If you know that you have had herpes – or blood tests show that you have – you will be given acyclovir tablets three times a day to prevent the infection reactivating. If you can't swallow tablets, you will be given this drug into your drip three times a day.

Herpes simplex is treated with acyclovir, orally or intravenously, at higher doses than for prevention.

Varicella zoster virus (VZV)

Infection with VZV is often called shingles or herpes zoster. It is the same virus that causes chickenpox and only occurs in those who have already had chickenpox.

Symptoms include an itchy blister-like skin rash that follows the path of the body's nerve branches. This rash can be extremely painful due to the involvement of the nerve endings under the skin. Even a gentle touch to the skin can hurt. The ophthalmic nerve to the eye can also be affected. The painful rash can affect the nerve path on the forehead and eyelids and, if not treated promptly, can damage the eye.

Up to 50% of BMT patients get VZV in the first year after the transplant, usually after day+100. It is most common in people who have GVHD.

Preventing and treating infection

Since VZV is highly contagious, patients who have never had chickenpox or who have had a negative blood test for the virus should avoid people with chickenpox or shingles for the first year after a BMT. It is treated with acyclovir either into a drip or orally, depending on the severity of the infection.

Other viruses

Many other viruses – such as adenovirus, Epstein-Barr virus (EBV), respiratory syncytial virus (RSV) and human papilloma virus (HPV) – can cause infections after a BMT but are not common.

Adenovirus and RSV infections can cause pneumonia and can be serious. Adenovirus can also cause infections in the kidneys or gastrointestinal tract and blood in the urine. In rare cases, the Epstein-Barr virus infects the lymph system, creating a lymphoma-like condition.

Commonsense measures, such as avoiding crowded public places or people with colds and flu, and having good personal hygiene, reduce the risk of these infections.

Protozoa

Protozoa are single-cell parasites and, like viruses, need human cells to replicate. Infections from protozoa are less common than other infections but can cause serious problems for BMT patients who are T-cell deficient.

Pneumocystis carinii is a protozoa that usually lives harmlessly in the trachea or windpipe of healthy people but can enter the lungs and form tiny cysts when the immune system is suppressed. This is called *Pneumocystis carinii* pneumonia (PCP). Bactrim and pentamidine are highly effective in preventing and treating this type of lung infection.

Toxoplasmosis

Another infection called toxoplasmosis occasionally develops in patients whose immune system is compromised. Toxoplasmosis is caused by a protozoan called *Toxoplasma gondii*, which is often transmitted in the faeces of cats. It may infect the brain, eyes, muscles, liver and/or lungs. A painful, inflamed retina in the eye is a common symptom of the disease, which, without prompt treatment can damage the eye.

It is vital to limit all contact with pets and to wash your hands thoroughly if you do have contact. Emptying the kitty litter is off limits.

Bactrim is effective in preventing toxoplasmosis infection.

Revaccination

Because your immune system has been destroyed, you will have lost immunity to certain infectious diseases and will need revaccination against these diseases, plus other vaccinations that you may not have had. Revaccination is a way of educating your new immune system to cope with common infections.

Revaccination will not be necessary or effective until at least a year after the transplant. Your BMT doctor will explain what you need, and organise the vaccinations through your GP. Depending on their individual situation, some people will need a different set of vaccinations to those listed below.

The recommended revaccination schedule is:

One year after BMT

- diphtheria, pertussis, tetanus (DTP acellular vaccine)
- Haemophilus influenzae B (Hib)
- pneumococcal disease (Pneumovax)
- polio (inactivated polio virus [IPV] only, Salk vaccine)
- hepatitis B (for those with risk factors for infection).

14 months after BMT

- diphtheria, pertussis, tetanus (DTP acellular vaccine)
- Haemophilus influenzae B (Hib)
- polio (inactivated polio virus [IPV] only, Salk vaccine)
- hepatitis B (for those with risk factors for infection).

Two years after BMT

- diphtheria
- tetanus
- Haemophilus influenzae B (Hib)
- pneumococcal disease (Pneumovax)
- polio (inactivated polio virus [IPV] only, Salk vaccine)
- hepatitis B (for those with risk factors for infection)
- meningococcal vaccine
- mumps, measles, rubella (MMR) – if no longer taking immunosuppressive drugs.

Annually

You and all members of your immediate family should have an annual Fluvax vaccination against that year's strain of the flu from one year after BMT onwards.

Drugs used to treat infections

Antibiotics

Initial treatment of infections consists of broad-spectrum antibiotics, which kill a variety of different bacteria and are effective against either Gram positive or Gram negative bacteria. These drugs are particularly important during the time of neutropenia early after BMT.

Commonly a combination of a cephalosporin or a penicillin is used, plus one of the aminoglycosides, usually gentamicin. Vancomycin may be started up front or added about two days after starting the initial combination therapy.

Cephalosporins

Cephalosporins are a group of antibiotics that kill certain bacteria by preventing the bacterial cell wall from forming. Brand names for these drugs include Cefepime, Ceftriaxone, Claforan and Keflex. They are effective against a variety of bacteria that cause infections in the respiratory, skin, blood, urinary and skeletal body systems.

Bacteria that are susceptible to the cephalosporins include streptococcus and staphylococcus species and *Escherichia coli* (*E. coli*). They should not be given if you have a history of allergy to penicillin.

Cephalosporins may be given into a drip or orally, but in BMT they are usually administered into the drip once or twice a day.

Possible side effects

- rash
- allergy
- decreased kidney function
- gut disturbances including nausea and diarrhoea.

Penicillins

The penicillins are a group of antibiotics that kill bacteria by preventing cell wall production. Brand names for these drugs include Timentin and Tazocin. The types used in BMT are broad spectrum and are used to treat infections caused by bacteria such as: *E. coli*, pseudomonas and staphylococcus. Substitutes are available if you are allergic to Penicillin.

They are usually given into your drip 3-4 times a day, with each dose taking about 30 minutes.

Possible side effects

More common

- rash
- pain at the site of infusion if not given via a central line.

Less common

- anaphylaxis
- nausea and vomiting
- decreased kidney or liver function.

Aminoglycosides

The aminoglycosides are a group of antibiotics that kill certain bacteria by preventing the formation of proteins essential for the maintenance of the bacteria. Brand names of these drugs are Gentamicin and Tobramycin.

They are effective against many Gram negative bacteria such as *E. coli* and pseudomonas, and some Gram positive bacteria such as the staphylococcus species. These organisms or bacteria cause infections in many body systems including respiratory, skin, blood, urinary and skeletal.

Gentamicin and Tobramycin are both given into the drip once a day.

Possible side effects

More common

- decrease in kidney function
- ringing in the ears or deafness (usually temporary and dependent on dose).

Less common

- rash
- allergy
- gut upsets (mainly diarrhoea).

Drug levels are monitored regularly – with doses changed if needed – to prevent or decrease the chances of hearing loss or kidney damage.

Vancomycin

Vancomycin is an antibiotic that attacks bacteria by preventing the bacterial cell wall from forming. It also damages the cell membrane, which eventually results in killing the cell.

It is effective against bacteria such as *Clostridium difficile*, and the streptococcus and staphylococcus species.

Vancomycin is given orally for clostridium infections and into the drip for all other bacteria up to four times a day.

Possible side effects

More common

- decreased kidney function
- ringing in the ears or deafness (usually temporary and dependent on dose).

Less common

- moderate to severe flushing of the upper body and head ('Red man syndrome'), low blood pressure or cardiac arrest. These are possible side effects of rapid infusion.
- gut disturbances, such as nausea, vomiting and diarrhoea
- hypersensitivity, causing chills, nausea, rash and fever
- resistance by some organisms, such as vancomycin resistant enterococcus (VRE). This can result from prolonged overuse of vancomycin.

As with aminoglycosides, the drug levels are monitored regularly to prevent or decrease the chances of hearing loss or kidney damage.

Antifungal drugs

Amphotericin

Amphotericin is the main drug used to treat infections caused by fungi such as candida (*Candida*), cryptococcus or aspergillus. It works by altering the membrane of the fungal cells to allow some of the small molecules in the cell to flow out, ultimately killing the cell.

It is given intravenously, usually daily over a period of 2-24 hours, but commonly over 4-6 hours. Treatment may continue for months depending on the fungal infection. Many patients will be given a premedication to prevent or decrease the severity of the infusion-related side effects.

Other preparations of antifungal agents are available. Examples include Amphocil, caspofungin, voriconazole and liposomal (lipid preparation) preparations such as AmBisome.

Possible side effects

More common

- infusion related, such as chills, rigors and fever (leading to the nickname 'Amphoterrible')
- decreased kidney function
- nausea and vomiting
- decreased appetite causing weight loss
- abnormal electrolyte levels, especially potassium
- pain at the site of infusion, if not given via a central line.

Less common or rare

- rash
- ringing in the ears or deafness, usually temporary
- hypotension, cardiac arrest
- abnormal liver function
- kidney failure.

Antiviral drugs

Ganciclovir

Ganciclovir is an antiviral drug used to prevent and treat viral infections, particularly with the cytomegalovirus (CMV). It works by becoming part of the virus's genetic makeup, preventing further production of the virus.

Ganciclovir is given via the drip. To prevent infection in those who are CMV-positive or who have a CMV-positive donor, it is given twice a day for seven days before BMT.

At day+28, or later if engraftment is delayed, the drug may be restarted, and given three times a week until day +84.

To treat CMV infection, it is usually given twice daily for 14 days.

Possible side effects

More common

- bone marrow suppression, especially low platelets and anaemia
- gut disturbances, such as diarrhoea, nausea
- irritation of the vein, if not given via a central line.

Less common

- rash
- infertility
- fits, unsteady walking and decreased level of consciousness.

Acyclovir

Acyclovir is an antiviral drug used to treat and prevent viral infections, particularly with herpes simplex or varicella zoster viruses. It works in a similar way to ganciclovir.

Acyclovir is given either orally or into the drip three times a day, depending on your ability to swallow and retain the dose. It will start on day+1 and continue until day+28, and sometimes longer.

Possible side effects

More common

- rashes, susceptibility to sunburn
- decreased kidney function
- nausea and vomiting.

Less common

- allergy
- confusion, hallucinations, changes in level of consciousness, agitation
- change in liver function.

Anti-protozoal agents

Cotrimoxazole

Cotrimoxazole (Bactrim DS) is an antibiotic consisting of two drugs, trimethoprim and sulfamethoxazole, which used to prevent and treat *Pneumocystis carinii* pneumonia (PCP) and toxoplasmosis infection. Cotrimoxazole works by interfering with the building blocks of the protozoal cell leading to cell death.

To prevent PCP, cotrimoxazole is given twice daily, twice a week. To treat PCP, cotrimoxazole is given in high doses by vein.

The use of Bactrim for several months is very important, otherwise there is a serious risk of getting PCP pneumonia.

Possible side effects

More common

- nausea and vomiting
- lack of appetite
- rash
- bone marrow suppression, particularly when receiving treatment doses or on long-term treatment
- increased risk of sunburn
- liver dysfunction.

Less common or rare

- kidney dysfunction
- light-headedness, dizziness, unsteady walking
- headache
- ringing in the ears
- low blood sugar levels
- allergic reaction, particularly to the sulphur component
- electrolyte disturbances, high potassium.

Graft-versus-host disease (GVHD)

GVHD is a common complication of allogeneic BMT. Once the donor marrow cells begin to engraft (grow) and function, the donor T lymphocytes may see your own body as foreign and try to destroy your tissues and organs. This occurs because the conditioning therapy has suppressed or eliminated your immune system to stop your body rejecting the donor marrow.

About 50% of BMT patients who have a matched related donor develop some degree of GVHD. Most of these cases are mild to moderate.

The rates of GVHD are significantly higher in some groups of people, such as those:

- who have a matched unrelated donor or mismatched donor transplant
- who are older (over 30 years)
- whose donor is a female with more than two pregnancies.

There is growing evidence that, however unpleasant and frustrating, GVHD can be beneficial. Studies have shown that GVHD reduces the risk of relapse of your cancer. This is due to the graft-versus-tumour effect, when donor T cells attack your cancer cells. This effect is strongest in some types of leukaemia and lymphoma, where the further infusion of donor cells into a patient who has relapsed after BMT can reinduce remission. This is known as a donor lymphocyte infusion (DLI).

There are two types of GVHD – acute and chronic. You may develop none, one or both. Each differs in symptoms, clinical signs and time of onset.

Acute GVHD

Acute GVHD occurs within 100 days after a BMT and mainly affects the skin, the liver and the gastrointestinal tract (gut). It may be mild, moderate, severe or life threatening.

Biopsy of the affected area is the only definitive way to diagnose acute GVHD. At times this may be too dangerous, so a diagnosis is made on clinical signs alone or by ruling out other possible causes.

Acute GVHD is classified into four grades:

- **Grade 1 (mild):** a skin rash over less than 25% of the body
- **Grade 2 (moderate):** a skin rash over more than 25% of the body, and mild liver or stomach and intestinal disorders
- **Grade 3 (severe):** redness of the skin and moderate liver, stomach and intestinal problems
- **Grade 4 (life-threatening):** blistering and peeling skin, and severe liver, stomach and intestinal problems.

Symptoms

Skin

- burning and redness on palms or soles
- a rash, along with burning and redness (similar to sunburn), which may spread to the trunk and eventually develop over the entire body

- blistering and eventually flaking of the skin, leaving raw areas underneath.

Gut

- nausea, vomiting, abdominal cramps and loss of appetite
- watery diarrhoea, which may become bloody.

Liver

- jaundice (yellow eyes and skin) and pain in the abdomen
- swelling of the liver
- abnormal blood tests for liver function.

Prevention

A number of drugs are effective in minimising and controlling acute GVHD. Drugs such as methotrexate, cyclosporin, tacrolimus, mycophenolate and prednisone are given to lessen the ability of donor T cells to attack tissues and organs.

At least some of these drugs are given from day-1 of the BMT and continue for about six months after the transplant. The combination, dosage and duration of medications will depend on the grade and duration of acute GVHD. (More detail about these drugs is given later in this section.)

T cell depletion, which means the removal of the donor's T cells from the graft before BMT, is a technique used to reduce acute GVHD. It is possible to remove all donor T cells from the donor stem cell mixture before being put into your body, to eliminate the risk of GVHD.

However, T cells also help engraftment and are responsible for the graft-versus-tumour effect, which can help cure you. This means your doctor would have to strike a balance between removing the right amount of donor T cells to reduce acute GVHD and prevent graft rejection, but leaving enough to give the graft-versus-tumour effect. Because of the difficulties in doing this, T cell depletion is not widely used.

Treatment

The following treatments are used for acute GVHD:

- **for skin symptoms:** topical steroid (cortisone) creams
- **for mouth symptoms:** topical steroid mouthwash
- **for mild to moderate symptoms:** increase or start oral steroids, such as Prednisolone
- **for moderate to severe symptoms:** high-dose methylprednisolone (intravenous prednisone) daily
- **for symptoms not responding to steroids:** anti-thymocyte globulin, daclizimab (or other similar drugs targeting donor T cells) or increased doses of tacrolimus or mycophenolate
- **for symptoms such as pain, cramps, diarrhoea, nausea and vomiting:** medication is given to relieve symptoms
- **for moderate to severe gut symptoms:** usually no food or fluids by mouth, intravenous fluids and total parenteral nutrition (TPN, or intravenous feeding) replace food and drink.

Chronic GVHD

Chronic GVHD, which develops more than 100 days after BMT, is thought to be caused by new T cells that are produced after the donor's bone marrow engrafts.

Types of chronic GVHD

Chronic GVHD is classified according to the onset and severity.

- **progressive:** arises directly from acute GVHD, usually severe and often hard to treat and control
- **quiescent:** acute GVHD that has resolved
- **de novo:** develops although there has been no acute GVHD
- **explosive:** affects multiple organs and usually follows from either a skin injury, such as sunburn, or when immunosuppressive drugs are withdrawn. This type of GVHD is extremely serious.

Characteristics of chronic GVHD

Chronic GVHD may be:

- **limited:** localised involvement only. Less than 50% of the skin is affected, plus mild liver problems or involvement of eyes or mouth/salivary glands.
- **extensive:** generalised involvement. More than 50% of the skin is affected, plus severe liver problems or the involvement of any other major organ (eg, lungs, gut). This is often difficult to control and is very serious.

As with acute GVHD, older people are more likely to develop chronic GVHD. About 75% of people who develop chronic GVHD will have had acute GVHD previously. Chronic GVHD is also more common in people whose donor is unrelated or whose marrow is not perfectly matched.

Common symptoms

- skin problems, including dry itching rash, change in skin colour, and tautness or tightening of the skin
- jaundice and abnormal liver test results
- dry mouth (chronic GVHD attacks the saliva glands that secrete mucus, saliva or other lubricants)
- a burning sensation in the mouth when using toothpaste or eating acidic foods
- dryness or stinging in the eyes, because the glands that secrete tears are impaired
- vaginal dryness
- infections (the immune system remains severely compromised due to both GVHD and its treatment).

Less common symptoms

- some hair loss or early greying
- scarring of the skin
- difficulty swallowing and eating (the glands that lubricate the oesophagus are affected)
- heartburn, stomach pain and/or weight loss (the glands that lubricate the stomach lining and intestines are affected and inhibit the body's ability to absorb nutrients properly)

- tightening of the tendons in joints, which makes it difficult to move arms and legs
- wheezing, bronchitis or pneumonia if the lungs are affected.

Treatment

Chronic GVHD is usually treatable with steroids such as prednisone and the immunosuppressive drug, cyclosporin. A treatment known as PUVA is a type of ultraviolet radiation treatment that is sometimes helpful in treating skin and mouth symptoms. PUVA stands for psoralens (P) and UVA (the long wavelength of ultraviolet). Other immunosuppressive drugs used to treat chronic GVHD include tacrolimus, mycophenolate and sirolimus.

Antibiotics such as Bactrim or penicillin, or both, are usually taken to reduce the risk of infection.

A newer treatment called extracorporeal photopheresis is being trialled in Australia. This treatment involves processing the blood through a special machine, separating the white cells and exposing them to UV light before putting the cells back into the body.

If you have chronic GVHD you should avoid vaccinations with live viruses, such as German measles and polio, until the GVHD is gone and you no longer need immunosuppressive drugs.

If you are having problems with eating or finding foods that suit you, talk to the dietitian because it is important to have good nutrition to help your body cope with chronic GVHD.

Long-term implications

Most people recover from GVHD, but some symptoms may persist long after the GVHD is resolved.

- **Sensitive skin:** most people find that their skin is extremely sensitive and need to take extra care to avoid sunburn. Use sunscreen and cover all parts of your body exposed to the sun.
- **Dry mucous membranes can cause problems such as:**
 - dry and irritated eyes: regular eye drops can help
 - lack of mouth saliva: have frequent sips of water and eat meals with gravies and sauces. Artificial saliva is also an option.
 - dry vagina: a variety of lubricants is available. Ask your doctor for advice if you need help.
- **Stomach problems:** GVHD of your gut can cause recurrent diarrhoea and inability to absorb nutrients from food.

It is very difficult to predict the severity, timing and location of GVHD. Remember that not all GVHD is bad news. Depending on your initial diagnosis, a mild episode of GVHD can be a positive sign that your new engrafted white cells are reacting to your old cells. Your BMT team are the best people to explain your specific disease and the positives and negatives associated with GVHD.

Drugs used to prevent GVHD

Cyclosporin A

Cyclosporin A, or CSA (Neo-oral), is an immunosuppressive drug that prevents acute GVHD by slowing down the growth and development of the donor T cells. It is started the day before the BMT and is usually continued until day +60 when, if there is no evidence of GVHD, the dose will be decreased slowly so that it is stopped by six months after the BMT.

Initially it will be given into the drip twice daily over 2-6 hours. It will be changed to oral capsules or liquid twice a day when you can eat and drink normally again.

Cyclosporin is also used to treat chronic GVHD.

Common side effects include:

- reduction in kidney function
- tremors in arms and legs
- increased blood pressure
- nausea, vomiting and diarrhoea
- increased risk of infection
- swelling of eyelids, hands and feet due to fluid build-up
- overgrowth of the gums (with long-term use)
- excessive hair growth, particularly on the face (with long-term use). This will go away when the drug is stopped.

Less common side effects include:

- anaphylaxis (severe allergic reaction) with IV use only
- burning sensation in the hands and feet, particularly in the first week of treatment
- fits
- liver toxicity
- thrombotic thrombocytopenia purpura (TTP – see page ?).

Methotrexate

Methotrexate (MTX) impairs the ability of the transplanted T cells to attack your organs and tissues. It is usually given into your drip on days +1, 3, 6 and 11.

Common side effects include:

- bone marrow suppression
- mouth and/or throat ulcers – doses may be withheld if your mouth is too sore
- sensitivity to sunlight – a rash may develop
- impaired liver function.

Less common side effects include:

- acne, itchiness and skin rash
- general tiredness.

Mycophenolate mofetil

Mycophenolate, MMF or CellCept, inhibits the formation of B and T lymphocytes, which reduces the risk of GVHD. It is usually given orally twice daily, or into the drip twice a day.

Common side effects include:

- nausea and vomiting
- diarrhoea
- increased risk of infection, particularly oral fungal infections
- suppression of blood counts.

Less common side effects include:

- inflamed oesophagus
- inflamed stomach
- gastrointestinal bleeding
- cytomegalovirus infection (see page?).

Tacrolimus

Tacrolimus (Prograf) is an immunosuppressive drug. It works by suppressing T cells that are thought to have a major role in GVHD and rejection. Tacrolimus is usually given orally twice a day, or into the drip as a continuous infusion.

Common side effects include:

- tremor
- headache
- diarrhoea
- nausea
- decreased kidney function
- increased blood pressure
- increased risk of infection.

Less common side effects include:

- allergic reactions
- high blood sugars – possibly requiring insulin.

Drugs used to treat GVHD

Methylprednisolone and prednisone

Methylprednisolone (Solumedrol) and prednisone (Prednisolone) are synthetic steroid hormones. They work by suppressing the immune response of the donor cells on your cells. Prednisone is used to treat grade 1 acute GVHD and chronic GVHD.

Methylprednisolone is given as first-line treatment of grades 2-4 acute GVHD. It is given via your drip in high doses for a number of days until it becomes clear whether you are responding or not. If there is no response or a worsening of the symptoms, your dose may be increased and/or the treatment changed. You will be changed to oral prednisone at some point.

If you are given high-dose steroids for more than a couple of days, you will need to be weaned off them slowly to avoid potential complications of abrupt withdrawal such as adrenal function suppression (see below).

Common side effects

The only significant side effects of short-term use are high blood sugar levels, sometimes requiring insulin, interference with sleep and increased appetite.

With extended use (more than five days) the following may occur:

- fluid and salt retention
- development of swelling of cheeks (moon face)
- excessive hair growth
- high blood pressure
- stomach ulceration and/or haemorrhage
- delayed wound healing
- increased risk of infection and masking the symptoms of infection
- muscle weakness
- thinning of skin and bruising
- mood changes
- acne
- increased appetite and weight gain
- osteoporosis (thinning of bones)
- erosion of the head of the femur or humerus (long bones in the legs and arms). This is called avascular necrosis (AVN) and can cause pain in the joints affected.
- suppression of the ability of the adrenal glands to make natural steroids if the drug is stopped suddenly (ie, without weaning). This may cause lack of appetite, nausea, depression and generalised aches and pains – people often describe the feeling like they have been “hit by a bus”.

Anti-thymocyte globulin

Anti-thymocyte globulin (ATG) is an immunosuppressive drug sometimes used in conditioning therapy to boost the effects on the immune system (see Chapter 7). ATG can also eliminate donor T cells, which cause GVHD, and is often used as a treatment when first-line treatments have failed. ATG is usually given for three days as an intravenous infusion over 4-6 hours.

Common side effects include:

- fever, chills, hives and low blood pressure during the infusion. Sometimes the infusion may need to be slowed or stopped temporarily if the symptoms are severe. Drugs such as hydrocortisone (a steroid), paracetamol and antihistamines are usually given before the infusion to minimise symptoms.
- increased risk of infection due to suppression of the immune system.

Less common side effects

- serum sickness, due to an allergic reaction to the foreign material in the animal serum. This can cause fever, skin rash and loss of protein in the urine.

Daclizumab

Daclizumab is an antibody that has an immunosuppressive effect on acute GVHD. It is used when GVHD does not respond to methylprednisolone and is used most often to treat grades 2-4 acute GVHD of the skin. It is usually given through a drip on five days spaced over four weeks.

Daclizumab appears to have minimal side effects, apart from:

- rare allergic reactions
- increased risk of infection.

Liver complications

[Ed's note: We need an illustration of the liver here]

How the liver works

The liver, which lies under the ribs on the right side of the upper abdomen, is responsible for a variety of essential functions. Liver cells cleanse the blood of toxins and other waste materials, produce a fluid called bile to aid digestion and control the excretion of bilirubin, a by-product of red-cell breakdown.

The liver also stores energy and makes proteins that control blood clotting.

As blood flows through the liver, it passes through smaller channels called sinusoids, which are lined with liver cells. The cleansed blood flows out of the liver through a network of veins back to the heart.

The bile travels through the liver in the opposite direction to blood. It enters the gallbladder via bile ducts, where it is stored until needed in the intestine to aid digestion.

The liver's many essential functions may be disrupted during the transplant process. If the sinusoids become obstructed or liver cells are damaged, the liver cannot properly rid the body of toxins, drugs and other waste products.

Similarly, if the bile ducts become obstructed, excess levels of bilirubin, cholesterol and other chemicals build up in the body, interfering with the function of the liver and other organs.

Disorders of the liver can be grouped in three types:

- those that directly affect the liver cells
- those that affect the vessels that transport blood through the liver
- those that affect the bile ducts that carry bile from the liver to the gallbladder and intestines.

More than one type of liver complication can occur at the same time. Most liver complications are temporary and reversible, but some can become serious and may be fatal. As many of the potential complications present in a similar manner, it may take time for the correct diagnosis to become clear.

Risk factors for liver complications

People who had abnormal liver function before the BMT may have a higher risk of developing severe liver complications during and after the transplant.

Before the BMT, you will be tested for signs of fungal liver infections, hepatitis (inflammation of the liver usually caused by a virus), and gallstones or other obstructions of the bile duct.

Any treatment— such as removing fungal lesions or gall stones – will be done before the transplant, allowing time to recover before admission. The pre-transplant tests also give the BMT team information that may help prevent serious liver problems.

Many tests are used through all periods of the transplant to detect and identify liver complications.

Tests include:

- blood tests, include measuring levels of bilirubin and other liver enzymes
- physical examination of the abdomen to feel the size of the liver
- ultrasound or CT scan
- measurement of abdominal girth
- daily or twice-daily weight measurement
- liver biopsy for a definitive diagnosis.

Symptoms of liver problems

- jaundice
- tender or swollen liver
- rapid weight gain, showing fluid retention
- swelling in arms, legs or abdomen
- high levels of bilirubin and liver enzymes in the blood
- confusion (this may also be a symptom of other, less serious post-BMT problems such as drug side effects).

Liver problems in the first 100 days

Acute GVGD of the liver

Acute GVHD can damage the liver. It disrupts the flow of bile out of the liver by affecting the small bile ducts, and can be mild, moderate or severe (see page?). Patients who receive unrelated donor marrow or mismatched donor marrow are at increased risk of developing acute GVHD of the liver.

Symptoms include:

- jaundice
- mild liver tenderness.

Veno-occlusive disease

Veno-occlusive disease (VOD) is a potentially serious problem that occurs when the vessels carrying blood through the liver become swollen and blocked, impairing the liver's ability to cleanse the blood of toxins, drugs and other waste products.

As waste products build up in the blood stream, the kidneys may malfunction, causing water and salt to accumulate in the body, leading to swelling of the legs, arms and abdomen.

Also, as a result of the decreased flow of blood through the liver, pressure and fluids increase in the liver, leading to swelling and tenderness.

Risk factors for VOD: VOD occurs as a result of the chemotherapy and/or radiotherapy given in conditioning therapy. The amount and types of chemotherapy given to treat the original disease may also affect the chances of developing VOD.

People who have malignant diseases such as leukaemia and lymphoma are at higher risk of developing VOD than people who have non-malignant conditions, such as aplastic anaemia or immune disorders, due to the intensity of the drugs required to treat them.

You will be considered to be at high risk of VOD if you have or have had:

- busulphan conditioning
- prior transplantation
- liver involvement in your disease
- liver dysfunction
- hepatitis B or C positive
- prior abdominal irradiation
- thalassaemia
- mismatched or unrelated donor marrow.

Symptoms of VOD: If you develop VOD, you may have any or all of the symptoms of liver problems, see page ???. [Ed note – needs to be crossreferenced.]

Also, in severe cases of VOD, the build-up of abdominal fluid may put pressure on the lungs and affect breathing. Waste products and toxins that accumulate in the bloodstream may affect brain function causing confusion. In severe and unresponsive VOD, other vital organs such as the kidneys, heart and lungs may also fail.

Symptoms of VOD usually show themselves in the first few weeks after conditioning therapy. Because the signs and symptoms of VOD are similar to, or the same as, other liver complications, the condition can be hard to diagnose. However, if an enlarged liver and sudden weight gain and jaundice occur early after transplant and cannot be explained by other causes, VOD probably exists.

Preventing VOD: People considered to be at low risk of developing VOD are given a drug called ursodeoxycholic acid twice a day, orally. Those at high risk of developing VOD will receive a drug called defibrotide twice a day through the drip.

Treating VOD: The most effective treatment for VOD is defibrotide, which works by helping to prevent the formation of blood clots and dissolving existing clots.

Other options for treating VOD include:

- stopping or avoiding, where possible, of drugs that may worsen the problem
- using diuretics (fluid-removing drugs) or dialysis (removal of excess fluid from the blood stream using a machine similar to that used to harvest stem cells) to reduce or remove excess fluid from your body
- reducing your intake of salt, which may worsen fluid retention
- maintaining a strict fluid balance
- increasing use of blood products (platelets and blood.)

Drugs used to prevent and treat VOD

Ursodeoxycholic acid (UDCA/Urso)

Ursodeoxycholic acid (UDCA/Urso) is a naturally occurring bile salt that helps prevent and treat a number of liver problems, including VOD and GVHD.

The exact mechanism of action is not clear, but it reduces the inflammatory response that decreases liver functioning. It is given orally in 2-4 doses.

Common side effects

- diarrhoea
- itchy rash in the first few weeks of treatment.

Less common

- allergic response
- nausea and vomiting
- sleep disturbances.

Defibrotide

Defibrotide has a number of complex actions that reduce clotting and blockage of small blood vessels in the liver. It is given twice daily into the drip. If being used to treat VOD, it is given for a minimum of 14 days unless there is a complete response earlier.

Defibrotide is generally well tolerated but occasional side effects include:

- dizziness
- low blood pressure
- nausea, vomiting and diarrhoea
- infusion-related effects including flushing and headache
- allergy.

Bloodstream infections

Occasionally, an infection elsewhere in the body may cause the liver to function abnormally, affecting the flow of bile. Symptoms include abnormal blood tests and possibly jaundice. Treating the infection with antibiotics will usually reverse the abnormal blood tests and restore the flow of bile.

Fungal liver disease

A fungal infection in the liver is a serious complication. Candida is the most common cause of fungal liver disease. The body's immune system and bacteria that normally live in the body usually control the spread of this fungus. However, a depleted immune system and the use of antibiotics that kill off these bacteria allow fungi to grow uncontrolled. (See chapter on the immune system and infection for more information.) Aspergillus is another type of fungus that may cause liver problems.

Risk factors for fungal infections: You are at higher risk of developing fungal liver disease if you have a fungal infection in your gut or bloodstream, you are taking prednisone to treat GVHD, or your white cell count is slow to recover.

Symptoms include:

- a fever not responding to antibiotics
- a swollen liver that is tender
- abnormal blood tests.

Preventing fungal infections: Throughout your transplant you will receive a drug called fluconazole once a day either orally, or into your drip if you cannot swallow the capsules, to reduce the chance of fungal infections.

Other steps that may be used to decrease the chances of developing a fungal infection include:

- using special filters in the air conditioning in your room
- high turnover rate of the air in your room to remove fungal spores
- eliminating fresh plants, fruits and vegetables from your environment.

Treating fungal infections: Fungal infections can be difficult to treat, especially when your immune system is not functioning normally. However, if you have a proven or suspected fungal infection, you will be given a drug called amphotericin. You may need to take the drug for some months until the infection in your liver is thought to be cured.

Drug-induced liver injury

Some medications routinely given during the BMT can temporarily cause, or worsen, liver abnormalities. These drugs include antibiotics, anti-nausea drugs, pain relief and GVHD treatments. Symptoms include jaundice and abnormal blood tests. Pain is not usually associated with this type of complication.

Viral hepatitis

Viruses can cause swelling of the liver, with or without mild pain. Viruses that can cause this include hepatitis B or C, adenovirus, herpes simplex, varicella zoster, cytomegalovirus (CMV) and Epstein Barr. The most common and important of these after BMT is CMV, which can cause severe viral hepatitis if not diagnosed and treated early (see infection, page ?)

Viral hepatitis is usually only mild and rarely causes serious complications, but early detection and diagnosis are important, as early treatment is the most effective.

Biliary disease

Another liver problem occurs as a result of being unable to eat for an extended period, usually due to severe mucositis or nausea. If you are not eating for a long period, bile builds up in the gall bladder. The bile thickens and becomes sludgy and may block the bile duct.

Symptoms include:

- pain after eating (when you start again)
- fever
- gallstones and gallbladder inflammation.

Usually this complication fixes itself once you return to your normal eating habits, but can occasionally lead to an infection of the bile duct and/or gall bladder.

If you have been unable to eat and have had intravenous feeding, you may also experience some temporary liver complications with possible liver inflammation and mild tenderness. A reduction in the amount and type of intravenous feeding or switching you back to eating (if possible) will usually correct these problems.

Liver problems after day+100

Liver complications are much less common after the first 100 days. If you have developed acute GVHD or viral hepatitis before day+100, you have an increased chance of developing liver problems after this time. Most liver complications that occur from now on are mild to moderate and are not fatal.

Chronic GVHD of the liver

Chronic GVHD affects the liver in the same way as acute GVHD – that is, it affects the flow of bile from the gall bladder into the intestines by interfering with the small bile ducts.

It is possible to have acute and chronic GVHD at the same time (see GVHD, page ??) The symptoms are jaundice and abnormal liver function blood tests.

Prednisone and other oral drugs such as cyclosporin or tacrolimus are the main treatments.

Chronic viral hepatitis

Viruses can remain dormant in the body for a long time after an acute infection and can reactivate at any time, particularly if your immune system is depleted.

Chronic viral hepatitis C can be difficult to treat, particularly as the drug most frequently used to treat it, interferon, can suppress the white cell count, increasing the risk of another infection.

Fungal liver disease

Fungal liver disease occasionally develops after day +100. The symptoms are the same as for fungal liver disease in the first 100 days – an ongoing fever, painful and swollen liver, and abnormal liver function blood tests.

Again, people who have chronic GVHD or low white cell count are more likely to develop a fungal infection. The treatment is amphotericin, possibly for an extended time.

Lung complications

A variety of problems can damage the lungs after a BMT. The complications can be a result of infections, bleeding, damage from chemotherapy drugs or radiation, GVHD or disturbances in the immune system.

Lung problems in the first 100 days

Bacterial pneumonia

Bacterial infection in the lungs is a relatively common complication in the 2-3 weeks after BMT. It is largely due to the low white blood cell counts that are typical during this time.

Pneumonia after a BMT results from infection with bacteria that are different from those that usually cause this condition in the community. These may be less responsive to antibiotics and more difficult to treat.

Symptoms include:

- fever and chills
- chest pains
- cough
- yellow or green sputum
- difficulty breathing.

The BMT team will order chest X-rays to diagnose the problem, and take blood and sputum samples to try to determine which bacteria are causing the infection.

Bacterial pneumonia is treated with antibiotics given into the drip. Oxygen will often be needed. Occasionally, when the infection is severe, artificial support on a ventilator may be necessary.

Fungal infections

Fungus infects the lungs because it is inhaled from the environment. The symptoms are similar to bacterial pneumonia (see page ??). [Ed note – needs to be crossreferenced]

Factors that increase the risk of fungal infections include:

- low white cell count, particularly neutrophils
- use of strong immune suppressive drugs, such as cyclosporin and ATG
- use of large doses of steroid drugs
- GVHD
- transplants from unrelated or mismatched donors
- previous fungal infections in the lungs.

Often BMT patients will be nursed in areas that have filtered air to reduce the risk of developing fungal infections, and may be given anti-fungal drugs as a preventive measure. Chest X-rays will diagnose the problem, and treatment is an anti-fungal drug, such as amphotericin.

***Pneumocystis carinii* pneumonia (PCP)**

This form of lung infection can occur in people with a suppressed immune system. It is due to a small parasite, called *Pneumocystis carinii*, which normally lives in the airways in the lungs without causing illness, but can grow when the immune system is damaged, causing pneumonia. The symptoms are fever, dry cough and difficulty breathing.

PCP is a potentially serious infection, but an antibiotic called Bactrim can prevent it. This drug is usually given before the transplant and started again after engraftment. Bactrim is given twice a week until the immune system recovers after BMT (see infections, page ? [Ed note – needs to be cross-referenced] for more information on Bactrim)

Pulmonary haemorrhage

This is a relatively rare complication, usually occurring in the first month after BMT. Bleeding or haemorrhage from the lungs results in coughing up blood and difficulty in breathing. The causes are usually thought to be faulty blood clotting, especially low platelet count, and damage from the drugs used in conditioning therapy.

Treatment consists of correcting the clotting problems with transfusion of platelets and plasma products, giving large doses of steroid drugs, and assisting breathing by giving oxygen and sometimes artificial support on a ventilator.

Interstitial pneumonia

This condition occurs less commonly, but is still a potentially serious complication. It may be due to viral or protozoal infection, damage from radiation and drugs, or from unknown causes. It usually occurs in the second or third month after BMT. Symptoms usually include fever, dry cough and difficulty breathing.

If it occurs, the BMT team will look for an underlying infection, such as a virus. Blood tests look for cytomegalovirus and other viruses. A bronchoscopy, which takes biopsies from the lungs, may also be needed. This procedure involves passing a fibre-optic tube through the mouth or nose into the large airways in the lungs under sedation.

Treatment involves drugs to treat any underlying infection, and giving oxygen, steroids and artificial breathing support as necessary.

Lung complications after day+100

Lung fibrosis

In this condition, scar tissue in the lungs causes stiffness and difficulty in expanding the lungs. The condition, which usually comes on gradually, can occur months or years after a BMT.

The symptoms are dry cough and difficulty breathing. It may be caused by drugs, especially busulphan, used in conditioning therapy or radiation therapy. Sometimes the cause is not known.

Diagnosis involves chest X-rays and breathing function tests. A lung biopsy by bronchoscopy or surgical operation may be necessary to confirm the diagnosis. Steroids are often used to treat fibrosis, but are not always successful.

Chronic GVHD of the lungs

GVHD can affect the lungs as well as other organs. The usual problem is damage to the bronchioles, which are the lining of the small airways in the lungs. This causes narrowing of the small airways, reducing the flow of air in and out of the lungs and increasing the risk of infection. Sometimes this produces a condition very similar to asthma, with wheezing and difficulty breathing out. There may be associated infection, such as bronchitis or pneumonia.

The diagnosis is often difficult to make, but is suspected in people with chronic GVHD who develop lung abnormalities. The diagnosis may require X rays, breathing tests and biopsies. Treatment usually consists of increasing the dose of the immunosuppressive drugs for GVHD, but not all patients will respond to this.

Recurring infections due to immune deficiency

Some BMT patients, especially those with active GVHD and on immune-suppressive treatment, have continuing defects in their immune systems that increase their risk of lung infection, either bronchitis or pneumonia.

Treatment includes antibiotics for each bout of infection and antibiotics to prevent infection. Some patients receive regular intravenous immunoglobulin, which is a source of antibodies.

Kidney and other complications

A variety of complications can affect the kidneys and urinary tract after a BMT. Often these are side effects of drugs, but infection and other complications may cause kidney problems.

Kidney failure

The function of the kidneys is to excrete excess water and eliminate waste products of cell metabolism in the urine. Some degree of the failure of normal kidney function is common after a BMT.

Kidney function is measured by the volume of urine produced each day and the amount of various breakdown products in the blood. The most commonly measured of these is creatinine, a normal breakdown product of muscle. Regular analysis of blood samples after BMT will allow doctors to monitor the ability of the kidneys to excrete substances such as creatinine. In some patients, this will show early signs of reduced kidney function, well before more serious problems, such as reduced production of urine, occurs.

Several drugs routinely used after BMT can damage kidney function. Cyclosporin, in particular, commonly impairs kidney function. Both the creatinine level and the concentration of cyclosporin in the blood need to be measured regularly, and the dose of the drug adjusted if there are signs of kidney failure.

A number of antibiotics and antifungal drugs, particularly gentamicin and amphotericin, can damage kidney function, and kidney function and drug levels need to be closely monitored. Low blood pressure, usually due to serious infection, can lead to poor kidney function and failure. Veno-occlusive disease of the liver (see page ??) can contribute to kidney failure.

Treatment of kidney failure will depend on the circumstances and its severity. Sometimes, it will involve only omitting or changing doses of cyclosporin, and waiting for the creatinine level in the serum to return to normal. In other situations, antibiotics will need to be changed, and supportive fluids and drugs given to improve blood pressure.

Uncommonly, dialysis will be needed for severe kidney failure. This involves processing of blood using a dialysis machine, to correct fluid and salt abnormalities. A central venous line, as well as any you already have, may need to be put in to allow dialysis to be done.

Severe kidney failure requiring dialysis is a correctable complication that can be fully reversible, but is a very worrying development that can contribute to a fatal outcome of BMT.

Haemorrhagic cystitis

This condition results from damage to the lining of the bladder from drugs or viral infections. Symptoms include pain when passing urine, increased frequency of urination, and blood and clots in the urine.

Haemorrhagic cystitis, which may occur weeks to months after BMT, can vary from mild to severe. It is often associated with the use of cyclophosphamide during conditioning therapy, which can damage the lining of the bladder.

Certain viruses, particularly cytomegalovirus and parvovirus, can also cause haemorrhagic cystitis. There is no proven effective treatment for this condition, and treatment is supportive, ie, blood and platelet transfusion, and washing the bladder out with fluids through a catheter as required.

Often the condition is mild and self-limiting, and resolves in a few weeks. Sometimes it is more severe, with considerable blood loss requiring transfusion. Clots in the bladder may block the passage of urine, and a catheter may need to be inserted into the bladder to drain the urine and wash out clots with saline solution.

Microangiopathic disease

This is an uncommon BMT complication. Microangiopathic disease means a disease process involving small blood vessels in vital organs, including the kidney. It is usually known by its complex medical name, thrombotic thrombocytopenic purpura or TTP.

This complication results from changes in small blood vessels, causing clotting and blocking of blood flow. Kidney damage and brain abnormalities, such as confusion, coma and seizures, commonly result. TTP also destroys red blood cells and platelets, causing anaemia and bleeding. Fever is also often present.

While the causes of TTP are often not clear, cyclosporin is often suspected as playing a role. This drug may be stopped when signs of TTP appear. Virus infections – especially cytomegalovirus – or previous radiation therapy may trigger the disease.

There is no proven effective therapy. Supportive measures include giving blood to correct anaemia, reducing cyclosporin doses, giving plasma products by transfusion or plasmapheresis, and kidney dialysis if kidney failure occurs.

Key points

- Every person who has a BMT is an individual with their own risk factors. You may get none of the following complications, or you may get one or more – there is no way of predicting your particular case.
- After a BMT, your immune system will not be at full strength for six months to a year, and longer for those with GVHD. You are extremely vulnerable to infections during this time, and it is important to follow the hygiene guidelines to minimise the risk.
- Because your old immune system has gone after a BMT, you will have lost the immunity you previously had to certain infectious diseases and you will need revaccination against these diseases, plus some other vaccinations that you may not have had.
- Graft-versus-host disease (GVHD) is a common complication of allogeneic BMT, but most cases are mild to moderate. It is caused by donor T cells attacking your body because they see it as foreign.

- Not all GVHD is negative. Depending on your initial diagnosis, a mild episode of GVHD can be a positive sign that your new engrafted white cells are reacting to your old cells.
- Acute GVHD occurs within 100 days after BMT and chronic GVHD occurs later. Both are treated with steroid and immunosuppressive medication.
- Most liver complications are temporary and reversible, but some can be serious and fatal. People who had abnormal liver function before the BMT have an increased risk of liver complications.

CHAPTER 11

Life after a BMT

Going home

After being in hospital for a long time, you may feel nervous about leaving. Some people say they feel a little daunted by the 'outside'.

Don't expect too much too soon. Like your experiences in hospital, just take life on the outside one step at a time. You will have some good days and some days when you don't have much energy. Try to be kind to yourself and realistic in your expectations. Remember to call or visit the BMT clinic if you have any concerns.

Start yourself on a gentle daily exercise program such as walking and gradually increase this as you feel able. Your body will be your best guide as to how much you can do.

Your carers will play a significant role in helping you adjust to life at home. In the first few weeks at home, you may need help with many normal daily activities until your strength improves. Early on, your carer may want to help you get to your clinic appointments.

You and your carer should also tell the team about any changes or difficulties you are having at home.

Preventing infections

Your immune system will need at least 3-6 months to fully redevelop after the transplant. It is important to be careful to prevent infections during this time, particularly if your white cell count and neutrophils are low. Some ways to help prevent infection include:

- Avoid crowded places like public transport, shopping centres and movie cinemas at peak times.
- Avoid or limit contact with people who are unwell, or who have had contact with others, particularly children with illnesses such as chickenpox or measles or who have been recently vaccinated.
- Don't go swimming if you still have a Hickman catheter or central line. If you want a bath, ensure the water level is below the exit site.
- Avoid gardening or contact with soil or potting mix because of the risk of contact with live bacteria.
- Don't wear contact lenses until you have discussed this with your team.

On discharge, your transplant team will give you information about how to care for yourself at home. Make sure you report any symptoms when you attend the clinic and call the clinic to get advice on your concerns.

Medications

When you leave the hospital, you will still be on medications to aid your recovery after the transplant. Continue to take your medications as directed by the team, as these are crucial to your recovery and the success of your transplant.

Your medications will be adjusted during your follow-up appointments with the transplant team. As your recovery progresses, the amount of medication should gradually decrease. Some people will need medication for several years after the transplant.

The BMT team will write out your medication schedule for you, and it will be helpful to take this information to each clinic visit. Remember to ask early for extra supplies.

Follow-up clinic visits

You will have regular checkups at the BMT clinic at the hospital where you had your transplant. These visits give you an opportunity to get feedback on your progress from the BMT team and to raise any concerns.

The frequency of checkups varies between individuals, but generally they become less frequent as you recover.

If you live outside Sydney, you may need to stay near the transplant centre for several weeks after you leave hospital. Some complications of a BMT, such as GVHD or an infection, can occur after discharge, so follow-up clinic visits allow the transplant team to keep a close eye on you.

The duration of clinic appointments varies. As well as seeing the BMT team, you may need blood or platelet transfusions or IV drugs, which can be done in the outpatient clinic.

It is not unusual to have to be admitted to hospital at some time after your discharge, usually for the treatment of GVHD or infections. Speak with your team about this, as it will be important to understand what this means for you.

It is normal to feel anxious before follow-up appointments, no matter how long it has been since your transplant. Talk about your worries with your doctor. Often just asking can help to put your mind at ease.

Returning to work or study

An important part of going home and being on the road to recovery will be your return to work or study. Your transplant specialist will say when you can do this.

It can be a good idea to initially work part time or reduced hours to see how you manage, and then increase gradually as you feel able. Most people find they can go back to work about 6-12 months after their transplant date. If you can't return to the type of work you did before the BMT, talk to your team social worker about options for financial support and vocation retraining services.

Surviving BMT: recovery and a new 'normal'

Side quote:

'Survival is a privilege beyond price. It is a testimony to the survivor's toughness and resilience, as well as a piece of good fortune. All these things may be true in part but there is another side to survival, and for many people it is a darker side.' (Little et al (2000))

“Surviving Survival, Life After Cancer”

Until recently, most people believed that once medical treatment was over, life could get back to how it was before the diagnosis. Recent research, however, has shown that many people don't simply “get back to normal” after a transplant.

The challenge of a life-threatening illness can leave people with a different sense of what is important in life. People may experience a range of physical, emotional and psychological changes and feel that the stress of treatment has changed their life and relationships.

Some may feel a stronger sense of gratitude for loved ones and find they are more mature, compassionate and accepting of other people and other situations.

Many people find their priorities have changed – that they are different to the person they were before the transplant. They may feel unsure about how they fit into the “post-treatment world”. This sense of unease is normal and is to be expected.

Research has shown that the best thing you can do after the transplant is to accept your new normal, whatever it is, and build on the new reality.

It may take some time to adjust. If you need help to cope, talk to family and friends. It can help to make contact with others who have had similar experiences. Stay in touch with your BMT team and talk to them about how you are feeling.

Side quote

“The single most important strategy survivors indicate is important in making a successful adjustment post-treatment is that of accepting an altered sense of normalcy. The challenge is not to return to your pre-diagnosis self, but rather to accept and build on you new reality.” (Pam McGrath, 19??)

Feelings about surviving BMT

Side quote

“Getting better forced me to re-evaluate everything I'd ever believed in and plunged me into a despair I could hardly contain, let alone explain.” (Miles S 2000)

Many BMT patients find it difficult to describe their feelings about surviving, even to their partners, families or friends.

Many have contradictory emotions about their cancer, their transplant and their ‘new’ self. While most are happy to be alive and to have got through the transplant, some feel scared, confused or depressed. Others may feel guilty about surviving the transplant where other people, some of whom became friends, have not survived. All of these emotions are common.

Fear of recurrence

People who have had cancer often describe a changed relationship with their body. They no longer trust their body or feel they can't rely on it to stay healthy, as it has failed them. This is especially true of haematological cancers, as many have few or no signs of symptoms, and are only revealed by abnormalities on blood tests.

These feelings sometimes become particularly apparent before follow-up visits, which may create significant anxiety. For many people, clinic visits bring fears about the disease coming back, making the time before each visit very stressful.

Many people worry that every symptom they experience, such as a cold or flu, is a sign that their disease has recurred. These are very real concerns, which most people have after BMT and should not be ignored or dismissed.

Altered body image or sense of self

[Side quote]

“I felt that I didn’t belong to either my old life or my new one.” (Miles 2000)

BMT survivors often experience many body changes. With hair loss, weight loss, loss of muscle tone and definition, skin changes from GVHD, chemotherapy or radiotherapy, and the effects of drugs such as steroids, it is little wonder some survivors say they are “no longer able to recognise themselves”.

Your body shape and size will change – sometimes often – throughout the BMT process, mainly because of medication. It is common to experience cycles of weight gain and then loss as your medication regime is changed. This can sometimes be hard but try to remain flexible as your body adapts to the treatment.

Hair loss is one of the most noticeable changes. When your hair grows back, it may have a different colour or texture or it may be significantly reduced. In a few cases, it does not grow back. Ask to be referred to your hospital’s wig library, if you haven’t been already.

Changing relationships after transplant

BMT is not only difficult for you, but for the people close to you. The experience can place great strains on relationships and change them in ways that are difficult to explain or cope with.

Partners live through the experience of treatment and see parts of it that are very frightening. They are also forced to consider the possibility that their loved one may die.

The experience of cancer treatment and BMT disrupts day-to-day roles in relationships. Partners often take on the role of the carer, and may find that the need to provide support at home and at the hospital threatens their work and financial security. All these changes significantly affect the dynamics of a relationship.

Partners may find it difficult to understand or adapt to how the cancer and BMT have changed their loved one. After the transplant, couples may feel like they have to start the relationship again as the experience has changed them both. These difficulties are not impossible to overcome but need time, patience and understanding.

Sexuality

You and your partner may experience problems in your sexual relationships resulting from the treatment process. The treatment involved and the emotional effects of BMT can impact negatively on the way you feel about your body image and sexuality.

The changes that occur in your body may leave you feeling less confident about the way you look. Side effects of the conditioning therapy or GVHD can impair your sexual functioning and libido. These physical effects, fatigue and emotional difficulties can combine to make sex an after thought.

Despite such physical and emotional hurdles, you can still have a fulfilling sex life. Sexuality is not only about you look; it is about who you are and what you feel. It is your touch and warmth – how you laugh and smile, how you care and your personality.

If you want more information about sexual issues, talk to your BMT team. The Cancer Council also has booklets on sexuality for men and women with cancer. Call 13 11 20 for a copy.

Eating well

By the time you leave hospital, you may have just returned to a more normal meal plan. Side effects, such as taste changes and poor appetite, while improving, may last for a long time and make it difficult to quickly regain weight.

It is important to eat well to restore weight, strength and condition, but remember that these are long-term goals. After discharge, weigh yourself weekly to check your progress.

You may need follow-up appointments with the dietitian until your nutritional status has returned to what it was before the BMT. Ask for the contact details for the dietitian before you leave hospital.

Medications, poor diet and illness may also make it difficult to control levels of electrolytes (essential for normal body function), particularly potassium and magnesium.

Your doctor may prescribe oral supplements but you can help by increasing your intake of certain foods that are good sources of these electrolytes.

Potassium is many foods but the best sources are fruits and vegetables including in:

- tropical fruit, such as bananas, mangoes and paw paws
- stone fruit, such as peaches, nectarines and plums
- melons, especially rockmelons and honey dews
- dried fruits, such as prunes, dates and raisins
- fruit juices
- potatoes, spinach, silverbeet and mushrooms
- dried peas and beans
- chocolate (including cakes and biscuits) and licorice
- dried fruits or nuts

- wholemeal bread and cereals
- meat, chicken, fish and eggs.

Potassium is also in drinks including:

- fruit and vegetable juices, vegetable soups
- broths made from meat, vegetable and yeast extracts, such as Bonox and Vegemite
- chocolate drinks such as cocoa, Milo, drinking chocolate
- beer and wine (check with your doctor first).

Magnesium also occurs widely in foods but the following foods are particularly good sources:

- wholemeal cereals and breads (especially wheat germ and bran)
- nuts
- green leafy vegetables
- legumes(dried peas and beans)
- dried fruit
- bananas and citrus fruits.

Diet and GVHD

If you are being treated for GVHD, it is important to continue the safe food hygiene practices recommended in hospital because of the risk of infection.

GVHD of the gut may cause symptoms such as abdominal discomfort, diarrhoea and nausea. You may need to start or continue with dietary changes, such as low-lactose and low-fibre diets, to help control these symptoms.

If any of the following symptoms occur during your recovery period, report them to your doctor or dietitian:

- mouth sensitivity or dryness
- difficulty swallowing food or medications
- weight loss
- persistent nausea or vomiting
- frequent or loose bowel movements or diarrhoea.

Recovery of normal food intake and nutritional condition may be a slow process. However, with regular monitoring and nutrition support, you should be able to adapt and cope with your body's changing nutritional needs.

Possible long-term side effects

Bone problems

Problems with bones are relatively common and are related closely to the amount of prednisone and other steroid drugs given during treatment, although other factors may play a role. The main bone problems are osteoporosis, osteopenia (low bone mass) and avascular necrosis.

Osteoporosis: which means thinning of bones, is a common problem in the elderly. It can happen in young people as well after BMT, causing bone damage and pain. The

use of steroid drugs is the main cause of osteoporosis, but women who develop early menopause after a BMT have the additional risk factor of oestrogen deficiency.

Your doctor will usually order a bone mineral density test about a year after transplant. If osteoporosis is diagnosed, calcium supplements, vitamin D and hormones may be given. Other useful drugs are bisphosphonates.

Avascular necrosis: is a condition that results from temporary or permanent loss of the blood supply to the bones and is also caused by steroid drugs. It results in damage to joints, often hips, and sometimes knees and shoulders. Joint pain is the main symptom. X-rays, MRI or bone scans may be used to diagnose this problem. The treatment is to reduce the dose of prednisone, pain-killing drugs and physiotherapy. Surgery to replace the damaged joint may occasionally be needed.

Infertility

Conditioning therapies can have serious long-term consequences for the endocrine and reproductive systems.

Infertility is a risk with any anti-cancer treatment. In BMT, the high-dose treatment used in myeloablative conditioning treatment will often cause women's periods to stop and reduce or stop sperm production in men. Occasionally, however, sperm production will return after some months or years. The production of male sex hormones by the testes is relatively unaffected, so hormone replacement is generally not required.

In women, the ovaries are usually severely affected. This results in infertility in most women, as well as premature menopause, with symptoms of hot flushes, vaginal dryness, ceasing of menstrual periods and mood changes. This can be diagnosed with a blood test, and is usually treated with hormone replacement therapy.

Although infertility is usual after a BMT, it cannot be taken for granted, so contraception is still needed.

Eye cataracts

Cataracts are a clouding of the lens in the front of the eye and are relatively common 1-2 years after the BMT. The main risk factors are steroid treatment and total body irradiation. The usual symptom is a gradual blurring of vision, especially at night with bright lights. The treatment is to surgically removed the damaged lens and replace it with an artificial lens.

Second cancers

Long-term survivors of BMT are at an increased risk of developing a second cancer, largely due to exposure to strong doses of drugs such as cyclophosphamide and to total body irradiation, which damages the DNA of cells.

The risk of second cancers is not great, but it is enough to justify careful follow-up of BMT patients in the long term.

Skin cancers are a particular problem in Australia because of the high levels of UV radiation, so it's important to stay out of the sun in the middle of the day, and to use sunscreen and protective clothing.

Key points

- Be easy on yourself when you go home. Don't expect too much too soon.
- Your immune system won't be fully recovered until at least 3-6 months after you leave hospital, so it's important to avoid sources of infection.
- When you leave hospital, your transplant team will give you information about how to care for yourself at home.
- You will need to visit the hospital BMT clinic for regular checkups. When you visit the clinic, make sure you report any symptoms. You can also call the clinic to ask about any worries.
- It is normal to feel anxious before follow-up appointments. Talk about your worries with your doctor. Often just asking helps you feel better.
- Most people return to work or study 6-12 months after the transplant. It's a good idea to work part time at first.
- Many people are anxious about their disease recurring after the BMT. This is an understandable concern, which should not be ignored or dismissed.
- There are many changes after a transplant, affecting your physical appearance, your emotions, relationships and sex life. It can take some time to get used to your 'new normal'.
- Medications, poor diet and illness may make it difficult to control levels of electrolytes, particularly potassium and magnesium, which are essential for normal body function. Your doctor may prescribe supplements but you can help by eating foods that are good sources of these electrolytes.
- It may take a long time to get back to your normal eating habits. However, with regular monitoring and support, you should be able to cope with your body's changing nutritional needs.
- Long-term side effects may include bone problems, infertility, eye cataracts and second cancers.

Glossary

allogeneic bone marrow transplant

A transplant that uses stem cells donated by another person.

apheresis machine

A machine like a big centrifuge, which spins blood and separates it into white blood cells, red cells and plasma. It skims off stem cells from donated blood.

aspergillus

A common type of fungus that grows on decaying vegetation, such as compost heaps and fallen leaves. It can also be found in air-conditioning systems and construction sites or where buildings are being remodelled.

autologous bone marrow transplant

A transplant that uses the patient's own blood stem cells.

avascular necrosis

A disease resulting from the temporary or permanent loss of the blood supply to the bones. Without blood, the bone tissue dies and causes the bone to collapse. It usually affects the joints and hips, and sometimes knees and shoulders.

bacteria

Microscopic organisms that can cause infection anywhere in the body.

bile

A thick digestive fluid secreted by the liver and stored in the gall bladder. It aids digestion by breaking down fats.

bilirubin

A by-product of the breakdown of red cells. It can be measured to monitor liver function.

biopsy

The removal of a small sample of tissue to help in diagnosing a disease.

bone marrow

The soft, spongy part in the centre of the bones where blood cells are produced. The bone marrow makes stem cells.

bone marrow harvest

A procedure in which bone marrow is collected from bone while the donor is under general anaesthetic.

bone marrow transplant (BMT)

A treatment option for some people who have life-threatening blood or immune system diseases. It is the process of replacing unhealthy bone marrow cells with healthy cells.

broad-spectrum antibiotics

Drugs that kill a variety of different bacteria.

bronchoscopy

A procedure to look at the lungs and take a biopsy if necessary, using a bronchoscope, which is a flexible tube that is inserted through the nose or mouth and down the windpipe.

Bu/CY protocol

Conditioning therapy with the drugs busulphan and cyclophosphamide.

candida

The common fungus that causes thrush. It normally lives inside the mouth, vagina or gut but beneficial bacteria that also live in these areas keep it under control.

cataracts

A clouding of the lens in the front of the eye.

central line

Also known as Hickman catheter. A catheter that is inserted under the skin of your chest into a vein. It is a long, hollow tube that usually has two or three passages (called lumens) which stays in place during the BMT and is used to collect blood samples and give medications and fluids.

committed progenitor cells

The offspring of myeloid and lymphoid stem cells that can only turn into one type of mature cell.

computerised tomography (CT or CAT scan)

A detailed picture of inside your body, made up of X-rays.

conditioning or preparative therapy

Giving very high doses of chemotherapy drugs, sometimes with whole body irradiation, before a BMT. This kills cancer cells and suppresses your immune system, allowing the donor's cells to engraft and start working in your body.

creatinine

A normal breakdown product of muscle.

CY/TBI protocol

Conditioning therapy with the drug cyclophosphamide plus total body irradiation.

dialysis

A process for removing toxic substances (impurities or wastes) from the blood when the kidneys are unable to do so. A dialysis machine is similar to the apheresis machine, which is used to collect peripheral blood stem cells.

dietitian

A health professional who specialises in human nutrition.

electrolytes

Salts in the blood and other body fluids that carry an electric charge and are mainly responsible for the movement of nutrients into cells and of waste out of cells.

donor lymphocyte infusion

Infusing more donor cells into a patient who has relapsed after BMT to try to reinduce remission.

engraftment

New cell growth. It takes place after the bone marrow transplant when there is a sustained rise in new blood cell production.

extracorporeal photopheresis

A newer treatment for chronic GVHD that involves processing blood through a special machine, separating the white cells and exposing them to UV light before putting the cells back into the body.

Flu/CY protocol

Conditioning therapy with the drugs fludarabine and cyclophosphamide.

Flu/Mel protocol

Conditioning therapy with the drugs fludarabine and melphalan.

gated heart pool scan (GHPS or 'gate')

A test for heart damage done in the nuclear medicine department of the hospital.

glomerular filtration rate (GFR)

A test of kidney function.

graft-versus-host disease (GVHD)

A common complication of allogeneic BMT, caused by the donor's immune cells killing healthy cells after a BMT. Acute GVHD occurs in the first 100 days after the transplant. Chronic GVHD develops more than 100 days after BMT. It is thought to be caused by new T cells that are produced after the donor's bone marrow engrafts.

graft-versus-tumour effect

When the donor's immune cells help a cure by killing cancer cells after a BMT.

granulocyte colony stimulating factor (G-CSF)

A synthetic copy of a naturally occurring bone marrow hormone. It stimulates the growth of bone marrow stem cells and releases stem cells from the marrow into the blood.

haemoglobin

A protein that carries oxygen from the lungs to all parts of the body and gives blood its red colour.

hepatitis

Inflammation of the liver, usually caused by a virus.

Hickman catheter

See central line.

human leukocyte antigen (HLA)

Also known as haplotypes. Proteins that found on almost all the cells in your body. They are one of the main ways your immune system can tell the difference between your own cells and foreign cells, such as bacteria, which should be attacked. The closer the match in HLA types, the better the chance of a successful transplant.

immunosuppressive treatment

Therapy that kills your immune cells so both the donor's blood-forming stem cells and immune cells can become established in your body.

jaundice

Yellowing of the skin, the mucous membranes or the eyes.

lactose

A type of sugar found in milk and some milk products.

leukapheresis

A process in which stem cells are collected or harvested from the donor's blood.

liver

The organ that lies under the ribs on the right side of the upper abdomen and is responsible for a variety of essential functions. Liver cells cleanse the blood of toxins and other waste materials, produce a fluid called bile to aid in digestion and control the excretion of bilirubin, a by-product of red-cell breakdown.

lumbar puncture

A test of the fluid surround the spinal cord and brain (cerebrospinal fluid) for certain diseases. A needle is carefully inserted between the bones in your spine to take a sample of the fluid.

lymphocytes

A type of white blood cell that fights viral infections and helps destroy parasites, bacteria and fungi.

monocytes

A type of white blood cell that ingests and destroys bacteria and fungi, and cleans up cellular debris left behind after infection.

mucositis

A side effect of BMT treatment that causes mouth and throat pain.

mucous membranes

Moist surfaces of the eyes, mouth and gut.

myeloablative treatment

A conditioning treatment that kills the patient's bone marrow cells and cancer cells before a BMT. Also known as a full allo.

neutrophils

A type of white blood cell that ingests and destroys bacteria.

non-myeloablative treatment

A type of conditioning therapy that suppresses the immune system and allows the donor's immune cells to engraft and attack the cancer. Sometimes called a mini-transplant.

nutrition

The process of eating and digesting food the body needs.

nutrition supplement

A food or drink that provides extra energy, protein and/or vitamins.

osteopenia

Low bone density that can be a risk factor for osteoporosis.

osteoporosis

The thinning of bone tissue and loss of bone density over time.

patient controlled analgesia (PCA)

A method of pain control where the patient presses a button on a remote control device to inject a preset dose intravenously.

peripheral blood stem cell harvest

A procedure in which donor stem cells are collected from the circulating blood.

peripheral blood stem cell transplant

A BMT using stem cells collected from circulating blood (the peripheral blood).

platelets

A type of blood cell that initiates clotting to stop bleeding.

pluripotent stem cell

A early-stage cell in the bone marrow that is able to make copies of itself. These cells also make lymphoid and myeloid stem cells, which evolve into the different types of blood cells.

precursor cells

Cells that are almost mature.

protein

An essential nutrient that helps the body build and repair connective tissue, cell membranes and muscle cells.

protozoa

Single-cell parasites which, like viruses, need human cells to replicate.

PUVA

A type of ultraviolet radiation treatment that is sometimes helpful in treating skin and mouth symptoms. PUVA stands for psoralens (P) and UVA (the long wavelength of ultraviolet).

red blood cells

Also called RBCs or erythrocytes. Contain haemoglobin, and transport oxygen to, and remove carbon dioxide from, the body tissues.

septic shock

A life-threatening condition that occurs when an overwhelming infection leads to low blood pressure and low blood flow. Vital organs, such as the brain, heart, kidneys, and liver may not function properly or may fail.

spleen

An organ that collects lymphocytes and destroys blood cells at the end of their lifespan. It is situated high in the abdomen on the left side.

stem cells

Early-stage cells that produce other cells. Each tissue in the body contains stem cells that renew and replace that tissue when needed due to damage or wear and tear. Stem cells generate all blood cells in the human body, including red cells, white cells and platelets.

T cell depletion

A technique used to reduce the risk of acute GVHD, which involves the removal of the donor's T cells from the graft before BMT.

thrombotic thrombocytopenic purpura

A complication that results from changes in small blood vessels, causing clotting and blocking of blood flow.

tissue typing

A process to check how closely your cells match the potential donor's cells. Also known as HLA typing.

total body irradiation

TBI, radiotherapy to the entire body.

total parenteral nutrition

TPN, nutrition that is delivered intravenously

viruses

Tiny parasites that need other organisms (hosts), such as human cells, to survive and multiply.

white blood cells

Also called WBCs or leukocytes. Fight infection and protect the body against foreign organisms.

