



Bone Marrow Transplant
Network N.S.W.



BLOOD & MARROW TRANSPLANT IN CHILDREN

Blood and Marrow Transplant in Children: A Guide for Parents and Other Family Members
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Introduction

This book has been written to provide background information about blood and bone marrow transplants in children and adolescents. While some older children who are receiving a transplant will find the book useful, it is primarily aimed at parents and other family members who wish to understand the transplant procedure. We recognise that the desire and need for information varies widely among families. For this reason, Chapter 1 has been written as a stand-alone chapter, covering the basics of the transplant process. For those who want to know more, detailed information is available in the other chapters.

The chapters in this book cover many important aspects of transplant, from identifying a donor, through to how a transplant happens and what occurs afterwards, the various complications and side effects, and how a transplant can affect the lives of children and adolescents in the long term. As you read through the book, you may find some concepts distressing or disturbing. It is suggested that you talk through these issues with the medical team looking after your child.

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 that are directly relevant. A glossary has been included at the back of the book to help you make sense of key medical terms – where each of these terms is first mentioned in the book it appears in **bold**.

The material covered in this book is, by necessity, general in nature and does not always refer directly to a patient or treatment hospital. The circumstances applying to each child being considered for a transplant vary widely, depending on the age of the child, the underlying disease being treated, the stage of the disease, and treatment that has been given previously. All of these factors will have an important influence on how the transplant is done, the risks, and the chances of success. These issues are not covered in any detail in this book. Each family should go through possible risks and benefits with the transplant doctor responsible for their child's care. A copy of the specific treatment protocol that will be used to guide therapy during the course of the transplant will be available from your doctor.

Foreword

Dear reader,

The transplant procedure usually occurs after a long period of therapy. By this stage, you will be tired and have received significant information surrounding your child's medical treatment, hospital procedures and the risks you live with on a daily basis.

This part of your journey though is very significant and involves acute attention to cleanliness, procedure and child support. This book offers you valuable information. If you are time poor, read the first chapter, if you have time between treatment (as I did), read the whole book and take advantage of the information included. It may assist you to better understand the transplant procedure and its importance.

Many parents research their child's particular illness and you should pay attention to advice from medical staff. This book offers information that either puts your mind at ease or at least offers you guidance on what to ask the dedicated staff at the hospital.

I hope you take the opportunity to read the book and that it assists you with the speedy recovery of your child.

Yours sincerely,

David Marko

Father of Melissa, who participated in the Bone Marrow Transplant Program.

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CHAPTER 1

The Basics of Transplants

A blood or **bone marrow transplant (BMT)** is a medical procedure used to treat diseases once thought incurable. The first bone marrow transplant was performed in 1968 in a child with an inherited immune disorder. Since this time, thousands of transplants have been performed worldwide. In Australia each year, around 1000 children and adults need a transplant. In New South Wales, there are over 300 transplants performed annually.

More recently, scientists have discovered that just like **bone marrow**, blood taken from a vein (**peripheral blood**) or the umbilical cord of a newborn baby (**cord blood**) also contains important cells (**stem cells**) that can be used for transplant. Stem cells are the basic building blocks of the blood and immune system, and are the most vital cells needed for a transplant.

There are lots of different terms used to describe transplants. These include stem cell transplant (SCT), haematopoietic cell transplant (HCT), bone marrow transplant (BMT), peripheral blood stem cell transplant (PBSCT) and umbilical cord blood transplant (uCBT). Throughout this book, the word transplant is used to refer to any of the above.

Why is a transplant necessary?

Transplants can be used to treat cancers, non-cancerous diseases of the bone marrow, immune deficiency and metabolic disorders.

Cancers

The first group of diseases in which a transplant may be the treatment of choice is cancer. In some types of cancer, very high doses of chemotherapy and/or radiation are needed to destroy all cancer cells in the body. However, the high dose or intensity of therapy needed to kill the cancer cells also destroys the patient's own normal bone

marrow cells. We need these bone marrow cells to make the blood and immune cells in our bodies – without them we could not survive.

using high doses of therapy, then giving the patient a transplant to replace destroyed normal blood and immune cells, allows doctors to treat cancer more effectively and improve cure rates.

Cancers treated with transplant may include:

- leukaemia
- neuroblastoma
- lymphoma
- Ewing's sarcoma
- brain tumours
- Wilms' tumour
- rhabdomyosarcoma

Non-cancerous diseases of the bone marrow

Children may be born with a congenital or genetic disease, or later in life may develop a defect in the cells that originate and grow in the bone marrow. This can result in life-threatening diseases such as:

- severe aplastic anaemia
- Fanconi anaemia
- thalassaemia and other haemoglobinopathies
- Wiskott-Aldrich syndrome haemophagocytic syndromes
- severe combined immunodeficiency syndrome (SCIDS)
- chronic granulomatous disease and other rare immune deficiency disorders
- severe autoimmune diseases

A transplant using healthy blood stem cells collected from a donor is used to treat these diseases. There are over 50 different inherited or acquired diseases such as those listed above that may be cured by a blood or marrow transplant.

Metabolic diseases

Children may be born with a disease in which there is a deficiency in the body's ability to produce a specific enzyme. This deficiency may lead to a serious and life-threatening illness. The transplantation of healthy blood stem cells may make available enough of the missing enzyme to slow down or even stop the progression of the illness. The most common metabolic diseases for which a transplant may be used are:

- adrenoleukodystrophy
- Hurler's syndrome
- metachromatic leukodystrophy

Types of transplant

Autologous or allogeneic transplants

There are several different types of transplant. The main difference relates to the source of the stem cell, or said another way, who the donor is. There are two broad categories:

- (1) **Autologous transplant** or 'self transplant'. In this type of transplant, stem cells are collected from the patient at a specific time in the treatment of their disease and cryopreserved (frozen) for future use. Following high dose chemotherapy and/or radiation (see Chapter 7) the cells are given back (re-infused) to the patient.
- (2) **Allogeneic transplant**. In this type of transplant, stem cells come from a donor - someone other than the patient. A donor may be a sibling or other family member, or someone who is unrelated to the patient.

Whether your child needs to have an autologous or an allogeneic transplant will depend on their diagnosis. Some diseases are treated only with autologous transplants, some only with allogeneic transplants and some can be treated with either. Your transplant team will discuss with you the most appropriate type of transplant for your child.

Allogeneic transplants are more complicated than autologous transplants. This is because the stem cells have come from another person and so are recognised by the body as different or 'foreign'. Two consequences can occur as a result of this. Firstly, the patient's immune system may attack and destroy the transplanted cells. This is called graft rejection. Secondly, the immune cells that came from the donor may recognise the patient's organs (particularly the skin, gut and **liver**) as foreign and attack them. This condition is known as **graft-versus-host disease** (GvHD). If severe, this can be life-threatening.

A third situation that can occur is known as **graft-versus-tumour effect**, also called **graft-versus-leukaemia** or graft-versus-lymphoma (GvL). In this situation, the donor's immune cells attack any residual cancer cells in the patient's body. Unlike graft rejection and graft-versus-host disease, GvL is a desired positive effect of the transplant.

In order to prevent or minimise graft rejection and GvHD, donors need to be matched as closely as possible to the patient. Blood tests, called **tissue typing** or Human Leukocyte Antigen **HLA** typing, are conducted to determine whether or not the donor's cells match the patient's. Tissue types are inherited from both parents in four different possible combinations (see Chapter 3). Siblings therefore have a 1 in 4 (25%) chance of being a perfect match.

Because only a small number of patients have a matched sibling donor available, most allogeneic transplants are done using donors who are unrelated to the patient. This is known as a matched unrelated donor transplant, often referred to as a MuD transplant. The cells used for the transplant may come from adult bone marrow or blood donors, or from a public umbilical cord blood bank (see section below). Donors can be located through international bone marrow and cord blood registries. There are over 10 million bone marrow donors and 400,000 umbilical cord blood units available, so the chance of finding an appropriate match for your child is very high.

Bone marrow, peripheral blood and umbilical cord blood transplants – what's the difference?

Transplants can also be categorised according to the type of cells given to the patient. There are three different types of transplants based on the stem cells used:

- (1) Bone marrow transplant (BMT)
- (2) Peripheral blood stem cell transplant (PBSCT)
- (3) umbilical cord blood transplant (uCBT)

Each of these types of cells works in exactly the same way – that is, they replace the diseased blood and immune system of your child.

Historically, bone marrow transplant is the most common type of transplant. Bone marrow stem cells are collected or 'harvested' from a donor using a simple procedure that sucks out marrow cells from the hollow space in the hipbones. This is called a **bone marrow harvest**. This is usually done under a general anaesthetic and is a simple and safe procedure. There are no long-term problems for donors and only minor discomfort for a day or two. Bone marrow can be collected safely from children as well as adults.

Stem cells can also be collected from a vein in the arm, much like when you have blood test, in a procedure called **apheresis**. This type of transplant is called a peripheral blood stem cell transplant. Children having autologous transplants will often have their own stem cells collected in this way, through their **central line**. Occasionally, the stem cells may come from the child's parent who is half matched (haplocompatible); this will depend on the disease and availability of other donors.

umbilical cord blood is a very rich source of stem cells and is now routinely used in transplants in exactly the same way that bone marrow is used. This is called an umbilical cord blood transplant. umbilical cord blood is collected immediately after birth, at no risk to mother or baby, then frozen and stored in cord blood banks around the world. Sydney Children's Hospital houses Australia's largest cord blood bank with over 10,000 frozen umbilical cord blood units ready for use in transplants.

Preparing for transplant

The transplant team

A successful transplant requires an expert medical team - doctors, nurses, and support staff (pharmacist, **dietician**, social worker, physiotherapist, psychologist, occupational therapist, etc) - who are experienced in transplants. The team can promptly recognise problems and emerging side effects, and know how to react swiftly and properly if problems do arise. A good transplant program will also recognise the importance of providing patients and their families with emotional and psychological support before, during and after the transplant, and will make personal and other support systems readily available for this purpose. Other members of the team may include music therapists, play therapists and schoolteachers.

The 'work up'

Your child's general physical condition, their underlying diagnosis and the stage of their disease are all important factors that will determine the type of transplant that he or she will receive.

Before the transplant goes ahead, a number of tests will be carried out to assess the health of your child, particularly their heart, lung and kidney functions. This is an essential first step in the planning of the transplant. These tests include:

- lung assessment - this can include a chest x-ray and/or chest CT (**computerised tomography**) and/or lung clearance scan and/or lung function studies
- heart assessment – this includes a ultrasound of the heart (a cardiac echo) and a recording of the heart rate and rhythm (an electrocardiogram or ECG)
- kidney assessment– this includes a blood test and a test to measure the capacity of the kidneys to excrete waste and toxins (the **glomerular filtration rate** or GFR)
- hearing and vision tests (audiometry and ophthalmological examination)
- dental check.

Other tests may also be needed, depending on the disease and the condition your child is in.

These tests are usually conducted one to two weeks before the transplant, and can often be done in the outpatient's clinic. Younger children may require sedation for the tests.

Children who will be receiving an allogeneic transplant from a donor who is not a matched sibling (e.g. cord blood or unrelated bone marrow donor) may require a 'back-up' collection. This is when bone marrow or peripheral blood stem cells (PBSC) are collected from the patient as a back-up, in case their body rejects the donor cells during the transplant. Bone marrow needs to be collected (harvested) in the operating theatre under a general

anaesthetic, while PBSC can be collected through a central line in a procedure called apheresis. Both procedures are safe and well tolerated. The collected cells are frozen and stored ahead of the scheduled transplant so that they are available if needed. Your doctor will discuss with you if back-up cells are needed for your child and if so, how they are best collected.

Hospital admission and conditioning treatment

Insertion of a central venous line (CVL)

If your child does not already have one, he or she will have a catheter known as a central line or **Hickman catheter** inserted under the skin of the chest. The central line will usually have two openings (lumens) to allow intravenous medications and fluids to be injected, and blood to be taken for various tests. The central line is usually inserted into a large vein



A central line in position

that runs beneath the collarbone, with the tip sitting near to the entry into the heart. The rest of the catheter remains outside the body for easy access. The catheter will be inserted in the operating theatre under a general anaesthetic. The central line can usually be removed about 3-4 months after the transplant, but this will depend on your child's condition and is at the discretion of his or her physician.

Conditioning treatment

Before the transplant can go ahead, your child will first undergo several days of chemotherapy and/or radiation, which destroys the bone marrow and cancerous cells and makes room for the new bone marrow. This is called **conditioning therapy** or the preparative regimen. You may also hear the phrase 'countdown to transplant', because conditioning treatment is recorded in medical notes in terms of the number of days until transplant. For example, Day-5 (minus five) means that you are 5 days away from transplant day, which is called Day 0.

The type and number of days of chemotherapy and/or radiation varies according to the disease being treated and the protocol or preferred treatment plan of the hospital where your child is being treated. The dosage of chemotherapy and/or radiation given to your child during conditioning is much stronger than the dosages he or she may have

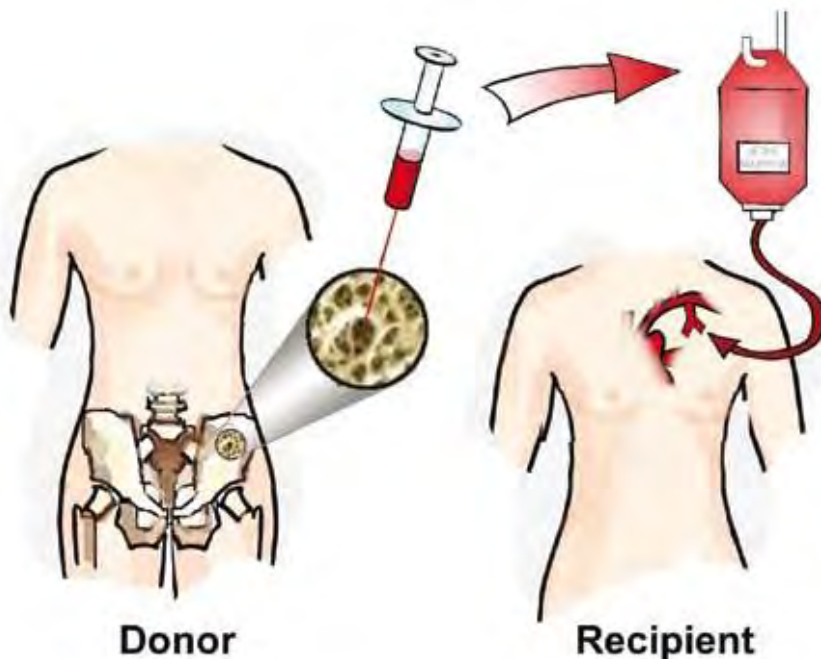
received in previous treatments. Children therefore often feel nauseous and sometimes irritable, although anti-nausea medications will help minimise discomfort. You will also notice that your child's blood counts go down at this time. This is no cause for alarm, as the desired effect of conditioning therapy is to empty the bone marrow in preparation for transplant day.

The transplant

One or two days after conditioning therapy finishes, the transplant will take place. The transplant is not a surgical procedure and can take place in the child's hospital room.

During the transplant, healthy stem cells are infused through the central line, in much the same way that a blood transfusion is given. The transplant does not take long and can seem like an anticlimax after all the build up, although some families find it to be an emotional event. You may choose to take photos or a video of the transplant.

In transplants where the stem cells have been frozen ahead of time, the stem cells are thawed in the child's room and are infused via the central line using a syringe. The preservative that is used to safely freeze the stem cells has an unusual odour, which you will notice within minutes of the infusion beginning. The odour is harmless but will persist for several days. The child is usually unaware of the odour, but visitors will almost certainly comment on it. The preservative often creates an unpleasant taste in the child's mouth and this can make them vomit. Some children find that sucking mints or citrus flavoured lollies helps to disguise the unpleasant taste.



Facial and neck flushing may occur during the infusion, but will go away on its own. You may also notice that your child's urine is dark red following transplant. This is due to the preservative used for the stem cells and is completely harmless. Your child's blood pressure may rise during and after the infusion and sometimes medication may be needed to treat this. Your child may also be given medication before the transplant to prevent a reaction to the transplant, depending on the source of the stem cells.

When the stem cells begin to grow (engraftment)

Engraftment means new cell growth. As a general guide, engraftment is said to have happened once the white blood cell (neutrophil) count rises above $0.5 \times 10^9 /L$. The first two to four weeks immediately following transplant are the most critical. The high-dose chemotherapy and/or radiation given to your child during conditioning will have destroyed the bone marrow, crippling the body's immune or defence system.

While waiting for the transplanted stem cells to migrate to the cavities of the large bones (this can happen within minutes or hours) and engraft (a process that may take between 10 and 28 days, depending on the type of transplant), your child will be very susceptible to infection and bleeding. Multiple antibiotics and blood transfusions may be administered during this time to help prevent and fight infection, while transfusions of **platelets** will be given to prevent bleeding. If your child has an allogeneic transplant, he or she will receive additional medications to prevent and control graft-versus-host disease (GvHD).

Although many infections arise from within the body, a number of precautions will be taken to minimise your child's exposure to **viruses** and **bacteria**. visitors and hospital personnel will wash their hands with antiseptic soap or alcohol rub and, in some cases, wear protective gowns, gloves and/or masks while in your child's room. Any visitors or relatives need to be made aware that they should not visit if they are unwell, for example, if they have a sore throat, runny nose, cold or flu symptoms, stomach upsets or diarrhoea. Fresh fruits, vegetables, plants and cut flowers are not allowed in the patient's room since they often carry fungi and bacteria that can pose a risk of infection. The transplant team will discuss in detail all the requirements for your child's transplant before the transplant goes ahead.

Blood samples will be taken regularly to monitor engraftment, as well as to check kidney and liver function. When the transplanted stem cells engraft and begin producing normal blood cells, your child will gradually be taken off antibiotics, and blood and platelet transfusions will generally no longer be required. Once the bone marrow is producing enough healthy blood cells, your child will be sent home from hospital, unless other complications have developed. Transplant patients typically spend four to eight weeks in hospital.

How your child may feel during the transplant

A transplant is a physically, emotionally and psychologically demanding procedure for your child and your family. *Seek as much help as you need to cope*, because this will help your child cope. During this period, your child may feel sick and weak. They may be clinging and reluctant for you to leave their sight. Walking, sitting up in bed for long periods of time, reading books, playing games, visits from siblings or even watching Tv may require more energy than they have available.

Complications can develop after a transplant such as infection, bleeding, mouth sores (**mucositis**), GvHD or liver disease. These complications can create additional discomfort. Any pain, however, is usually well controlled by medication, which may include intravenous morphine or other strong pain relievers. Mouth sores can develop that make eating and swallowing uncomfortable and difficult. Temporary mental confusion can also sometimes occur and can be quite frightening for the child and/or parents who may not realise it is only temporary. The medical and nursing staff will help you deal with these problems.

Emotional and psychological concerns

Having a child diagnosed with a life-threatening illness is a traumatic experience. Feeling overwhelmed by the amount of information you receive and the need for urgent treatment is common. Each family feels differently and responds differently to these situations. You may find that your family finds some aspects of the treatment process more stressful than others.

It is important to understand that transplant is a team effort and that your child and family are the central people in this team. Understanding your child's treatment plan, and clear communication with the rest of the transplant team are essential elements in maintaining your family's emotional and psychological well-being. Families often comment that it is the unexpected symptom, complication or treatment that upsets or frightens them the most. It is therefore very important that you *do not hesitate* to clarify any aspect of the process that you are unsure about.

People vary in terms of the amount of information they want about the transplant. Some want to speak to others who have been through a transplant. Some want to be well researched on all aspects of the transplant process. Others only want to have minimal facts about their child's proposed treatment. Whichever category you fall into, it will be important for you to have all the information you need, relating to your child's 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 your child against infection whilst his or her immune system is not working properly. Your child will be nursed in a single room,

which can be decorated to make it feel more like home, with a favourite blanket, toys, photos and posters. While visitors will be restricted, lack of privacy is another common issue during transplant, and you may like to talk to your nurse about setting aside some time when your child will be left 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 improve and disappear can be very frustrating and lead to increased stress. Try to remain positive and be realistic in your goals. Transplant 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 transplant. relationships within families are likely to change and recognising this change is important – feel free to talk to the social worker if you need help. Each family member or close friend will cope with the transplant 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 do not care – they may just be taking some time out as their way of coping.

Some families are separated for long periods of time during the treatment process and this can add to the emotional burden. It is sometimes difficult to know how to find time for yourself, your sick child and the rest of your family. If you are finding this to be a problem, feel free to talk to your transplant team.

Having a sick child can also lead to financial difficulties. Please talk to the social worker about ways in which you can be helped.

Psychological discomfort, like physical discomfort, is a normal part of the transplant experience. It is important to know that social workers, psychologists and psychiatrists are also part of your medical team. There is no right or wrong way of managing all the challenges and stresses that transplant presents you with. There is only the method that works best for you.

Going home

recovering from a transplant continues for some months after being discharged from hospital. Your child will need to make regular visits to hospital to monitor his or her progress and to administer any medications and/or blood products needed. Lots of patience and encouragement are required during this time.

Your child's new marrow is still in its infancy and does not provide the normal protection from bacteria and viruses encountered in everyday life. It is therefore important that you protect them from potential sources of infection. Your child can play outdoors and go to the park, but it is important to keep sick friends and relatives away, follow the safe food guidelines and don't take your child to the shops or the movies until you have been advised that it is alright to do so.

Making informed decisions



When a transplant is being considered, there are many issues that need to be discussed and many decisions to be made. You may feel bombarded with a lot of information about the transplant process. Some families choose to research extensively and think through every possible scenario, while others just want enough information for the next day or stage. Other families only want enough information to be informed but choose not to read or listen to anything negative, as this is a time when they need to stay very motivated and focused.

It is important that you are well informed and that you clearly understand what the transplant really means for your child and your family. In order to achieve this, you will need to establish good communication with your transplant specialist and other members of the team. You will find that at your initial visits with your child's specialist, you will receive a lot of information about the proposed transplant treatment, its side effects and possible complications. It is particularly important to consider some of the possible long-term effects of a transplant, such as changes to fertility, growth patterns, IQ or hormonal balance and discuss these issues with the transplant specialist.

To help absorb all this new information, it may be useful to take notes during consultations or to take a tape recorder with you, so that the information can be replayed afterwards. Do not be afraid to ask questions or to request that information be repeated as often as needed. Questions are a good indication that you are working in a partnership with the medical team. It is very important to be involved in your child's care and to express your concerns throughout this process.

Transplant is a team effort, and your child and family are important people in this team. Communication is the key, so remember to keep the medical team informed about your needs. Don't underestimate how crucial your role is as a parent/carer, particularly when relaying information about how your child is feeling and any symptoms that your child is experiencing.

If you decide to go ahead with the transplant, you will be asked to sign a consent form in the days approaching transplant day. Not every family will decide to go ahead with a transplant. After considering all the possible risks and benefits, some families reach the conclusion that transplant is not for their child. In this case, you need to inform your child's specialist and discuss with them what alternative treatments are possible. You can expect your child's doctor to continue to provide your child with the best available form of treatment for his or her illness.

Frequently asked questions

What is a bone marrow transplant?

A bone marrow transplant is a standard treatment option for some people who have life-threatening blood or immune system diseases. A bone marrow transplant is the process of replacing bone marrow cells (stem cells) that are unhealthy, with stem cells that are healthy. The healthy stem cells are re-infused intravenously after very strong chemotherapy and/or radiation to kill unhealthy stem cells. The re-infusion of healthy stem cells essentially rescues the patient from the chemotherapy and/or radiation, by enabling his or her bone marrow to start producing new blood cells.

What is the difference between bone marrow transplants (BMT), peripheral blood stem cell transplants (PBSCT) and umbilical cord blood transplants (UCBT)?

All three types of transplants aim to do the same thing – that is to replace bone marrow stem cells in the patient who has had their bone marrow ablated (destroyed) by large doses of chemotherapy and or radiation. Bone marrow is the spongy substance found in the hollow of bones of the hips, legs and arms. There are cells in the bone marrow called stem cells (you may also hear them called CD34 cells) that produce all the different types of blood cells - **red blood cells** that carry oxygen, **white blood cells** that make up the body's immune system, and platelets that help blood to clot and therefore stop bleeding. 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 hipbone area, is called a bone marrow transplant. umbilical cord blood transplants use stem cells collected from the umbilical cord and placenta at the delivery of a baby.

What is the difference between an allogeneic and an autologous transplant?

An allogeneic transplant involves finding a donor whose tissue type closely matches that of your child. The donor can be related or unrelated. **r**elated donors are usually a brother or sister. If there is no matching relative, the Australian Bone Marrow Donor **r**egistry (ABDM**r**) will conduct a search to find a suitable donor (see Chapter 3). An autologous transplant uses your child's own blood stem cells, rather than those from a donor.

If my child has a common blood group, will they have a common tissue type?

No, not necessarily. There is no link between blood type and tissue type. Tissue type is determined by different sets of genetic **proteins** called human leukocyte-

associated antigens (HLAs) found on the surface of most T-cells. A person's tissue type is identified by a test called tissue typing. A donor can therefore be a bone marrow match for your child even though they may have a different blood group.

Is an operation needed for a transplant?

No, the stem cells will simply be infused through a central line (Hickman's catheter) in the same way that blood transfusions are given.

What is engraftment and when will it happen?

Engraftment means new cell growth. This takes place after the transplant when there is a sustained rise in new blood cell production. This generally occurs within two to four weeks after the transplant. The first obvious sign may be a rise in the white blood cell count. This is an indication that the new bone marrow cells are starting to produce new blood cells. Up until this time, the patient is particularly at risk of infection and therefore needs to be careful of possible sources of infection.

What are the possible side effects of a transplant?

The main side effects caused by the conditioning treatment used in transplants are an increased risk of infection and bleeding. This is due to the high doses of chemotherapy and/or radiation used to kill the unhealthy stem cells. Short-term effects may include nausea, vomiting, fatigue, mouth ulcers, weight loss, hair loss, and skin reactions. Long-term effects may include fertility issues and possible complications in the liver, kidneys, lungs, joints and/or heart. If **total body irradiation** (TBI) is required, possible long-term effects will be discussed with your radiotherapy doctor, before starting the treatment.

Allogeneic transplants carry the risk of a complication called graft-versus-host disease (GvHD). This occurs when the white blood cells from the donor (the graft) identify the cells of the patient's body (the host) as foreign and attack them. This can range from mild, in the form of skin rashes on the hands and feet, to very severe affecting the skin, liver and gut (see Chapter 9).

When will I know if the transplant has been successful?

This is very difficult to answer, as there are many individual issues involved. The outcome of your child's transplant is strongly influenced by the original disease, the stage of the disease and the general condition of your child at the time of transplant. The best person to discuss possible transplant outcomes with is your transplant doctor. He or she can discuss your child's individual factors that may influence the outcome of the transplant.

Resources

CanTeen

Provides support for young people aged 12-24yrs who either have cancer, or are the sibling of someone who has cancer.

Sydney & Central 9382 1563

Hunter & Northern NSW 4927 1500

ACT & Southern NSW 62628133

Website: www.canteen.org.au

Centrelink

Appointments 13 1021

Centrelink multilingual 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

TTY toll free 1800 810 586

Disability, sickness and carers 13 2717

Family Assistance Office 13 6150

Youth and Student Services 13 2490

Web Resources

Sydney Children's Hospital www.sch.edu.au

Children's Hospital at Westmead www.chw.edu.au

Sydney Cord Blood Bank www.sch.edu.au/departments/acbb

Bone Marrow Transplant Network NSW www.bmntsw.com.au

Australian Bone Marrow Donor Registry www.abmdr.org.au

National Marrow Donor Program www.marrow.org

Arrow Foundation www.arrow.org.au

Leukaemia Foundation www.leukaemia.org.au

Cancer Council NSW www.cancercouncil.com.au

Cancer Council Australia www.cancer.org.au

Kids with Cancer www.kids-cancer.org

CHAPTER 2

All About Blood Cells

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



Table 1. Blood cell functions and blood tests

Cell type	Function	Relevant blood tests
red blood cells (rBC), also called erythrocytes	Contain haemoglobin , which carries oxygen around the body. The oxygen is released in the tissues in exchange for carbon dioxide, which is transported to the lungs to be breathed out.	red blood cell count Haemoglobin (oxygen carrying capacity)
White blood cells (WBC), also called leukocytes	To fight infection and protect the body against foreign organisms, including bacteria, viruses, parasites and fungi. Types of WBC include neutrophils , lymphocytes , eosinophils, basophils, and monocytes .	White blood cell count
Neutrophils (Neut/N)	A type of white blood cell able to ingest bacteria	Absolute neutrophil count (ANC)
Platelets	Initiate clotting of blood	Platelet count

Table 2. Blood tests - normal ranges at different ages

Blood test	1 month	1 year	3 years	5 years	9 years	16 years
Haemoglobin (g/L)	102–130	104–132	107–136	110–139	113–143	115–165 (Female) 130–180 (Male)
White cell count (x 10 ⁹ /L)	6.4–12.1	5.4–13.6	4.9–12.8	4.7–12.3	4.7–12.2	3.5–11
Neutrophils (x 10 ⁹ /L)	0.8–4.9	1.1–6.0	1.7–6.7	1.8–7.7	1.8–7.6	1.7–7.0
Platelets (x 10 ⁹ /L)	270–645	205–553	214–483	205–457	187–415	150–450

Blood cell production



The body is constantly producing new blood cells. In healthy children, an estimated 100 billion red cells and 400 million white cells are produced each hour. The vast majority (95%) of the body's blood cells are made in the bone marrow, with the rest being made in the **spleen**. While most blood cells that leave the bone marrow go directly into the bloodstream, **T-cells** (a type of white blood cell) first travel to the thymus gland (hence the name 'T-cells') where they receive further education or programming before being released into the bloodstream.

All mature blood cells are believed to originate from primitive cells in the bone marrow called **pluripotent stem cells**. Pluripotent stem cells are not only capable of making copies of themselves, but also of producing lymphoid and myeloid stem cells, from which the various types of mature blood cells evolve.

Like pluripotent stem cells, myeloid and lymphoid stem cells can make copies of themselves (self-renew) as well as produce offspring that eventually evolve into mature cells. However, their ability to self-renew is believed to be more limited than that of pluripotent stem cells and they are capable of producing fewer different types of offspring. While lymphoid stem cells only produce cells that evolve into lymphocytes (T-cells or B-cells), myeloid stem cells can only evolve into red blood cells, platelets, or white blood cells other than lymphocytes.

Some of the cells that myeloid and lymphoid stem cells produce are called **committed progenitor cells**. Unlike stem cells, committed progenitors are only capable of developing into one specific type of mature cell. Cells passing through the final stages of maturation are called **precursor cells**.

In healthy human beings, the number produced of each type of stem cell and their offspring is limited. Certain proteins (such as interleukins and colony-stimulating factors) play a key role in determining whether a stem cell will copy itself, produce offspring that evolve into mature blood cells, do both, or do neither at any given time. These proteins also control how precursor cells mature. If this regulatory process breaks down, too many or too few stem cells will be present in the bone marrow, and/or a high number of certain progenitor or precursor cells will be made and fail to mature properly. For example, in patients with leukaemia, the white blood cells fail to properly mature. These cells stall at one stage of development and self-replicate uncontrollably.

A transplant enables physicians to destroy a patient's diseased bone marrow with high-dose chemotherapy and/or radiation, then replace it with healthy stem cells that will go on to produce normal blood cells.

Searching for a Suitable Donor

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

What is tissue (HLA) typing?

To determine how well matched a stem cell donor is to a transplant recipient (the person receiving the transplant), a test called tissue typing is done. Your own tissue type will depend on your Human Leukocyte Antigen (HLA) markers. These markers are found on nearly all the cells in your body, and are what enables your immune system know which cells belong in your body, and which do not (such as invading bacteria) and should be attacked. To determine the tissue type (HLA type) of a potential donor, a blood sample is taken and analysed.

Why is HLA typing important?

The outcome of a transplant is strongly influenced by how well the HLA of the donor matches that of the recipient. The closer the donor and recipient match, the less likely it is that the transplant will be rejected.

The function of the immune system is to fight against foreign particles such as bacteria and viruses. If the stem cells used for a transplant are not well matched to the recipient, the recipient's immune system may recognise the transplanted cells as 'non-self' or foreign and attack the cells as if they were bacteria or viruses. This can lead to rejection of the transplanted stem cells. Likewise, the donor's immune cells (the graft), introduced into the recipient's body along with the transplanted stem cells, can recognise the

recipient's cells (the host) as foreign and attack them. This is called graft-versus-host disease (GHvD).

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

How is HLA typing done?

A 10-40ml sample of blood is needed for HLA typing, depending on the size of the child. A further blood sample is collected shortly after this to confirm the results of the first test. Tissue typing is performed by two different methods:

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

When DNA testing is performed, confidentiality is maintained. The DNA is not used for any reason other than tissue typing and ethically approved research purposes, and remains the property of the tissue typing laboratory.

Preliminary tissue typing takes about two weeks. Further high resolution (more detailed) tissue typing of the patient and any potential donor may take another 2–4 weeks. Results of the HLA typing of family members and/or unrelated donors, along with the patient's own HLA results, will be reported to the patient's doctor by the laboratory that performed the tests. The doctor, or the hospital's transplant coordinator, will then inform the patient and family of the results.

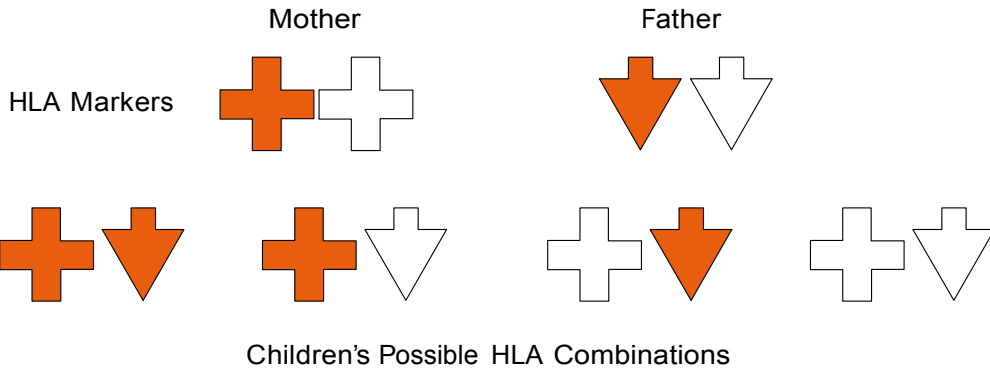
Searching for a related donor

An HLA type is made up of two main groups of markers. These are called Class I antigens (HLA A, B, and C) and Class II antigens (HLA Dr, DQ and DP).

The most important antigens for matching a donor and a recipient are two A antigens, two B antigens, two C antigens and two Dr antigens. These antigens are reported as a series of numbers. For example: A 3, 32; B 7, 37; C 01, 03; Dr 1, 15.

You inherit a set of HLA-A, B, C and Dr antigens from each of your parents. The two sets of antigens you inherit determine your HLA type. Because each parent has two sets (called haplotypes), there are four possible combinations that their children can inherit. This means that each child has a one in four chance of having the same HLA markers as a brother or sister.

HLA matching is not related to appearance or personality, blood group or sex.



Typing family members

The hospital's transplant team will begin searching for a compatible family donor at the request of your child's doctor, usually at the time of diagnosis. HLA typing of family members will be carried out on the basis of their genetic relationship to the patient. Since typing of family members is done systematically, it is best that family members do not come forward for testing without first contacting the transplant coordinator or transplant physician.



Immediate family

To carry out the search for a compatible related donor, the transplant coordinator will need:

- the patient or their representative to approach immediate family members to check their willingness to be tested, and
- contact details for all members of the immediate family.

If a member of the family would like more information about being a donor, they should contact the child's doctor or transplant coordinator *before* they have their initial blood test.

Extended family

An extended family search may be considered if a matched sibling is not found and the patient has at least one set of HLA markers (one haplotype) that is commonly found in the general population.

The search is done systematically, exploring the side of the family from which the least common haplotype has been inherited. The aim is to find a person who has inherited the less common haplotype by descent, but who has inherited the more common haplotype by chance through marriage/partnership. The Australian Bone Marrow Donor registry search coordinator, who is in close contact with the transplant coordinator, coordinates the search.

For an extended family search to be undertaken, the transplant coordinator will need:

- a family tree that clearly shows the relationship to the patient, sex, age and number of children of each family member willing and available for tissue typing
- a designated contact person within the family to liaise with the ABMDr search coordinator
- contact details for all those family members who are willing and available for tissue typing.

Again, if any member of the family would like more information about what is involved in being a bone marrow donor, they should contact either the child's doctor or transplant coordinator *before* they have their initial blood test. It is preferred that family members who do not feel able to donate are not tested, as this avoids potential family conflict. There is absolutely no compulsion to be tested – it is entirely voluntary.

Typing friends

The best chance of finding a matched donor is within the immediate family (siblings). The chance of finding a suitable donor decreases as you move away from the immediate family to the extended family. The chance of an unrelated person (friend) having the same tissue type as your child is actually quite remote.

Friends who wish to be tissue typed as potential donors for your child must be prepared to donate blood at least once and must also be willing to join the Australian Bone Marrow Donor registry and to donate stem cells for any patient in need if required. They cannot be typed for your child only.

Searching for an unrelated donor

What are bone marrow donor and cord blood registries?

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

Over 10 million donors from more than 35 countries are listed on Bone Marrow Donors Worldwide (BMDW), an international database managed by The Netherlands. Of these, more than 400,000 are cord bloods units.

Bone marrow donor registries

Bone marrow donor registries contain the details of volunteers who are willing to anonymously donate stem cells to any patient worldwide in need of a transplant. On joining, preliminary tissue typing of the donor is done and the results are recorded on a computerised database. Australia's registry is called the Australian Bone Marrow Donor registry (ABMDr)

Cord blood registries

Blood collected from the umbilical cord and placenta from newborn babies is a rich source of stem cells, suitable for transplant in children and some adults. Cord blood registries record details of stored cord blood units, donated by mothers at the time that their babies are born.

How are registries searched?

If the doctor considers that your child would benefit from a transplant using an unrelated donor, a registry search will be carried out. The search process is performed by a team that includes the transplant unit staff, tissue typing laboratory staff, and ABMDr coordinators. Parents do not have direct access to registries.



The search process is made up of a number of steps:

1. 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 national office.
2. 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.
3. If a potential donor is not found on the ABMDr, an international search of bone marrow donor and/or cord blood registries may be initiated after discussion with your transplant doctor.
4. A search of the Bone Marrow Donors Worldwide website is conducted, giving an immediate overview of potential donors worldwide.
5. Whether from the ABMDr or one of the international registries, the relevant donor will be selected for confirmation of their tissue type, or for high resolution DNA sub-typing to be undertaken if not already known. Samples are sent to the ABMDr tissue typing laboratory for testing.

Donors are volunteers and may change their mind about donating at any time, up until the time that the patient is admitted for the transplant.

How long does it take to identify a donor?

On average, the time it takes from the start of the search to the identification of a suitable donor is about four months for bone marrow, and 3-4 weeks for cord blood. However this varies greatly, depending on the circumstances. The steps involved in this process and the time involved are outlined below:

- If the donor is member of your immediate family, you will usually know whether the match is suitable within 2-3 weeks of testing.
- The identification of an extended family donor may also be known relatively quickly. However, if your family is widespread or international, the time frame is longer due to the time taken to coordinate the whole process.
- The initial identification of a potential donor from a registry may be very quick if the donor has previously had the high resolution DNA typing performed. Sometimes there are multiple donors identified. However if the potential donor has not had these tests already performed, it may take up to four weeks to find out.
- All initial results must be confirmed, whether or not the donor is a family member. 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 is a family member, the process will usually take about 2-3 weeks.
- Blood samples will be tested for infectious diseases.

Below is an example of a fully matched donor with both Class I and II typing:

Patient	A3, 32; B7, 37; C01, 03; DRBI*0101, 1501
Donor	A3, 32; B7, 37; C01, 03; DRBI*0101, 1501

Sometimes, it is not possible to find a completely matched donor and a mismatched donor must be used. Below is an example of what is called a 'single-antigen mismatch':

Patient	A3, 32; B7, 37; C01, 03; DR1,15
Donor	A3, 17; B7, 37; C01, 03; DR1,15

The transplant doctor will explain the typing results and donor options that are available.

If a suitable donor is identified, what happens next?

The transplant team will decide on the urgency of the transplant, depending on the type and stage of the disease and the patient's condition. If the transplant is urgent, the search coordinator will request the 'work up' of the compatible donor. The work up involves a series of medical tests and appointments to determine the donor's suitability.

If an unrelated donor is identified, but transplant is not urgent, the donor can be reserved for that patient for a period of up to nine months. After that time, the donor is released from the patient search and details of the donor ID, registry and tissue type are recorded in the patient file for easy recall when transplant is ready to proceed.

The ABMDr does not encourage contact between donors and patients. However it is acceptable for a letter to be given to your transplant coordinator to be sent to the donor, provided that no personal details (name, date of birth or address) are disclosed. After a period of 12 months, if both the donor and the patient consent, the ABMDr may release personal details. It is up to the donor and recipient how they wish to proceed. This is a personal decision and one that can carry both positives and negatives.

Sources of Stem Cells

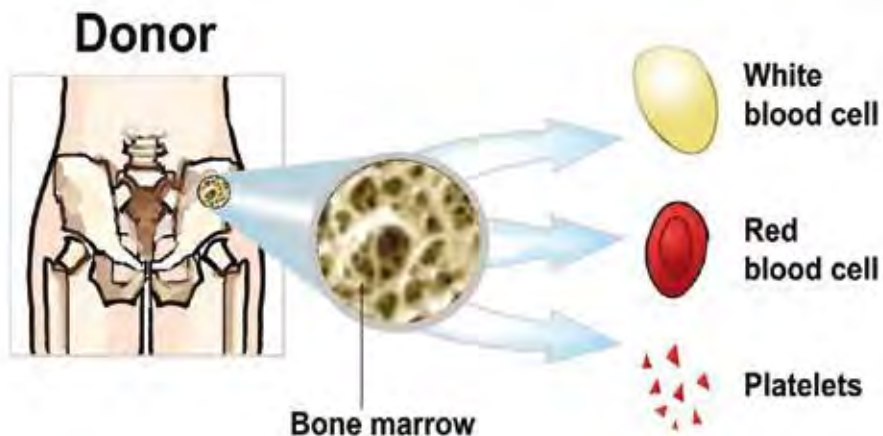
As explained in Chapter 1, there are two categories of transplant. Allogeneic transplant involves using stem cells that have come from a donor. Autologous transplant or 'self transplant' involves using stem cells that have been collected from the patient. Depending on the type of transplant, the stem cells may be collected by different methods.

Allogeneic transplants

The stem cells used in allogeneic transplants may come from a related donor (member of the child's family), an unrelated donor, or cord blood.

HLA matched brother or sister

When the donor is a matched sibling, a bone marrow harvest is usually the preferred method of collecting stem cells. The harvest takes place in a hospital operating room, under a general anaesthetic. It is a low-risk procedure, but does involve some discomfort post operatively (after the operation).



While the donor is under anaesthesia, a needle is inserted into their rear hip bone (iliac crest), an area that contains a lot of bone marrow. The bone marrow - a thick, red liquid - is extracted using a needle and syringe. Several skin punctures on each hip and multiple bone punctures are usually required to extract the amount of bone marrow needed. There are no surgical incisions or stitches involved - only skin punctures where the needle was inserted.

The amount of bone marrow that is harvested depends on the size of the child who will be receiving the cells. The procedure usually takes at least one hour.

When the anaesthetic wears off, the donor will feel some discomfort in their hips. The pain is similar to that felt after a hard fall and can usually be controlled with paracetamol. There may also be some colourful bruising at the back of the hips after the harvest. The donor may require an overnight stay in hospital, but can usually resume their normal activities a few days later.

Partially matched parent

A partially matched (haplocompatible) parent is only used as the donor if no other, more compatible, donor can be found. Every parent is usually half matched with his or her child, since the child inherited half of his or her HLA genes from that parent.

The preferred method of collecting stem cells from a haplocompatible parent is apheresis. This involves being attached to an apheresis machine – a machine that collects blood from a vein, separates out its components, removes the stem cells,

then returns the rest of the blood to the donor. One procedure is usually enough to collect the amount of stem cells needed, although sometimes a second collection (done the next day) is needed.

Stem cells collected by this method may require special treatment before they can be used for transplant. During this treatment, the donor's T lymphocyte cells (a type of cell in the immune system) are removed so that, when transplanted, they cannot attack the patient's cells. This is called a 'T-cell depleted' transplant, and can reduce the risk and severity of GvHD.

The parent needs to begin preparing for the stem cell collection about five days in advance. The stem cell collection centre will prescribe a drug called **granulocyte**



An apheresis machine

colony stimulating factor (G-CSF for short), which is a bone marrow stimulating growth hormone. This is given by injection under the skin once or twice a day. Some parents choose to inject themselves, but others prefer a relative, a nurse, or their local doctor to give the drug.

The parent will usually receive at least four doses of G-CSF before stem cell collection, which takes place on the fifth day. Common side effects of G-CSF include flu-like symptoms (aches, pains and fatigue), which can be relieved by using paracetamol. G-CSF makes the spleen (a large organ under the rib cage) grow in size, and there have been very rare reports of the spleen rupturing in some donors. However, many thousands of donors have received G-CSF without any serious short- or long-term side effects.

Matched unrelated donor

When there is no matched sibling, an unrelated donor search is conducted using the Australian Bone Marrow Donor registry and, if necessary, various international donor registries. The chances of any two unrelated individuals being matched for all HLA genes ranges from one in a hundred to one in a million, depending on how common your child's particular HLA genes are in the general community.

The stem cells provided by an unrelated donor will either come from peripheral blood (collected by apheresis) or bone marrow (collected by bone marrow harvest). Which source of stem cells is used will depend on the request of the transplant doctor and the policies of the donor collection centre.

Umbilical cord blood

umbilical cord blood is a rich source of stem cells and therefore can be used for transplants. Studies in children have shown that that unrelated cord blood transplants and unrelated bone marrow transplants produce equivalent results.

Stem cells from a cord blood bank will be considered in the following circumstances:

- there is no matched sibling donor
- the transplant is urgent.

There appears to be less risk of graft-versus-host disease with cord blood transplants than other types of transplants. This means that cord blood can be used even if it is not fully HLA matched with the transplant recipient.

In some cases, it may be necessary to use two cord blood donations to provide an adequate number of stem cells for transplant.

Autologous transplants

Autologous transplant is the recommended treatment for some childhood cancers. This allows very high doses of chemotherapy (anti-cancer drugs) to be given to the child. Stem cells for autologous transplant may come from peripheral blood or bone marrow.

Peripheral blood stem cell collection (apheresis)

The blood circulating in the veins, peripheral blood, contains small numbers of stem cells called peripheral blood stem cells (PBSC). It is possible to increase the numbers of these cells by administering certain drugs such as G-CSF either alone or in conjunction with chemotherapy. The cells can then be easily collected or harvested by apheresis.

For this procedure, it may be possible to collect the stem cells through an existing Central venous Line (CvL). However this is not always successful for technical reasons, and your child may need to have a stiffened double lumen CvL called a vascath inserted under general anaesthetic.

Before collecting the stem cells, your child will usually be given high-dose chemotherapy. At first, this treatment suppresses bone marrow function. The day after chemotherapy is completed, your child will begin a course of treatment with G-CSF. This is given as a small injection just under the skin. The G-CSF will be given for 10-14 days, stopping only when the stem cell harvest has been successfully completed. The bone marrow will work overtime to produce lots of stem cells. Excess stem cells spill over into the peripheral blood, where they can be collected using the CvL.

In some cases of autologous transplant, the patient's stem cells need to be collected before chemotherapy begins. If this is the situation with your child, he or she will receive G-CSF on its own for four to five days before the stem cells are collected by apheresis.

A number of blood tests need to be carried out before apheresis begins. One such test is called a CD34+ count, which is a stem cell count. The harvest can't be carried out until the CD34+ count reaches a certain level. The apheresis nurse will discuss this with your doctor.

The stem cell harvest will take place in the oncology ward or the day-only unit. Your child may need more than one collection, depending on the number of stem cells that are needed for transplant. Each collection may take up to four hours.

At the beginning of each collection, a nurse will connect a line from the apheresis machine to each opening (lumen) of your child's CvL. The machine draws blood from the child through one lumen, collects the stem cells, then gives the rest of the blood back to the child through the other lumen.

Children who weigh less than 20kg have less blood circulating around their body. In this case, blood that is matched to the child's blood group will need to be added to the apheresis machine.

Any potential side effects of the stem cell harvest, however minimal, will be discussed with you on the day.

During the collection, watching videos and television can help to pass the time, and you may like to bring in games and toys for your child to play with. The play therapist or school may also visit to help relieve boredom.

After the stem cells have been collected, they are frozen (cryopreserved) and stored in the transplant laboratory until your child needs them.



An apheresis machine connected to a child through the CVL.

Bone marrow harvest

If bone marrow cells are needed for the transplant, a bone marrow harvest will take place. The harvest takes place in a hospital operating room, under a general anaesthetic. It is a low-risk procedure, but does involve some discomfort.

While under anaesthesia, a needle is inserted into the rear hip bone (iliac crest), an area that contains a lot of bone marrow. The bone marrow - a thick, red liquid - is extracted

using a needle and syringe. Several skin punctures on each hip and multiple bone punctures are usually required to extract the amount of bone marrow needed. There are no surgical incisions or stitches involved - only skin punctures where the needle was inserted. The amount of bone marrow that is harvested depends on the size of the child, and the procedure usually takes about an hour.

When the anaesthetic wears off, the child will feel some discomfort in the hips. The pain is similar to that felt after a hard fall and can usually be controlled with paracetamol. There may also be some colourful bruising that develops.

Preparing for a Transplant

The 'work-up'

When preparing for a transplant some routine medical tests will be carried out. These can usually be done in the outpatient's clinic, about four weeks before admission for transplant. The tests are to determine that your child's body is fit enough to endure the physical stresses that will be placed on it during transplant.

Some or all of the tests outlined below may be done, depending on the particular disease type. Your doctor will give you more detailed information on the specific tests needed for your child. Please note that sedation may be needed, depending on the age of the child.

Cardiac echo +/- Stress echo

This is a test of the heart's functioning and is done by the cardiology department of the hospital. The test is necessary because certain chemotherapy drugs can affect heart function and any existing heart problems need to be determined before transplant. Also, during transplant your child may be given large volumes of intravenous fluid and it is important that your child's heart is functioning well enough to cope with these extra fluids.

Glomerular Filtration Rate (GFR) +/- DTPA

This is a test of your child's kidney function. Specifically, it measures the rate at which the kidneys can filter and remove waste products. The test will be performed in the nuclear medicine department of the hospital. It is necessary to ensure that your child's kidney function is adequate to cope with the large number of drugs and the volume of fluids that will be required during transplant. If any pre-existing kidney damage shows up in the test, some drug doses may be need to be adjusted.

Lung clearance

This is a test of your child's lung function. To carry out the test, the child breathes a radioisotope or chemical through a mask, then a series of lung scans are done.

Lung function studies

This test measures how well your child's lungs can fill with air and then empty. It is only performed on children who are five years or older, as the child needs to breathe through a mouthpiece.

Chest X-ray

If your child is new to the hospital and has not had a recent chest x-ray, he or she will need to have an x-ray taken to check the lungs. If your child has had serious lung problems before, such as pneumonia, a CT scan of the lungs may also be needed. Your doctor will let you know if this test is necessary.

Sinus-ray

If there is any suspicion that your child has an existing problem with the sinuses, he or she may be required to have an x-ray of this area. It is important that you tell your clinician if you think your child may have chronic sinus problems, as this will need to be fixed prior to transplant.

Dental assessment

Because the mouth is one of the major sources of bacteria that can cause infection during transplant, your child will need to see the hospital dentist before the transplant to check for any cavities or holes. Treatment may be required pre-transplant.

Audiometry (hearing test)

Certain medications can cause some hearing loss. Your child will be given a hearing test before transplant if he or she is receiving such medications.

Ophthalmological exam (eye test)

Your child will be seen by an eye doctor to check vision, and to check behind the eye for infections. Eye drops may be needed to dilate the pupils. If your child is given drops, it is advised that he or she wear sunglasses and a hat to protect the eyes from the sun for six to eight hours afterwards, while the pupils return to normal.

Radiation planning

If radiation is part of your child's conditioning therapy, a planning meeting will be held and the radiation oncologist will discuss with you all the associated issues.

CT scan

A CT scan may be needed if your child is receiving radiation as part of their conditioning therapy. This test will give doctors the information they need to calculate the correct dose for the radiation treatment.

Disease status assessment

All children with cancer need a recent assessment of their disease to be carried out before transplant. Your child may require a bone marrow aspirate and **lumbar puncture** as part of this assessment. If your child has previously had scans (CT scan, Gallium scan, Mri) as part of their normal follow up, these tests will be repeated just before the transplant.

Dietary considerations

If your child is having difficulty eating or maintaining weight, you should arrange an appointment with the haematology dietician in your area.

Good nutrition before a transplant 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
- improving energy levels and ability to cope with the treatment.

Some children may require feeding via a nasogastric tube for 2-4 weeks prior to transplant. For further information on nutrition, see Chapter 8.

Emotional Aspects

The information in this chapter may be relevant before, during and after the transplant. It is important to consider these issues before the transplant, so you can plan for the challenges you and your child may face during transplant.

Having a child diagnosed with a life-threatening illness is 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. Some find certain aspects of the treatment more stressful than others.



Dealing with stress

You don't have to cope alone

Everyone has his or her own way of coping with emotional stress, but you don't have to cope alone. Social workers are an integral part of your transplant team. It is helpful to establish a relationship with your social worker early on in treatment.

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 the challenges and stresses of transplant. There is only the method that works for you.

Focus on your goals

Before admission for transplant, parents need to feel comfortable with their decision for their child to undergo this treatment, recognising and accepting that it may offer the best chance of cure. Coming to terms with this decision can be a very stressful time for you and your family. During the transplant, when your child is very unwell, it will be important to remember why you decided to have the transplant. It can help you see past the setbacks and focus on a brighter future.

Communicating with your team

A transplant is a team effort. understanding your child's treatment plan and communicating clearly with team members are essential. *Remember, don't hesitate to clarify any aspect of the process you are not clear about.* It is important that you have all the information you need.



Before proceeding to transplant, you will be asked to participate in a formal meeting with your child's transplant team. This is to ensure that you fully understand all the potential risks and benefits of the treatment. Depending on your child's age, he or she may also be required to join in the meeting.

Privacy

Your concept of privacy may change once you have spent some time in hospital. You may feel that your family are living in a fish bowl, always visible and visited by a range of hospital staff. Privacy is one of those things that is unique to the individual. On some days, particularly when you and/or your child are feeling vulnerable, privacy can become very important. Nurses, specialists and cleaners can constantly interrupt you when you are trying to have a private phone conversation or some personal time with your child.

There are strategies you can use to try to create some privacy. Discuss this issue with the nurse looking after you and work out some time during the day that you can set aside to minimise disturbance to you and your child. There are signs that can be put on your door, and if you need time alone with no phone calls, you can disconnect the phone.

You may choose to organise a 'telephone chain', so that one or more relatives or friends can keep others informed and relay messages of support without you having to answer endless calls.

Impact on relationships

Role changes

Not surprisingly, transplant 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 become the main carer for the rest of the family. There can be other changes to the position and the roles that people have in a family.

The experience of caring for a seriously ill child and being away from home can alter the relationships you have with your loved ones. Because of the hospital stays and recovery time involved, your partner and others in your family may take on some of your usual day-to-day roles.

It is important that you and your family discuss these changes and recognise that they are essential, even if they are difficult for some members of the family, especially siblings. 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. Parents have different ways of coping when their child is going through a transplant. Some need to talk openly about their 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. It is important to respect different ways of coping – one way is not necessarily better than another. Try as much as possible to keep the lines of communication open with family and friends throughout the transplant process.

It can be stressful and tiring to be the main carer for your child, and to see them distressed and in discomfort. At times, you may feel frustrated at not being able to comfort them. Sometimes they will seem dependent on you for their care, while at other times they may not respond to you. Remember that if they don't respond or they reject your affection, this does not mean that they do not want you by their side. It is a fine balance.

It is vital to look after yourself if you want to properly care for your child throughout the transplant. Ensure you get regular breaks and have your own support in place, including close family and friends where possible. Support services to help you care for your child, such as ward volunteers or ward grannies, are available. The transplant team can help organise this for you.

Talking to your child and his/her siblings

It is difficult to know how to talk with your child about the transplant and about being in hospital for long periods. However, it is important to always be open and honest with him or her. As a parent, you have the best understanding of your child and their strengths and needs. If you need help, the transplant nurse coordinator and/or social worker in your team can give you information and support.

Protecting children by not telling them about their transplant can sometimes make things worse, because children often imagine things that are worse than reality.

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

Your child's understanding and ability to cope with the transplant process may depend partly on their age, and you may see changes in your child's behaviour during this time.

Changes in your family

Not surprisingly, transplant does affect relationships within families. Some family members will find that their main role changes. This may include temporarily not being the primary income earner, or the main carer of children. There may be other changes to the position and/or roles that people play within your family unit. The reality of long hospital stays can mean that the family is geographically divided, particularly if you live outside the Sydney metropolitan area, or interstate. This is particularly difficult when you have other children.

It is important that you and your family discuss these changes. recognise that the changes are inevitable and also that they may be difficult for some members of the family. Discussing these issues with your social worker can be helpful.

Transplant and child development

Disruptions to development

There are a number of factors involved in transplant that have the potential to adversely affect your child's development. These include:

- the imposition of a prolonged stay in an isolation room in hospital
- reduced social contact
- reduced sensory stimulation
- inhibition of motor activity
- increased dependency and a loss of a sense of control
- loss of privacy
- physical discomfort and pain
- changes in physical condition and appearance
- prolonged disruption of normal eating habits
- difficulties taking oral medications
- awareness of the seriousness of the disease and the possibility of a shortened life span
- awareness of the life-threatening nature of transplant and the uncertainty of its outcome.

Normal development can be disrupted during and following transplant, because isolation and illness reduce the opportunity your child has to engage in activities that are normal for their age. Emerging skills can be delayed, and newly acquired skills can be temporarily lost due to lack of practice. While the impact of transplant varies according to age, and from child to child, you can help minimise the effects by giving your child as many opportunities as possible to do the things they would be doing, were they not in transplant.

Babies and toddlers

In the case of young babies and toddlers, certain constants are needed for normal development. These include a primary caretaker, consistency in caretaking, and opportunities to explore and interact with the environment.

Where possible, you can minimise transplant-related disruptions to the development of your baby or toddler by:

- encouraging him or her to play and interact with their environment
- regularly holding, cuddling and talking to him or her
- maintaining the primary caretaker's nurturing role, while making sure there is opportunity for time out when needed
- keeping the number of other caretakers to a minimum.

Pre schoolers

For normal development, pre-schoolers need behavioural boundaries as well as support for their efforts toward independence. They also need socialisation with peers and adults outside of the family.

Where possible, you can minimise transplant-related disruptions to your preschooler by:

- keeping the time that he or she is separated from the primary caretaker and other family members to a minimum
- developing a plan to help him or her cope with medical procedures
- avoiding pampering, over-protecting and overindulging him or her
- reassuring and encouraging him or her in the event that recently acquired skills and motor functions are lost
- providing opportunities for play (especially play that involves peer interaction and/or development of motor skills).

Primary aged children

Primary school-aged children need a number of things to develop normally. These include participation in formal school and other social settings, opportunities for developing their skills, opportunities to experience success, for comparison of self with peers, and social acceptance.

You can help minimise transplant-related disruptions to the normal development of your primary school-aged child by:

- keeping the time that he or she is separated from the primary caretaker and other family members to a minimum
- developing a plan to help him or her cope with medical procedures
- encouraging open discussion about his or her illness and treatment
- encouraging interactions with peers both in and out of hospital
- encouraging a return to normal chores and responsibilities as soon as possible
- encouraging a return to school and extra-curricular activities as soon as possible

- preparing your child and the school for his or her re-entry
- recommending that teachers do not lower their expectations of your child
- helping your child to achieve his or her potential
- getting help for your child if he or she feels behind with schoolwork.

Adolescents

For adolescents to develop normally, they need to be able to achieve a stable identity or self-image, adjust to their own sexual development, enter into mature relationships with peers, achieve independence from their family unit, and begin to prepare for their future (for example, by making decisions about a possible career path). Adolescence is a difficult period of life. Most adolescents are concerned about their body image, privacy, independence and freedom. They need affirmation from their peer group that they 'fit in', and they need to feel able to pursue social, romantic and sexual experiences.

You can help minimise disruptions to the normal development of an adolescent who needs a transplant by:

- being aware of, and respectful of, his or her needs and concerns
- making sure you communicate openly and discuss things in detail throughout his or her treatment
- discussing the likely outcome of treatment, and outcomes in the future
- allowing him or her to have as much input as possible into plans for their care
- encouraging self-care and as much autonomy as possible
- helping them develop self-control strategies to use during various aspects of treatment (for example, during medical procedures)
- striving to return to normal activities and school attendance as much as possible
- encouraging him or her to explore new areas and to gain new expertise or mastery in cases where a return to some prior activities is not possible
- addressing concerns about body image
- exploring ways to 'look normal' despite changes to appearances
- discussing with other adolescent patients, and/or other peers, ways to cope with feeling as though he or she is different.

Music therapy

Music therapy is the planned and creative use of music to address the physical, emotional, intellectual and/or social needs of an individual. The registered music therapist at the hospital is a university-trained professional, who uses the medium of music to achieve positive therapeutic outcomes.

Music therapy can help children and adolescents cope with the hospital environment by providing a sense of familiarity and security. As music is often a natural part of a child's life, its use in hospital can provide links to home, family, friends and school.

During your child's transplant period, the music therapist may:

- encourage him or her to express feelings about hospitalisation in a creative and non-threatening way
- promote coping skills by allowing him or her to exercise some control of musical activities and games
- alleviate stress and anxiety, as well as control pain through distraction and/or relaxation
- facilitate social interaction between the child, family members and staff.

There are lots of different activities that the music therapist may engage your child in:

- singing familiar songs
- action songs and games
- playing musical instruments
- creative musical improvisation
- music and storytelling
- music and relaxation
- song writing and audio recording
- digital video recording and editing of familiar and/or original compositions
- ongoing musical stories ('songstories') created with and for the child
- listening to and discussing song lyrics
- accessing the music therapy CD library.

The Engraftment Song (sung to the tune of "Dancing Queen" by ABBA)

Grow, white cells grow

Don't be slow

O-o-h make a show

White cells grow

Feel the glow

In your bone marrow

Oh yeah

You can grow

And multiply

White cells, come on, don't be shy

O-o-h, sing out loud

Sing out strong

Sing the Engraftment song!

© 2001 Lyrics – verena Clemencic-Jones, rMT

Play therapy

When your child goes into an isolation room for the transplant, he or she will be able to participate in a variety of experiences and activities led by the play therapist. The play therapist's role is to support your child through the transplant process. This may involve:

- organising experiences and activities that help to distract your child, so that the days may not seem so long
- working with your child to find strategies to reduce stress and anxiety
- helping with relaxation therapy by using videos and CDs
- providing diversion therapies during unpleasant activities, such as the insertion of a nasogastric tube or a finger prick, using music, games, visualisation or just talking.

Here are some ideas of things that you and/or your child may like to do during transplant. Have a look at the list and talk to the play therapist about different options.

- Make a book or keep a journal about the transplant process and what happens each day, including photos.
- Work on a project together.
- Paint your own picture or window.
- Make plaster moulds and ceramics.
- Draw, or colour-in pictures.
- Make a collage (by cutting and sticking shapes or pictures together).
- Make picture frames, door signs, cards, necklaces, bracelets, or other things.
- Do a puzzle, build things using lego, ello or mobilo.
- Do some 'medical play' – use medical equipment and learn about the stay in hospital.
- Blow bubbles.
- Play with cars, train and farm sets, dinosaurs, dolls and dolls' houses.
- read a book or magazine.
- Play a board game or other games.
- Make something out of papier mache.

Practical issues

Personalising your child's room

You are encouraged to personalise your child's transplant room so it feels more like their space, and allows them to feel connected to life outside of the hospital. Personal possessions such as doona covers, toys, posters, photos, CDs, DVDs, game boys etc can help provide comfort and reassurance.

The play therapist can assist you in decorating the room. Please discuss this with the transplant coordinator before the transplant. A favourite stuffed toy or blanket is allowed, but it must be thoroughly washed and dried immediately prior to transplant. Plants and fresh flowers are not permitted in the room.



An isolation room

Financial considerations

If you have had to relocate for your child's treatment, the costs associated with living in Sydney and maintaining another home elsewhere can be considerable. Your social worker can assist you with any difficulties you may be experiencing.

Schooling for siblings

It is a Department of Education requirement that school-age children attend school. Schooling for siblings can be arranged through the hospital's schoolteacher and social worker.

Facilities in the hospital ward

On the transplant ward there are kitchen facilities for use by families. The kitchen contains a microwave, oven and stove. The ward also has laundry facilities, which can be used for the patient and family's clothing. Each transplant room has a microwave and a small refrigerator for your family's use. Of course, each transplant unit is slightly different, depending on the hospital.

Conditioning Therapy and the Transplant

As discussed in Chapter 1, conditioning therapy, also called preparative therapy, is a crucial part of the transplant process. This usually starts 1–2 weeks before the actual stem cell infusion. For some types of transplant, conditioning may only take a few days. This period of time is sometimes referred to as ‘the countdown’.

Allogeneic transplants

In allogeneic transplants (transplants using a donor), conditioning involves giving one or more high dose chemotherapy agents, with or without total body irradiation (TBI). Your child may not have received some of these chemotherapy drugs before. The choice of conditioning therapy will depend on the disease being treated.

The goals of conditioning therapy before an allogeneic transplant are:

- to kill off any residual cancerous cells
- to create space for the donor cells in the bone marrow
- to suppress the immune system to allow the donor cells to engraft (grow) and begin producing healthy blood cells.

Myeloablative therapy

The most commonly used conditioning therapy is called **myeloablative therapy**. This therapy aims to totally eradicate the patient’s existing bone marrow.

Reduced intensity therapy

Some people are unable to tolerate myeloablative therapy, and in such cases, ‘reduced intensity therapy’ is used. As the name implies, the doses of drugs and radiation used are reduced and do not necessarily kill all the patient’s stem cells, nor does the treatment have as strong an effect on the patient’s cancer. Instead, intensive immunosuppressive

treatment is given (treatment to destroy the patient's immune system) which allows the donor's immune system to take over after transplant. The concept behind this treatment strategy is to rely on the graft-versus-tumour effect to cure the cancer.

Autologous transplants

In autologous transplants (transplant using the patient's own cells), conditioning therapy involves giving one or more high dose chemotherapy drugs.

The goal of conditioning therapy in this situation is to kill off any residual malignant disease (cancer), then 'rescue' the patient with his or her own stem cells, which have been collected and stored earlier on.

For information on specific drugs your child may be given, please see the Appendix at the back of the book.

Collecting the stem cells

The sibling donor

If the donor for your child's transplant is his or her brother or sister, and they are over the age of 10, they may be required to donate a unit of their own blood (autologous collection) about a week before stem cell harvest. This purpose of collecting the blood is to use it to infuse into the donor at the time their stem cells are being harvested. If such a collection is necessary, your doctor and transplant coordinator will discuss this with you.

If the donor for the transplant is a child, he or she will be admitted to either the transplant ward or another ward at the hospital. A paediatrician at the hospital will independently assess him or her, but the actual harvest will take place under the direction of the transplant team. If the donor is an adult, they will be referred to an adult haematologist.

Bone marrow harvests are performed under general anaesthetic in the operating theatre. The donor lies on his or her stomach, while the transplant team collects marrow from the back of the hipbones. The process usually takes 1–2 hours, depending on the amount of marrow needed. In general, about 15ml of bone marrow is needed for every kilogram of the recipient's weight. The marrow, which looks like thick blood, is put into a bag containing an anti-clotting agent. Inside the donor, new marrow cells grow over 1-2 months to replace those that were taken.

The donor will wake up in the recovery room before being taken back to his or her hospital bed. A large bandage will cover the area where the marrow was taken from – this will remain in place for at least 24 hours. A number of needle insertion marks will be visible

on their hips, and they will be sore and bruised following the donation. The amount of pain varies from donor to donor. It usually lasts 1 or 2 days, but can last longer. Medication will be given to relieve the pain.

There are generally no long-term effects of donating bone marrow. The donor will be discharged the following day and may require iron supplements for several weeks.

Unrelated donors

For unrelated donor transplants, the procedure is similar to that outlined above. The main difference is that the collection will take place at the hospital nearest to the donor's home. The stem cells will then be transported to the recipient's hospital, where the laboratory will process them before they are given to the patient. unrelated donors may choose to donate bone marrow or peripheral blood stem cells.

Cord blood



Cord blood

Cord blood used as a source of stem cells is collected at the time of birth, frozen and stored in cord blood banks throughout Australia and the world. The selected cord blood is transported to the recipient's hospital before conditioning therapy begins. The blood remains frozen until the day of transplant, when it is thawed.

On the transplant day

On the day of the transplant (Day 0), your child will receive the stem cells collected from the donor. The stem cells are stored in a special bag and are given to your child in their room, through their central line. If conditioning therapy consisted of chemotherapy, the stem cells will be given 24 hours or more after the chemotherapy ends. If conditioning involved total body irradiation (TBI), the stem cells can be given immediately after TBI is finished.

If the stem cells or marrow are from a matched sibling, they are infused in a similar way to a blood transfusion. If the stem cells are from an unrelated donor or a parent, they may be treated in the laboratory to remove the T-cells (one type of immune cells) to reduce the risk of graft versus host disease. This process may take six hours or more.

If the stem cells are from cord blood, or if it is an autologous transplant, the stem



cells are thawed in the hospital room and given via the central line. The preservative (called DMSO) used to protect the stem cells during freezing and thawing has an unusual odour, which you will notice within minutes of the infusion beginning. The odour, which will be on your child's breath, is harmless but will persist for several days. The preservative usually also gives the child a bad taste in their mouth, which may make them feel like vomiting. If this is the case, it may help if they suck lollies or strong mints, or chew gum, to disguise the taste. Your child will be monitored before, during and after the stem cell infusion, as the DMSO can cause high blood pressure. This sometimes needs to be treated with medication.

Transplant day is often a very emotional day for families, especially when the donor is a sibling, and you may choose to have a camera on-hand to record the event.

After the transplant

Within hours of the transplant, the new stem cells will find their way to the recipient's bone marrow where they will grow and start making new blood cells. It will take the new stem cells about 10 to 28 days to 'bed down' and start producing new blood cells. This is known as engraftment.

Signs that the stem cells are starting to grow are a gradual increase in the white blood cell count, often associated with an improvement in mucositis. Once the cells start to engraft, the rate that the total white cell count continues to rise can vary. This is normal in all patients undergoing transplant. The most important thing is that there is an overall trend upward. This can feel like a roller coaster ride for families watching and waiting.

The time it takes new platelets to grow is much longer than for white blood cells, so the platelet count may remain low even when the white cell count is normal.

Side effects of transplant

Unfortunately the process of transplant is often accompanied by a number of unpleasant side effects. The most common of these, and how they can be controlled, are described below.

Bone marrow suppression

Within several days of completing the conditioning therapy, your child will have a very low white blood cell (WBC) count. This condition is referred to as neutropenia. During this time, it is likely that he or she will develop a fever and intravenous antibiotics will be needed.

The infections that are most common at this time are bacterial infections. The intestinal tract (gut) is often not intact, because of small abrasions from the mucositis, and the bacteria in the intestinal tract can get into the blood stream. Without neutrophils (a type

of white blood cell) it is difficult for your child to fight off these infections, and the only way to treat these infections is by intravenous antibiotics. Your child will need several different types of antibiotics to fight the infections, and may need a change in antifungal medications as well.

Sometimes, fevers can persist for many days. While bacterial infections are treatable, an infection can be life-threatening and possibly even fatal. The longer a child is neutropenic, the higher their risk of having a life-threatening infection.

Your child will also need platelet and red blood cell transfusions to make sure they have safe haemoglobin and platelet counts. Before engraftment has had time to take place, bleeding is a potential problem, and platelet transfusions help avoid this problem. While your child is waiting for their new stem cells to engraft, platelet transfusions will be given routinely to maintain the platelet count above 20,000. red blood cell transfusions will also be given to maintain a haemoglobin level of 70-80g/L. All red cells and platelets are irradiated in the blood bank before they are used for transfusion. As your child's new stem cells begins to engraft, the need for blood and platelet transfusions will decrease.

Nausea and vomiting

Many of the treatments given as part of your child's transplant can cause nausea and vomiting. There are a number of drugs available to control nausea and/or vomiting and sometimes it can take a while to find the combination that works best for your child. As soon as the conditioning therapy begins, your child will be given regular anti-nausea medications and these will continue as necessary.

Diarrhoea

Just as for nausea and vomiting, many of the treatments given to your child during transplant can cause diarrhoea. Infections and GvHD of the gut can also cause severe diarrhoea. Stool specimens will be collected regularly. Large amounts of fluid can be lost very rapidly as a result of diarrhoea, so it is very important that all nappies and bed pans are kept so that the nurses can assess and measure your child's output.

Pain

Children who undergo transplant experience varying degrees of pain. Your child's pain and their need for pain relief will be assessed regularly throughout the day and night, and pain relief will be given as required. Most children, at some time during transplant, need intravenous analgesics (pain relievers) such as morphine or fentanyl via their central line.

Mucositis

Mucositis is painful ulceration of the mouth, throat and gut, caused by conditioning therapy. It is often accompanied by large quantities of very thick and sticky saliva, which may be difficult to swallow due to pain and/or swelling of the mouth and throat. For many children, mucositis is the most distressing side effect of the transplant.



Mucositis can make eating and drinking difficult, or even impossible. In most cases, children require feeding by a nasogastric tube and/or a tube fed through a vein – this is called intravenous **total parenteral nutrition** (TPN). Mucositis can also cause cramping, abdominal pain and diarrhoea.

Hair loss

Your child's hair will fall out as a result of the conditioning therapy. The time taken for this to happen will depend on the treatment they are given. Although hair loss can be distressing, remember that it will grow back over time.

Nutrition

Nutrition before transplant

Good nutrition is essential for your child's normal growth and development. During a transplant this is even more vital, as it can help your child's body cope with the side effects of treatment. It is important for your child to be well nourished and as close to their ideal weight as possible before they enter transplant. The dietitian can help your child reach this goal by reviewing their nutritional status.

The role of the dietitian

The dietitian's role is to make sure your child receives the best nutrition they can to help engraftment, minimise side effects, and achieve normal growth and development during the transplant period. The dietitian will assess your child's current growth, and during transplant, will provide nutrition in the means that is best suited to your child's needs. This may be oral (through the mouth), enteral (through a tube) or total parenteral nutrition (into a vein), or a combination of these. You will meet the dietitian when your child is admitted to hospital for the transplant. If you are worried about your child's nutrition or growth before this time and would like to see a dietitian earlier, just ask your doctor, clinical nurse coordinator or social worker.

The importance of food safety

During a transplant, your child is less able than normal to fight off infections. Many of the normal bacteria found in food can cause your child to become ill. Two common types of bacteria found in foods are Salmonella and Listeria. Good food hygiene is very important to minimise the risk of contamination of food with these bacteria, which can lead to infection. Food safety involves using the correct methods to cook, store, prepare and transport food. It also means avoiding certain foods. These restrictions begin from

the beginning of the transplant period. Your dietitian will give you information about food safety once you come into hospital.

The impact of side effects

Due to the chemotherapy and/or radiotherapy your child receives as conditioning therapy, he or she may develop side effects, such as:

- loss of appetite – not wanting to eat and/or only being able to eat or drink small amounts before feeling full
- mucositis – difficulty eating due to pain in the mouth and throat
- taste changes and/ or a dry mouth
- diarrhoea – this may lead to not wanting to eat because of the stress or discomfort caused
- nausea and vomiting – the sight and smell of food may make your child feel sick.

These side effects make it harder for your child to achieve a balanced diet. This is very normal and can be managed.

Poor appetite

Your child is likely to experience a poor appetite early on during the transplant period. It is fine to offer your child food and drinks, but it is important to realise they may not want anything in their mouth at all due to the side effects of the treatment. Don't let meal times become a battle. Instead, offer small amounts of food during the day instead of large meals, as too much food on a plate can be off-putting. Try to make meals fun and relaxing and, when you can, eat with your child as this can encourage them to eat too. Nutritious drinks can also be used as a supply of much-needed calories and nutrition while your child's appetite improves. This is something your dietitian will talk to you about during the transplant.

Dealing with mucositis

During treatment, the cells in the mouth, throat and anywhere down the digestive tract can become damaged. This is why your child may feel pain anywhere from their mouth to their bowel. Swallowing can also be painful, and this can be a reason why he or she may not eat enough to meet nutritional requirements.

Children with mucositis may find eating and drinking too painful and will require enteral nutrition (tube feeding) or total parenteral nutrition (nutrients given through a vein). If your child is able to eat and/ or drink, he or she should choose soft, bland and moist foods. Adding extra moisture such as sauces to foods should make them easier to swallow. It is best to avoid spicy or salty foods as these may sting the mouth. Your child

will be the best guide as to the most suitable temperature of foods. very hot or very cold foods may be uncomfortable to eat.

Special nutritional supplements may be recommended by your child's dietitian to help provide adequate calories, protein, fat, vitamins and minerals.

Preventing weight loss

Children in hospital undergoing transplant are usually weighed daily so that their fluids can be monitored. Weight loss in the form of body fat and/or muscle mass is usually due to not eating enough to provide the body with the energy it needs. The energy requirements of children receiving a transplant are higher than the average child.

If your child is able to eat but is losing weight, here are some strategies to try.

- Encourage him or her to eat small, frequent, nutritious meals.
- Increase the calories in his or her food and drinks by adding fats (such as margarine, cheese, mayonnaise), carbohydrates (such as sugar, honey), and protein (such as skim milk powder, cheese).
- Limit non-nutritious and low calorie foods and drinks such as soft drinks and cordials.
- Try nutritional supplements as recommended by the dietitian.

While weight loss can occur quickly, weight gain can take a lot longer, so it is important to take action early on.

Diarrhoea

If diarrhoea becomes a problem, offer your child small frequent meals, and avoid foods with too much fibre or fat as well as those that are very spicy.

Fluids are particularly important if your child has diarrhoea. Choose hydrating fluids such as water, or diluted fruit juice. A low lactose diet may also be needed. Speak with your doctor or dietitian before making any dietary changes.

Taste changes

Don't be surprised if your child tells you that all their favourite foods taste strange or have no flavour. This is normal and will slowly improve. During this time, encourage him or her to eat foods with lots of flavour such as salty or savoury foods (if there is no mucositis). If drinking fluids becomes a problem, try getting your child to drink through a straw, as this will help by-pass their taste buds.

High protein foods such as meat and dairy products can often have a metallic taste. It may take time and encouragement for your child to want to eat these foods again.

regular mouth washes and good oral hygiene will help minimise taste changes.

Nausea and vomiting

Many children experience nausea and vomiting both during conditioning therapy and the transplant. Here are some hints to help you to encourage your child to eat.

- If your child is afraid of vomiting, tell them that, while unpleasant, it is not serious and should stop by the end of the treatment. It is not a sign of their illness getting worse.
- Foods rich in fat, such as fried foods, chocolates, and takeaway foods, can increase nausea and so are best avoided. Be guided by what your child wishes to eat.
- Your child may prefer to eat foods that are cold and without much smell, such as fruit, jelly or bread.
- Keep small snacks available for when your child feels able to eat.
- Avoid giving favourite foods when your child is experiencing nausea or vomiting, because this may result in a long-term dislike of that food type.

Encouraging your child to eat

Parents often ask for strategies to encourage their child to eat. It is important to find ways of encouraging your child without them feeling bullied or force-fed. If your child feels bullied into eating, he or she may see eating as a chore, rather than an enjoyable experience. Offering your child small amounts of food is less overwhelming than larger portions. It is also better to only offer two or three choices of food at a time. The dietitian will help develop strategies for your child if poor eating is an ongoing problem.

Think about why your child may not want to eat. Is he or she experiencing taste change or mucositis? Is nausea an issue? Does he or she associate food with vomiting? Understanding why your child is not eating may help you decide which strategies to try.

During transplant, most children find it difficult to eat and will require enteral and/or parenteral nutrition at some time. This may only be needed for a short time and will be stopped once your child starts eating again.

Enteral nutrition

Enteral nutrition, also called nasogastric feeding (NGF), is when liquid nutrition is given through a fine tube placed down the nose and into the stomach. This is the best method of giving nutrition if your child cannot manage to eat enough, as it makes sure the gut keeps working properly. Enteral feeding can help your child to start eating sooner after the transplant is done.

The nasogastric tube will be put in place when your child is not experiencing severe mucositis. There may be some discomfort while the tube is being put in, but once it is

taped in place there should be very little discomfort. Your child will still be able to eat and drink if they feel like it, even when the tube is inserted.

Enteral nutrition will be cut down as your child becomes more able to eat and drink normally, and/or as the doctor or dietitian considers his or her weight to be adequate.

Specialised formulas are used for enteral feeding to help provide complete nutrition. The dietitian will monitor your child's tolerance of the feeding and will modify it as needed throughout the transplant.

Parenteral nutrition

If your child is unable to get the nutrition they need by eating, or via a nasogastric tube, total parenteral nutrition (TPN) can be used to help meet their nutritional needs. This is a special mixture of glucose, protein, fat, vitamins, and minerals and is given intravenously via the CvL. TPN goes straight into the blood system and does not involve the gut.

Your child will be weaned off TPN as he or she becomes more able to gain nutrition by eating or tube feeding.

Leaving hospital

It is very common for children who have undergone transplant to have a poor appetite when they are discharged from hospital. This is due to treatment side-effects as well as ongoing limited physical activity. Being hospitalised for an extended period of time can affect the appetite, but things usually improve after a child goes home. As your child's activity increases, you will find that their appetite will also increase.

Getting a child to eat after a transplant can be very frustrating for parents. If your child cannot manage to eat enough after transplant, they may need oral nutrition supplements or enteral feeding. If your child is on enteral nutrition when they are discharged from hospital, the dietitian will organise the feeds for you and will explain what you need to know. The enteral nutrition is not likely to be needed for long. For many parents, knowing their child is getting adequate nutrition through the tube is a relief.

Most children who have had a transplant will be put on a multivitamin, to replace vitamins lost during transplant and to make up for poor absorption. Your dietitian or pharmacist can recommend the most suitable vitamin formula.

Review

The dietitian will review your child as an outpatient once he or she is discharged from hospital. How often a review takes place will depend on your child's needs. The dietitian

will arrange reviews as required; however parents are welcome to contact the dietitian in the interim if necessary.

Alternative therapies

While following prescribed medical treatments, some people like to explore alternative dietary therapies. These therapies need to be assessed carefully before beginning them, as some alternative diets do not provide complete and balanced nutrition.

Despite research conducted over many years, there is no evidence to suggest that any special foods or diets can cure cancers.

Diets that restrict food groups such as meat and dairy can make it difficult to achieve adequate protein and energy intake, and may lead to weight loss and increased tiredness.

Before changing a 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 purchase, or time consuming to prepare
- has any proven health benefits.

If you are in any doubt, please discuss dietary changes with the dietitian or your doctor.

Alternative products such as herbs, high-dose vitamins, anti-oxidants and other health food preparations can contain contaminants such as bacteria and fungi. Some may also interfere with treatments, or even be toxic to organs such as the kidney and liver. Discuss these products with your doctor or dietitian before using them.

Other alternative therapies, such as meditation and relaxation, can complement treatment and help your child feel better.

Complications

This chapter covers the most common complications that may occur following transplant and may seem frightening. Remember while you are reading that each child is an individual with his or her own specific risk factors. Your child may experience one or more of these complications, or may experience none of them. There is no way of predicting a particular situation.

After reading this chapter, you may feel overwhelmed by all the possible complications that could occur. You may want to ask questions about these, or talk to someone who has experienced a complication, for example GvHD, following transplant. It is important to keep in mind that each person's experience is unique to them and will not necessarily apply to your child.

Talk to your medical team about your concerns and any questions you may have.

Infections

Everything we do in our day-to-day activities is a potential source of infection. This includes breathing, eating, and contact with other people or animals. For those of us with a normal immune system, such everyday encounters are not usually a problem. The body and its immune system work to protect us from infections, by recognising and destroying any harmful organisms that enter the body.

For people who have had, or are about to have, a transplant, the normal function of the immune system is disrupted. The conditioning therapy that your child receives prior to transplant involves drugs and/or radiation that are not able to distinguish between cancerous and normal cells, and so affect all the cells of the body. In particular, these treatments affect rapidly dividing cells – these are found in the mouth and gut, bone marrow and hair. Changes to the immune system that result from the conditioning therapy lead to a decrease in circulating blood cells. This includes white blood cells,

which are responsible for fighting infection (especially the neutrophils).

The skin and **mucous membranes** that line the mouth and nose are the body's first line of defence, and repel millions of potentially harmful organisms and foreign substances every day. Normally, if you cut yourself, white blood cells (leukocytes) spring into action to fight any infectious organisms that may enter the body through the cut. However, during transplant and in the months following, this process is disrupted.

Antibodies, which we all make over our lifetime in response to contact or infection with a variety of bacteria or viruses (such as measles or chicken pox), are also depleted or destroyed during transplant. This means that your child may develop infections that they had earlier in childhood.

until your child's immune system returns to normal, he or she is extremely vulnerable to infections and in some cases these can become life-threatening.

The first two to four weeks following transplant is a particularly 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. Although the risk of infection steadily decreases once the transplanted marrow successfully engrafts, your child's immune system remains compromised (that is, not functioning efficiently) for six to eighteen months after transplant. This can be even longer for those who experience GvHD. This is due to the actual process of GvHD as well as the medication given to treat it, which prolongs the period of immune suppression.

To help avoid infections, good hygiene is extremely important.

- Ensure that *all* visitors (including staff) carefully wash their hands with antiseptic soap and alcohol rub prior to touching your child (since hands are a primary carrier of infectious agents) – ask them if you are unsure.
- Ensure your child has a daily shower or wash (including hair or scalp wash), using the antibacterial skin wash or liquid soap provided. Do not use cake soap.
- use disposable wash cloths.
- Bed linen and your child's clothes should be changed daily.
- report any abnormalities when your child is passing urine – burning, stinging or the presence of blood in the urine.
- Perform mouthwashes thoroughly at least four times per day. Good mouth care may not prevent your child forming ulcers, but it will reduce the risk of infection. use the mouthwashes provided by your hospital.
- Toothbrushes should be avoided when your child's counts are low.
For further guidance talk to your transplant coordinator.
- Limit the number of family and friends that visit your child when in hospital – refer to your transplant coordinator for more information. Apart from the risk of infection, it can be very tiring for you and your child to have a lot of visitors.

Inform all visitors that they are 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 are not sure they should check with staff before visiting you.

- Flowers and plants (both live and dried), which can harbour harmful bacteria or fungi, are not permitted in the room. People with muddy shoes should wash their shoes before entering your child's room.
- Eating sensibly and avoiding foods that may be a potential source of infection is very important. The dietician will discuss the sorts of food your child should eat and also those that they should avoid until their immune system has returned to normal. (See Chapter 8 for more information.)
- Fresh fruit should be kept in the fridge in the room and not left out.



Bacterial infections

Bacteria are microscopic organisms that have the ability to cause infection anywhere in the body. They secrete toxins that can interfere with normal organ functioning (such as the maintenance of blood pressure), or cause problems due to their ability to multiply rapidly. Some pneumonias, for example, are caused by bacteria which fill up the spaces in the lungs where air is normally absorbed by the body.

Bacterial infections are the most common type of infections during the first two to four weeks after a transplant. These occur in more than half of all transplant patients. Post-transplant bacterial infections are most common in the gastrointestinal tract (gut), on the skin (especially where the central line is inserted) 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 sometimes can prove fatal.

If your child has an infection, they may have some or all of the following symptoms:

- a high fever ($>38^{\circ}\text{C}$) (but not always)
- a fast breathing rate
- pale and clammy skin (sweaty)
- diarrhoea
- a high pulse rate
- low blood pressure
- a runny nose and/or cough
- nausea and vomiting.

Once it is apparent that there is an infection, your child will be monitored closely for any signs of sepsis (contamination of the blood). Sometimes, however, complications can occur suddenly and can progress very quickly. These complications can lead to a life-threatening condition called **septic shock**, where the body has difficulty maintaining blood pressure. If this happens, large volumes of intravenous (iv) fluids or other drugs are given in an attempt to increase blood pressure. If this does not work, it may be necessary to move your child to the intensive care unit where his or her condition is monitored even more closely, and he or she can be given special drugs to maintain blood pressure. This is important, as a prolonged period of low blood pressure can lead to major damage to body organs (especially kidneys) due to inadequate oxygen being supplied to the lower part of the body.

Treating bacterial infections

If your child's temperature goes above 38°C, blood and urine samples will be taken to try to find the source of infection. Treatment with antibiotics will be started immediately, without waiting for the source of infection to be identified. This can take a few days, although often the source of infection is not found. Antibiotics are administered through a vein (intravenously). You may find that your child's drugs are changed around until the correct combination to combat the particular infection is found.

Fungal infections

Fungal infections are common during the first three months after transplant, particularly in patients with graft-versus-host disease. Moulds, such as those found on bread, are an example of common fungi. Certain fungi usually live within our bodies without causing problems, and are kept under control by bacteria that live alongside them. However, the use of antibiotics pre- and post-transplant destroys these beneficial bacteria in the body, allowing the fungi to grow out of control.

Prevention of fungal infections

To try to prevent fungal infections, your child will be given a drug called Fluconazole (orally or iv daily). This will continue until after discharge from hospital, or until your doctor advises that it can be stopped. If your child has had an *Aspergillus* fungal infection in the past, they may receive Amphotericin or an oral drug called Itraconazole, instead.

Candida and *Aspergillus* are the most common post-transplant fungal infections.

Candida, (commonly known as thrush) lives inside the mouth, vagina or gut and is normally kept under control by the bacteria that also live in these areas.

Aspergillus fungi are frequently found around construction sites or where buildings are being remodelled. Infections with this type of fungus most often occur in the sinus passages or lungs, and can cause pneumonia.

Special air-filtering equipment called HEPA filtration is installed in the transplant rooms to remove fungi and other potential infections from the air. These rooms also have positive pressure air conditioning.

Treating fungal infections

As well as being used to prevent *Candida* infections, Fluconazole is effective in treating *Candida* infections if they do occur. Liposomal Amphotericin is used to treat both *Candida* and *Aspergillus* infections. If your child develops an *Aspergillus* infection, they may be treated with liposomal Amphotericin for a prolonged period and this may continue after discharge from hospital. Infections caused by *Aspergillus* and less common fungi can be difficult to treat. (See the Appendix at the back of this book for information on drugs used to treat fungal infections.)

Viral infections

viruses are tiny parasites that require the help of other organisms, to survive and multiply. When a virus enters a host cell – for example, a cell in the human body – it changes the genetic machinery of the cell, turning the cell into a factory that produces more and more of the virus. The virus eventually destroys or cripples the host cell and moves on to neighbouring cells to continue its reproduction.

In healthy people, immune cells called T-cells and antibodies produced by B-cells work together to keep invading viruses in check (see Chapter 2). However, people whose immune cells are destroyed or depleted during conditioning therapy are far more at risk of developing a viral infection. Infections caused by viruses can be difficult to treat, as they tend to reoccur.

viral infections following a transplant can occur either as a result of exposure to a new virus, or the reactivation of an old virus that has been lying dormant (inactive) in the body.

viral infections are most common during the 12 months immediately following a transplant, but can occur as late as two years after transplant. The most common viral infections in transplant patients are caused by the cytomegalovirus (CMV), *Herpes simplex* virus (HSV), varicella zoster virus (VZV) and respiratory syncytial virus (RSV).

Cytomegalovirus (CMV)

Almost one third of patients undergoing a transplant develop CMV infection, usually during the second or third month after transplant. CMV infections can develop in several different organs including the liver, colon, eye, and lungs.

Many people in the general population are exposed to CMV during their lifetime, particularly those who live in cities. You may have even been infected with CMV and not known, as

CMV produced general flu-like symptoms. It causes no long term effects, unless your immune system is compromised.

Your child will have had a blood test prior to transplant to determine whether or not they have been exposed to CMV. If your child tests CMV-negative, a CMV-negative bone marrow donor will be used if at all possible.

Wherever possible, only blood products that are CMV-negative are given to transplant patients. In addition, special filters are used when transfusing blood products to stop viruses entering the blood.

The risk of developing CMV infection increases with age, and is more common in patients with graft-versus-host disease.

Prevention of CMV

If your child tests CMV-positive (showing that he or she has been exposed to CMV before), IV Ganciclovir will be given twice a day for seven days before the transplant. Depending on the transplant protocol, Ganciclovir may be given again after engraftment. Your transplant team will discuss this with you and your child.

Your child will have routine blood and urine tests to check whether they are developing a new or reactivated CMV infection.

Treating CMV

If your child develops a CMV infection, they will be treated with Ganciclovir or Foscarnet IV for a minimum of 14 days.

Herpes simplex virus (HSV)

Herpes simplex virus (HSV) infections are caused by two separate viruses: Herpes 1 and Herpes 2. The Herpes 1 virus causes cold sores, which are painful blisters around and in the mouth. Most people are exposed to the Herpes 1 virus at some time in their life, usually during childhood. This virus is highly contagious and is transmitted through contact with people who have active herpes sores on their mouths.

HSV infections often re-occur again and again. The virus can lie dormant in the body for many years, usually flaring up at times of stress or over-exposure to sun or wind. Even if a person does not recall having had an active case of herpes, the virus may nonetheless be present in the body. This can be determined by a blood test.

Prevention of HSV

Your child will have a blood test prior to transplant to determine whether or not he or she has been infected with HSV. If the blood tests show up positive, IV Acyclovir will be given for a minimum of 3 weeks, starting Day 0, to prevent reactivation of the infection.

Treating HSV

HSV infections usually occur in the first month after transplant and are usually due to the virus already being present in the body. As well as the usual mouth sores associated with a Herpes 1 infection, skin lesions can occur in transplant patients. In rare cases, infection can also occur in the brain or lung.

HSV is treated with Acyclovir administered intravenously, at higher doses than those used for prophylaxis (prevention).

Varicella zoster virus (VZV)

Infection with *Varicella zoster* virus (vZv) is commonly referred to as shingles or herpes zoster. vZv is the same virus that causes chicken pox. vZv infections occur in people who have had chicken pox, when the virus which has been lying dormant is reactivated.

Transplant patients may develop a vZv infection during the first year after transplant, usually after 100 or more days have passed. This infection is most common in allogeneic transplant patients with graft-versus-host disease.

Symptoms of vZv infection include an itchy, blister-like skin rash that extends along any one of the body's nerve branches. This rash can be extremely painful due to the involvement of the nerve endings under the skin. Pain can result from the gentlest of touches to the skin.

The ophthalmic nerve to the eye can also be affected by vZv. The rash may occur along the nerve path on the forehead and eyelids and, if not treated promptly, can damage the eye. Since vZv infections are highly contagious, children who have never had chicken pox or who have tested negative to vZv in their blood test should avoid any contact with people who have chicken pox or vZv infections, for the first year following transplant.

Treating VZV

vZv infections are treated with Acyclovir, either into a drip or orally, depending on the severity of the infection.

Other viruses

There are many other viruses that can create problems after transplant, although the incidence of these infections is quite low. Such viruses include adenovirus, Epstein-Barr virus (EBv), respiratory syncytial virus (rSv), and human papilloma virus (HPv). Adenovirus and rSv infections can cause pneumonia and can potentially be very serious. Adenovirus can also cause infections in the kidneys or gastrointestinal tract and bleeding in the urine. In rare cases, the Epstein-Barr virus infects the lymph system of allogeneic transplant patients, creating a lymphoma-like condition.

The risk of developing these viral infections can be reduced by using common sense measures such as good personal hygiene, limiting time in crowded public places, and limiting contact with people who have colds and flu-like symptoms.

Protozoan infections

Protozoa are single cell parasites. Like viruses, protozoa need living cells in which to replicate. Infections from protozoa are less common than other infections. However, they have the potential to cause serious problems for transplant patients who are low in T-cells.

Pneumocystis carinii is a protozoan that lives harmlessly in the windpipe of healthy people, but can enter the lungs and form tiny cysts in people who have a suppressed immune system. This condition is called *Pneumocystis carinii* pneumonia (PCP). Bactrim and Pentamidine are highly effective drugs used to prevent and treat this type of lung infection, and your child will take such medications for at least 6-12 months after transplant.

Another infection, 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 (cat poo). It may infect the brain, eyes, muscles, liver and/or lungs. A painful, inflamed retina in the eye is a common sign of the disease, which, without prompt treatment, can result in damage to the eye. It is therefore crucial that all contact with pets is limited and hands are thoroughly washed after contact. Emptying the kitty litter is definitely not a task for a transplant patient.

Revaccination

Because conditioning therapy destroys the immune system, your child will have lost their natural immunity to certain infectious diseases. For this reason, he or she will need to be revaccinated against these diseases, as well as receive some additional vaccinations to protect against new diseases. Your transplant doctor will explain this at the appropriate time. vaccination will not be necessary until at least 12 months after the transplant, and should only go ahead after consultation with the transplant doctor. A revaccination schedule will be provided for you.

The following revaccination schedule shows what is recommended, although there may be times when this is altered and will depend on your child's individual situation.

Vaccination schedule at 12 months post-transplant:

- Diphtheria, pertussis, tetanus (DTP) acellular vaccine
- *Haemophilus influenzae B* (HiB)
- Pneumococcal

- Polio - inactivated polio virus (IPV) only (Salk vaccine)
- Hepatitis B (for those at risk of this infection)

Vaccination schedule at 14 months post-transplant:

- Diphtheria, pertussis, tetanus (DTP) acellular vaccine
- *Haemophilus influenzae B* (HiB)
- Polio - inactivated polio virus (IPV) only (Salk vaccine)
- Hepatitis B (for those at risk of this infection)
- Pneumococcal

Vaccination schedule at 24 months post-transplant:

- Diphtheria
- Tetanus
- *Haemophilus influenzae B* (HiB)
- Pneumococcal
- Polio - inactivated polio virus (IPV) only (Salk vaccine)
- Hepatitis B (for those at risk of this infection)
- Meningococcal vaccine
- Mumps, measles, rubella (MMr) - if the child is off
all **immunosuppressive therapy**
- varicella

Annually:

It is also recommended that your child, and all members of the immediate family, have an annual Fluvax vaccination, to protect against each year's new strain of the flu. Children under the age of three require two doses.

Leaky capillary syndrome

Leaky capillary syndrome is a common complication in the first three weeks after transplant. This is a result of damage to the cell lining of blood vessels, caused by combination chemotherapy and radiation therapy. The blood vessels leak fluid into the surrounding tissues, causing swelling in the hands, feet, face and lower back as well as weight gain. This syndrome can be treated by drawing the fluid out of the tissues and returning it to the blood vessels. This is achieved by giving an infusion of albumin (a protein) via the CvL.

Kidney and bladder dysfunction

A number of complications can occur in the kidneys and urinary tract after transplant. Often these are side-effects of the drugs used after transplant, although infection and other complications can cause kidney problems.

reversible abnormal kidney function is relatively common after transplant and may range from mild to severe. The function of the kidneys is to rid the body of excess water and waste products by producing urine. Kidney function is measured both in terms of the volume of urine produced each day, and also the amount of various products left in the blood.

The most commonly measured product is creatinine, a normal breakdown product of muscle. regular blood tests, during and after transplant, will allow the transplant team to monitor the ability of the kidneys to excrete such substances. In some children these tests will show up early signs of reduced kidney function, well before more serious problems such as reduced production of urine occur.

Kidney damage after transplant can result from a variety of factors. The most important and common of these factors is drugs. Several drugs routinely used after transplant can damage the kidneys. In particular, Cyclosporin (a drug used to help prevent GvHD) commonly impairs kidney function. Both creatinine and the concentration of Cyclosporin in the blood need to be measured regularly in allogeneic transplant patients. The dose of the drug will be adjusted if signs of kidney failure develop.

A number of chemotherapy agents, antibiotics and antifungal drugs can damage kidney function. For this reason, kidney function and some drug levels are closely monitored. Low blood pressure, usually the sign of a serious infection, can lead to poor kidney function and even kidney failure. Some diseases of the liver can also contribute to kidney failure.

Treatment of kidney failure will depend on its severity and the particular circumstances. Sometimes, this will involve stopping or changing doses of Cyclosporin and waiting for the creatinine level in the blood to return to normal. In other situations, antibiotics will need to be changed and increased fluids and drugs may need to be given to improve blood pressure.

If there is severe kidney failure, **dialysis** may be needed. This involves using a dialysis machine (similar to the apheresis machine used to collect peripheral blood stem cells) to take over from the kidneys. An additional central venous line may need to be put in to allow for dialysis. Kidney failure requiring dialysis is sometimes fully reversible. However, it is a very serious condition and, in some cases, it can prove fatal.

Haemorrhagic cystitis

Haemorrhagic cystitis is a complication resulting from damage to the lining of the bladder, caused by drugs or viral infections. Symptoms include pain on passing urine, increased frequency of urination, and blood clots in the urine. Haemorrhagic cystitis can occur weeks or months after transplant, and can vary from mild to severe. It is

often associated with the use of Cyclophosphamide during conditioning therapy, as the breakdown products of Cyclophosphamide damage the lining of the bladder. Certain viruses, particularly Parvovirus, can also cause haemorrhagic cystitis.

There is no treatment for this condition that has been proven to be effective. Often the condition is mild and resolves (disappears) in a few weeks. Sometimes it is more severe, with considerable blood loss requiring a blood transfusion. The passage of urine may be blocked by clots forming in the bladder, and a catheter may need to be inserted into the bladder to allow the urine to be drained and clots washed out with saline solutions.

Lung complications

The lungs may be affected by a variety of different problems after transplant. These complications can be a result of infections, damage from chemotherapy drugs or radiation, graft-versus-host disease, disturbances in the immune system or bleeding. Occasionally, when infection is severe, support with a ventilator in the intensive care unit may be necessary.

Early lung complications

Bacterial pneumonia

Bacterial infection in the lungs is a relatively common complication in the first two or three weeks after transplant. This is due to very low white blood cell counts during this time. Pneumonia can result from infection with bacteria that would not normally cause this condition, and these infections can be more difficult to treat. Symptoms include coughing, difficulty breathing, an increased breathing rate, increased oxygen requirements and fever.

An x-ray of the chest will be taken to attempt to diagnose the problem. Blood cultures and nasopharyngeal aspirates (NPA) (samples taken from the nose) may also be needed to establish which bacteria are responsible. Antibiotics will be given intravenously, and oxygen may be given via a mask or nasal prong.

Fungal infections of the lungs

The lungs can be infected with a fungus in the first few months after transplant. The fungus causing infection may be a yeast (*Candida* or thrush is the best known example), or a mould (*Aspergillus* is the most common one found in transplant patients). A fungus that infects the lung commonly does so because it is inhaled from the surrounding environment.

There are a number of factors that can contribute to bringing about fungal infections. These include a low white cell count (particularly neutrophils), use of strong

immunosuppressive drugs (like Cyclosporin and ATG), use of large doses of steroid drugs, graft-versus-host disease, transplants from unrelated or mismatched donors, and previous fungal infections in the lungs.

All transplant patients are nursed in single rooms that receive filtered air (HEPA filtered rooms) to reduce the risk of developing fungal infections. Anti-fungal drugs may also be given, such as Fluconazole, as a preventative measure. While symptoms of fungal infections are often similar to those of bacterial pneumonia, a chest x ray can show that the cause is a fungus rather than a bacterium. A CT scan and sometimes a lung **biopsy** are commonly used to confirm the diagnosis. To treat a fungal lung infection, anti-fungal drugs may need to be changed, and/or their doses increased.

Pneumocystis carinii pneumonia (PCP)

This is a lung infection that can occur in children who have a suppressed immune system. It is caused by a small parasite called *Pneumocystis carinii*. This organism normally lives in the airways in the lungs without causing illness, but can grow out of control when the immune system is not functioning properly. If this happens, PCP can result, causing fever, dry cough and difficulty breathing. This is a potentially serious infection and preventative therapy will be given in the lead up to transplant and started again after engraftment. Despite therapy, PCP can still occur. It is treated with high doses of antibiotics.

Pulmonary haemorrhage

This is a relatively rare complication, usually occurring in the first month after transplant. Bleeding (haemorrhage) from the lungs results in blood being coughed up and difficulty in breathing. The cause is usually thought to be a fault in blood clotting, especially due to a low platelet count, and damage caused by the drugs used in conditioning therapy. The condition can be treated by giving transfusions of platelets and plasma products, large doses of steroid drugs, and assisting breathing by giving oxygen or using a ventilator machine.

Interstitial pneumonitis

Interstitial pneumonia can result from infection by a virus or protozoan, damage by radiation and drugs, or unknown causes. It usually occurs in the second or third month after transplant. Symptoms include fever, a dry cough, and difficulty breathing. If this complication occurs, medical staff will try to find out if there is an underlying infection, such as a virus. Cytomegalovirus and other viruses will be tested for using blood tests and sometimes by taking samples from the lungs by **bronchoscopy**. This involves giving sedation, then passing a fibre-optic tube through the mouth or nose

into the airways leading to the lungs. Treatment may include drugs to treat underlying infection, steroids, giving oxygen, and artificial breathing support as necessary.

Late lung complications

Lung fibrosis

This problem may occur months or even years after transplant. It can be caused by drugs used in conditioning therapy (especially Busulphan), radiation therapy, or unknown causes. Lung fibrosis means that the lungs are affected by scar tissue, which results in stiffness and difficulty in expanding the lungs. The condition usually comes on gradually, with symptoms such as a dry cough and difficulty breathing. Chest x-rays and breathing function tests are used to diagnose the problem. A lung biopsy by bronchoscopy or surgical operation may be necessary to confirm the diagnosis. Treatment is often steroid drugs, but these are not always successful.

Chronic GVHD and the lungs

Graft-versus-host disease (GvHD) can affect the lungs as well as other organs. The usual problem is damage to the lining of the small airways of the lungs - thin tubes called bronchioles. This causes narrowing, which reduces the flow of air in and out of the lung and increases the risk of infection. Sometimes this situation produces a condition very similar to asthma, with wheezing and difficulty breathing out. In other patients, there may be associated infection such as bronchitis or pneumonia.

The diagnosis is often difficult to make, but is suspected in any patient with chronic graft-versus-host disease who develops lung abnormalities. The diagnosis may require x-rays, breathing tests and even biopsies. Treatment usually consists of increasing the dose of the immune-suppressive drugs used for GvHD, but not all patients will respond to this.

Recurring infections

Some people who receive a transplant, especially those with active GvHD and on immune-suppressive treatment, have continuing problems with their immune systems which put them at risk of bronchitis or pneumonia. Treatment may consist of giving antibiotics each time a bout of infection occurs and/or a preventative basis, and regular intravenous immunoglobulin, a source of antibodies.

Liver complications

The liver lies under the ribs on the right side of the upper abdomen. This organ carries out a variety of essential functions in the body. The liver cleanses the blood of toxins

(including drugs) and other waste materials, produces a fluid called **bile** to aid in digestion, and controls the excretion of **bilirubin** (a by-product of red blood cell breakdown). The liver is also the site of energy storage and is responsible for the manufacture of proteins that control blood clotting.

The essential functions that the liver performs can be disrupted during the transplant process. If the sinusoids become obstructed, or liver cells are damaged, the liver becomes unable to properly rid the body of toxins, drugs, and waste products. Similarly, if the bile duct becomes obstructed, excess levels of bilirubin, cholesterol and other chemicals will build up in the body, interfering with the function of the liver and other organs.

Disorders of the liver can be grouped in three categories:

- those that directly affect the liver cells
- those that affect the vessels that transport blood through the liver
- those that affect the bile ducts.

Liver function tests are highly sensitive and some abnormality is to be expected after transplant. It is important to note that more than one type of liver complication can occur at the same time. The majority of liver complications are temporary and completely reversible, although some can become serious and may even be fatal. As many potential complications show up in a similar manner, it may take time for the correct diagnosis to be made.

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

These tests include:

- blood tests – includes measurement of bilirubin level 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 weights recordings
- liver biopsy.

Signs of liver problems include:

- jaundice (yellowing of skin and eyes)
- a tender or swollen liver
- rapid weight gain (fluid retention)
- swelling in arms, legs or the abdominal cavity
- high levels of bilirubin and other liver enzymes in the blood
- confusion (this can also be a symptom of other less serious post-transplant problems, or a result of certain drugs).

Liver problems during the first 100 days

Drug-induced liver injury

Some of the medications given to your child during transplant can temporarily cause, or worsen, liver abnormalities. These include drugs such as antibiotics, antifungals, anti nausea drugs, pain relief and drugs given to treat GvHD.

Your child may have abnormal blood tests or occasionally be jaundiced. Pain is not usually associated with this type of complication. If your child is having intravenous feeding (TPN), they may experience some temporary liver complications, possibly with inflammation and mild tenderness. Reducing the amount and type of intravenous feeding your child receives may help with these problems.

Veno-occlusive disease/sinusoidal obstructive syndrome

veno-occlusive disease (vOD), also known as sinusoidal obstructive syndrome (SOS), is a potentially serious liver problem which occurs when the vessels carrying blood through the liver become swollen and blocked. This interferes with the normal processes the liver carries out, such as cleansing the blood of toxins, drugs and other waste products. Because of the decreased flow of blood through the liver, pressure and fluids build up, leading to swelling and tenderness. This build up of waste products in the blood stream can cause the kidneys to malfunction, which in turn causes water and salt to build up in the body, leading to swelling of the legs, arms and abdomen.

vOD occurs as a result of the combination of chemotherapy and/or radiotherapy given for conditioning therapy.

Some of the signs and symptoms of VOD are:

- abnormal liver function tests
- pain and tenderness below the ribs on the right side of the abdomen
- significant weight gain
- an enlarged liver
- the build up of abdominal fluid (ascites) - this may cause pressure on the lungs, making it harder to breathe
- jaundice
- limited response to platelet transfusions.

In severe 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 following 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 occur early after transplant and cannot be explained by other causes, vOD is considered and your child will be treated accordingly.

Risk factors for developing VOD

- certain conditioning therapies
- certain chemotherapy, received before conditioning therapy began
- prior transplant
- prior liver dysfunction
- prior radiation to the abdomen
- thalassaemia.

Preventing VOD

To try to prevent vOD, ursodeoxycholic acid is given orally twice a day. Those who are considered to be at high risk of developing vOD will also be given Defibrotide intravenously. Despite giving preventative drugs, vOD may still develop.

Treating VOD

The most effective treatment for vOD is Defibrotide. This drug works by helping prevent the formation of blood clots and dissolving existing clots. Other treatments may include:

- stopping or avoiding drugs that could worsen the problem (where possible).
- restricting intravenous and oral fluids.
- using diuretics (fluid-removing drugs)
- infusion of blood products (platelets and packed cells)

Weight and girth (width) measurements will also be taken regularly.

Severe vOD is a very serious development that can contribute to a fatal outcome of transplant.

Acute GVHD of the liver

Patients receiving an allogeneic transplant are at risk of developing liver damage from acute graft-versus-host disease (GvHD). Acute GvHD occurs during the first 100 days after transplant and can affect the small bile ducts, disrupting the flow of bile out of the liver.

Signs and symptoms of this complication may include:

- jaundice
- mild liver tenderness
- abnormal liver function tests.

use of unrelated stem cells increases the risk of developing acute GvHD of the liver. Patients transplanted with stem cells from a donor that is not fully matched are also at increased risk.

Bloodstream infections

Occasionally, an infection elsewhere in the body may cause the liver to function abnormally, affecting the flow of bile. Symptoms may include abnormal blood tests and possibly jaundice. The cause of the infection is generally viral or fungal and will be treated with anti-viral or anti-fungal agents.

Graft-versus-host disease (GVHD)

Graft-versus-host disease (GvHD) is a common complication of allogeneic transplant. About half of all patients who have a matched related donor transplant develop some degree of GvHD. Most of these cases are mild to moderate.

Once the donor stem cells begin to engraft (grow), the T lymphocyte cells that came from the donor may recognise your child's own body cells as foreign and try to destroy them. This happens because your child's own immune system has been suppressed or eliminated by the conditioning therapy before the transplant. (remember, this is necessary to stop the donor stem cells from being rejected.)

There is increasing evidence that GvHD is actually beneficial in children with leukaemia, reducing their risk of relapse. This is due to a graft-versus-leukaemia (GvL) effect, whereby donor T-cells fight directly against leukaemia cells in the recipient's body. However, in children having transplants for non-malignant disorders, GvHD is of no benefit.

There are two distinct types of GvHD – acute and chronic. Each differs in their symptoms, clinical signs and time of onset. Chronic GvHD is uncommon in children.

Acute GVHD

Acute GvHD occurs within the first 100 days of transplant and primarily affects the skin, liver and gastrointestinal tract (gut). GvHD may be mild, moderate, severe or life-threatening (see below).

GvHD is classified within 4 grades.

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

Symptoms of acute GVHD

Your child may experience none, some, or all of the following symptoms.

Skin

- burning, itching and redness on palms or soles
- a rash, along with burning and redness (similar to sunburn), on part or all of the body
- blistering - eventually the skin may flake off, leaving raw areas underneath

Gastrointestinal (Gut)

- nausea, vomiting, abdominal cramps, and loss of appetite
- large quantities of offensive smelling, watery diarrhoea, which may become bloody

Liver

- jaundice and pain in the abdomen
- swelling of the liver
- abnormal liver function tests

Preventing acute GVHD

A number of drugs can help control acute GvHD. Drugs such Methotrexate, Cyclosporin, Mycophenolate, Prednisone and Tacrolimus - depending upon the type of transplant - are given to lessen the ability of donor T-cells to attack your child's tissues and organs. Depending on the conditioning therapy, the choice of drug and the timing and duration for which it is given will vary.

The removal of T-cells from unrelated donor cells prior to transplant (**T-cell depletion**) is a technique that may be used to reduce the incidence and severity of acute GvHD. It is theoretically possible to remove all donor T-cells and therefore all risk of GvHD from the donor stem cell product. However, this has a downside, in that donor T-cells also seem to contribute to engraftment and are responsible for the desirable graft-versus-leukaemia (GvL) effect. It is therefore necessary to find a balance between reducing the risk of acute GvHD, preventing graft rejection and maximising the GvL effect.

Diagnosing acute GVHD

Diagnosis of GvHD may be difficult, even with a biopsy. However, biopsy of the affected area is the only definitive way to diagnose acute GvHD. For skin a simple punch biopsy is performed for diagnosis. An endoscopy and/or colonoscopy and biopsy, under general anaesthetic, is usually required to diagnose gut GvHD. A liver biopsy is more complex; at times this may be too dangerous, therefore a diagnosis of liver GvHD is

often made on clinical signs alone, or by ruling out other possible causes for presenting symptoms.

Treating acute GVHD

The combination, dosage and duration of medications chosen to treat your child will depend on the grade and duration of acute GvHD. Treatments for acute GvHD include:

- topical steroid creams for the skin
- intravenous steroids
- non-steroidal drugs such as ATG, Infliximab and Daclizumab
- medication to control symptoms such as pain, cramps, diarrhoea, nausea and vomiting.

If your child has moderate to severe GHvD affecting the gut, they will need to fast in order to rest their gut. Fluids will be replaced intravenously and calories provided by total parenteral nutrition (TPN).

GvHD is very difficult to predict in its severity, timing and location. remember, GvHD is not necessarily a bad thing. Depending on your child's diagnosis, a mild episode can be a positive indication that the new engrafted white cells are working. Your transplant team are the best people to explain the positives and negatives associated with GHvD in your child's case.

Life after Transplant

Going home



Your child will be able to leave hospital and return home as soon as the doctor assesses that he or she is well enough and blood counts are rising. The length of the time your child will be in hospital will depend on the type of transplant they have received. On average, children having autologous transplants are in hospital for at least four weeks, while those receiving allogeneic transplants are in for at least six to eight weeks.

While your child will be excited to leave the hospital, this is often a very anxiety-provoking time for parents, as your child leaves the security of the hospital where nursing and medical staff are available 24 hours a day.

If you live in NSW country areas or interstate, your child will go from the hospital to Ronald McDonald House for a period of continuing treatment and follow up.

All children need to remain in isolation for a while after returning home from hospital. The length of this isolation period will depend on the type of transplant your child received, any complications that may have occurred, and ongoing therapy that is required. Your transplant nurse coordinator will discuss this with you in detail.

Once your child has left hospital, there are certain signs and symptoms you will need to watch for. If your child has any of the following symptoms, it is important that you contact the hospital straight away. Your transplant coordinator will give you a list of appropriate numbers to call.

Please remember that it is much easier to call the hospital to discuss concerns, rather than sit at home worrying.

You should call the hospital if your child:

- has a fever of 38°C or higher
- has a cough, breathlessness, or rapid breathing
- has a runny nose
- experiences nausea and/or vomiting
- bleeds excessively from any cuts or sores
- has nose bleeds
- has bruising anywhere on the body
- has diarrhoea
- has a rash anywhere on the body
- is unable or refusing to take medications
- is not eating or drinking enough
- has accidentally removed the nasogastric tube
- has any redness, swelling, oozing and/or pain at the site of their central line (CvL)
- has chills or fever after flushing the CvL
- has had exposure to chicken pox, measles or any other infectious diseases
- is lethargic (unusually tired) or shows any abnormal behaviour
- has aches and pains.

Sun exposure

All children who receive a transplant should be very careful with sun exposure, and wear sunscreen at all times. If your child received total body irradiation, he or she should always wear sunscreen, a hat and cover up with clothes while out in the sun. This should become a life-long habit, to lessen the risk of serious skin cancer (melanoma).

Preventing infections

Once your child has returned home from hospital, it is important that you remain cautious about preventing infections.

Here are some ways of helping prevent infection.

- Avoid public transport and attending crowded places like shopping centres, leisure centres, play grounds and movie cinemas at peak times.
- Avoid or limit contact with people who are unwell, or who have had contact with others who are unwell, particularly children with infections such as chickenpox or measles or who have recently been vaccinated for these.
- Children should not be allowed to help with gardening, and should avoid any contact with soil or potting mix due to the bacteria that live there.

- Avoid contact with poo and wee from the family pet, or any other animals including birds.

Going back to school

School is a major part of a child's growth and development. It is important that your child is reintegrated into their school system as soon as is practical after transplant. Otherwise, feelings of isolation and exclusion from schoolmates and friends can occur.

During transplant, regular contact in the form of cards, letters, telephone calls, faxes, emails and SMSs is encouraged from school friends. This is important, as it allows your child to stay in touch with the day-to-day happenings at school. The hospital school will liaise with your child's school teacher – however, you will probably find your child will not be interested in school work for the first couple of weeks after transplant.

Most children return to school within six months of transplant. How soon your child can return to school will depend on his or her condition, the type of transplant, and whether there are complications such as graft versus host disease. Your transplant team will advise you on when a return to school is appropriate. You may find that half days, alternate days or attending favourite subjects only may be best, until your child's energy levels have returned. If your child has any physical limitations, or requires any special considerations, the outreach/community clinical nurse coordinator will talk to the school's teachers about these when your child is preparing to return to school. Teachers will be also be given information about central lines (if necessary), and the importance of avoiding chicken pox and measles and notifying the appropriate person quickly if the need arises.

Teachers play an important part in integrating children back into school. They can be helpful in monitoring your child's progress and advising you if and when problems arise.

Should your child, or his or her siblings, require any letters of support throughout the transplant or treatment phase, feel free to ask the oncologist, transplant coordinator, social worker, or clinical nurse coordinator.

Late effects

Some side effects of transplant can occur much later on, well after your child has returned home from hospital. The late side effects of transplant vary, depending on the age of the child, the underlying disease, and previous treatments including conditioning therapy. There are many different aspects of your child's health that will need long-term follow up.

Below is information about late effects that some children can experience after transplant. Not all children will have these late effects - your child's consultant will be able to talk to you about which effects may be potential issues for your child.

Effects on the glands

The use of total body irradiation (TBI) can affect the endocrine system – the system of glands and hormones in the body. In particular, TBI affects the pituitary gland and thyroid gland (glands in the head and neck area) and the gonads (sex organs). These glands regulate growth and physical development.

radiation affecting the pituitary gland can cause your child to have growth hormone deficiency, leading to poor growth, particularly during the pubertal growth spurt. As a result, your child may not reach their full height potential. Height will be measured at every clinic visit and, if there is significant slowing of growth, the doctor will discuss with you a suitable plan for your child. This may include the use of a synthetic growth hormone, given to your child via a small injection.

The thyroid gland is also sensitive to radiation. However, the method by which TBI is given today means that damage to this gland can usually be avoided. However, blood tests will be carried out to check that the thyroid is functioning properly. If an insufficient amount of thyroid hormone is being produced, the hormone can be replaced by taking a tablet daily.

The gonads (testes in the male, and ovaries in the female) produce hormones that are necessary for normal sexual development. TBI and some chemotherapy drugs can affect the way that the gonads function. There are many factors involved in whether the gonadal hormones will be affected, such as age at treatment, dose of chemotherapy and dose of radiation. Your child's doctor will discuss this with you. When your child is entering into puberty, hormone blood tests will be done to check that the gonads are functioning properly. If your child has already entered puberty, hormone testing will be done at around 6-12 months after transplant. If hormone replacement therapy is required, the endocrinologist will discuss the options with you.

Effects on fertility

Fertility can be affected by chemotherapy and TBI. If your child has had TBI, the risk is very high. If he or she has had chemotherapy without TBI, the risk is moderate. The doctor will explain the likelihood of this complication occurring in your child.

If your child is a boy and has already reached puberty, it may be possible to store some of his sperm for future use. There is also now technology to store ovarian tissue for girls at any age. However, this is very new technology and the outcomes of this procedure have yet to be proven. To collect the ovarian tissue, the girl must have laparoscopic (keyhole) surgery. After collection, the tissue is stored until needed.

It is important to say that infertility does not prevent normal sexual activity. If you would like more information on this topic, ask your child's specialist.

Effects on learning

Some children who have received radiation or drugs in the brain (cranial irradiation and/or intrathecal chemotherapy) can develop learning difficulties due to changes in the brain. The younger the child at the time of treatment and the more irradiation or intrathecal chemotherapy they receive, the more likely these effects are. Your specialist will discuss with you the likelihood of your child having learning difficulties as a result of his or her treatment.

The most important thing is to follow your child's progress in school. If your child has difficulty in school it is important that you inform your specialist. You may also like to talk to the child psychologist on your child's transplant team. It is also important to watch your child's social development and interactions with others, as this can be an important indication of how he or she is developing.

Effects on the eyes

Cataracts (clouding of the lens in the eye) can be a complication of TBI. About 80% of children who receive TBI develop cataracts. Although this percentage is high, less than 10% of the children who do develop cataracts require cataract repair. This surgery has become simpler over the years, and is now an outpatient procedure. If your child does receive TBI, it is important to have regular ophthalmologic (eye) check-ups.

Effects on the teeth

Children who are less than two years old when they receive chemotherapy and/or radiation therapy can have problems with their teeth. Some teeth end up smaller than expected and the enamel of the teeth can also be affected, placing them at risk of tooth decay. regular dental checkups are strongly recommended. Older children may also have tooth enamel affected and they too should see a dentist regularly.

Effects on the kidneys

Some chemotherapy drugs, antibiotics, cyclosporine and/or TBI may affect kidney function. Tests will be carried in your child every few years over the long-term to check that the kidneys are working properly.

Effects on lung function

The lungs can be affected by certain medications, radiation, GvHD and infections. Lung function will therefore be checked in your child over the long-term. For the first year after transplant, your child will also be checked for signs of chronic GvHD (e.g. skin rash, diarrhoea, weight loss, dry eyes, shortness of breath), as this condition can cause a range of problems including scarring on the skin, or chronic inflammation of the liver, bowel, eyes or lungs.

Secondary cancers

Anyone who receives chemotherapy and/or radiation is at risk of developing a secondary cancer later in life. This is because these therapies disturb the DNA of the body's cells. These effects are desirable in cancer cells (this is how these treatments work), but not in normal cells, which need healthy DNA to grow properly.

If your child is currently being treated for cancer, simply having cancer puts him or her at risk of developing a secondary cancer later in life. If your child received a transplant as treatment for cancer, their risk of secondary cancer is less than 4%. This is much lower than the risk of the first cancer re-occurring (relapse). If your child had a transplant for a condition other than cancer, their risk of developing cancer is about 2%.

In the years following transplant, your child will need to attend the long-term follow-up clinic at the hospital for ongoing monitoring of any late effects, including secondary cancer.

APPENDIX

Commonly Used Drugs and Other Treatments

This section of the book contains information about drugs and other types of treatments most commonly used in transplant. Each treatment is covered separately, with a list of possible side effects, including rare but potentially serious side effects. *If you have any questions about treatments, please talk to your doctor, pharmacist or nurse.*

Conditioning therapy

Side effects of the chemotherapy used in conditioning therapy can occur at different times after the drugs have been given:

Early side effects may occur during administration and for the first 24 hours after chemotherapy has stopped.

Delayed side effects may occur from Day 2 through to about three weeks after chemotherapy has stopped.

Late side effects may occur many years after chemotherapy is stopped. For some newer drugs, these late effects are not yet clear.

Chemotherapy affects all of the cells in the body, particularly rapidly dividing cells such as hair, bone marrow and the cells that line the mouth and gut. Some side effects are therefore common and are often expected.

Common side effects of chemotherapy

- mucositis (sores or ulcers in the throat or mouth, often accompanied by pain on swallowing)
- infection - indicated by fever, cough, chills, sore throat, aching joints, swollen glands, skin sores or discomfort on urination

- a drop in blood cell counts or myelosuppression (a decrease in the number of blood cells made in the bone marrow, leading to increased risk of infection)
- alopecia (hair loss)
- anorexia or loss of appetite
- nausea (feeling sick in the stomach, which may be accompanied by vomiting)
- oral thrush (a fungal infection of the mouth, often accompanying mucositis)
- infertility (inability to have children)

Less common or rare side effects are listed under each drug in the section below. These side effects may have only occurred in a few patients. However, they are possible and can have severe effects.

Special precautions when handling urine, faeces or vomit are necessary after chemotherapy has been given. This is because of the way the drugs are broken down and excreted by the body. The exact number of days that precautions are needed for depends on the individual drug given.

Precautions

- Wear gloves when changing nappies, soiled bed linen or vomit bowls.
- Put dirty nappies in a plastic bag and then dispose of as advised by the nursing staff.
- Double flush the toilet after your child uses it.
- If your child wets or soils the bed, remove the linen and put in the linen skip in his or her room.
- If your child is vomiting, use a bowl you do not use for anything else, tip the contents into the toilet and double flush. Wash the bowl after each use.
- If you are pregnant or planning pregnancy, it is particularly important that you follow these guidelines for handling the drugs and body waste.

Chemotherapy drugs used in conditioning therapy

BUSULPHAN

Busulphan can be taken by mouth or be given by intravenous injection, diluted in fluid and given into a vein.

Possible side effects

Early

- nausea and vomiting
- diarrhoea

- low grade fever
- dizziness
- rash and itching
- seizures or convulsions (medication will be given to prevent this)

Delayed

- liver damage (may lead to severe veno-occlusive disease)
- increased skin pigmentation (darkened colour) especially in creases of skin
- in adolescent girls menstrual periods may become irregular or stop; in adolescent boys sperm production may decrease or be absent
- mucositis (can occur 5 to 10 days after treatment)

Late

- infertility (largely dependant on total dose given)
- secondary cancer (dependant on total dose given)
- lung problems (may lead to a dry cough and, uncommonly, difficulty breathing)

urine, faeces and vomit need to be treated with caution during treatment and for 48 hours after completion of treatment.

CARBOPLATIN

Carboplatin is given by intravenous infusion, diluted in fluid and given into the vein over 15 to 60 minutes.

Possible side effects

Early

- moderate nausea and vomiting

Delayed

- slow recovery of platelet count (may take longer than other types of blood cells)

Late

- increased risk of developing a secondary cancer

Uncommon

- metallic taste in mouth
- pins and needles in the hands and feet
- altered hearing, noises or ringing in the ears (tinnitus)
- kidney damage
- liver damage

urine, blood, faeces and vomit need to be treated with caution during treatment and for 48 hours after completing treatment.

CISPLATIN

Cisplatin is given by intravenous infusion, diluted in fluid and given into a vein over 6 hours.

Possible side effects

Early

- nausea and vomiting (may begin within 2 hours and last about 24 hours; may continue or re-occur for several days. Anti-nausea medication is given to prevent this).
- metallic taste in mouth
- diarrhoea (usually subsides within a few days)
- loss of appetite
- flushing and tightness of the face (temporary)

Delayed

- kidney damage (largely dependant on total dose given)
- high tone hearing loss or ringing in the ears (tinnitus)
- drop in magnesium and sometimes calcium levels in the blood, due to loss from the kidneys
- tingling or numbness in the fingers or toes, usually after more than one dose
- seizures (rare)

Late

- increased risk of developing a secondary cancer

urine, faeces and vomit need to be treated with caution during treatment and for 7 days after completion of treatment.

CYCLOPHOSPHAMIDE

This medication may be abbreviated as CPA. Cyclophosphamide can be given by mouth or injected into a vein slowly over 5 minutes, or diluted in fluid and infused into a vein.

Possible side effects

Early

- nausea and vomiting (may occur 4 to 8 hours after the medication is given)
- metallic taste in the mouth during the infusion or injection
- bladder irritation, developing hours to weeks later (noticed as pain on urinating; may be blood or blood clots in urine. Large volumes of fluids and a drug called Mesna lessen the risk of this uncommon side effect.)
- fluid retention and confusion (uncommon, but can occur due to abnormal secretion of a hormone within the brain)

Delayed

- irregular or absent menstrual periods in adolescent girls
- decreased or absent sperm production in adolescent boys
(may occur during treatment or begin 6 to 7 months after treatment)
- increased pigmentation of the skin (colour of the skin may darken), allergic skin reactions, and nail ridging

Late

- heart damage (following single high doses; rare)
- lung damage (scarring of lung tissue)
- secondary cancer (dependant on the total dose given; rare)
- infertility (dependent on total dose given)

Special Instructions

Frequent voiding of large volumes of urine is extremely important to decrease bladder irritation and keep the kidneys working well.

urine, faeces and vomit need to be treated with caution during treatment and for 5 days after completing treatment.

ETOPOSIDE

This medication is abbreviated as vP-16. Etoposide can be given by intravenous infusion, or by mouth.

Possible side effects

Early

- nausea and vomiting
- loss of appetite
- dizziness due to a lowered blood pressure, particularly if given too quickly into the vein (uncommon)
- allergic reactions during infusion (fever, rash, shortness of breath, dizziness due to lowered blood pressure) if drug is given too quickly into the vein (rare)

Delayed

- liver toxicity
- mucositis
- diarrhoea

Late

- secondary cancer (rare; dependant on total dose given)
- heart damage

urine, faeces and vomit need to be treated with caution during treatment and for 7 days after completing treatment.

FLUDARABINE

Fludarabine is used for a limited range of cancers, mostly lymphatic cancers, but is used in conditioning therapy because of its strong immunosuppressant properties. It is the most commonly used drug for non-myeloablative transplants. Fludarabine is given into a vein over 30 minutes, usually over 3 to 5 successive days.

Possible side effects

Early

- mild nausea (and rarely vomiting)
- fever and chills
- loss of appetite
- diarrhoea (transient)

Delayed

- 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)
- fatigue and weakness.
- raised levels in liver function tests
- mucositis (uncommon)
- skin rashes
- pneumonia or hypersensitivity of the lungs (reversible after completing treatment)
- visual disturbances, seizures, numbness, confusion and agitation (more commonly seen when given in high doses)
- damage to nerve tissue resulting in difficulty with concentration, memory, balance and walking
- kidney damage (rare)

urine, faeces and vomit need to be treated with caution during treatment and for 48 hours after completing treatment.

MELPHALAN

This medication is known by the trade or brand name 'ALKErAN'. Melphalan is given intravenously.

Possible side effects

Early

- loss of appetite
- nausea and vomiting
- diarrhoea

- low blood pressure (rare)

Delayed

- mouth ulcers
- irregular or absent menstrual periods in adolescent girls
- decreased or absent sperm production in adolescent boys

Late

- lung damage
- secondary cancer (rare; dependant on the total dose given)
- infertility (dependant on total dose given)

urine, blood, faeces and vomit need to be treated with caution during treatment and for 7 days after completing treatment.

MESNA

Mesna is usually given intravenously but may also be given orally. Mesna is a non-cytotoxic medication used in the prevention of bladder toxicity in patients treated with Cyclophosphamide.

Mesna is not very toxic and does not usually cause side effects.

Possible side effects

- diarrhoea
- headache
- limb pain
- bad taste in the mouth (particularly when given orally)
- fatigue
- low blood pressure (temporary)

THIOTEPA

Thiotepa is usually infused into a vein, but occasionally may be given into the cavity of the chest or abdomen or into the cerebro-spinal fluid.

Possible side effects

Early

- mild nausea and vomiting
- dizziness or headache
- local pain at site of injection
- sudden high fever
- confusion and drowsiness, if administered at high doses (uncommon)
- allergic reactions (skin rashes, hives or itching); rare

Delayed

- mucositis
- raised levels in liver function tests
- increased skin pigmentation (darkened colour)
- skin rash (dry scaling and peeling of the palms and soles); regular baths necessary
- irregular or absent menstrual periods in adolescent girls
- decreased or absent sperm production in adolescent boys

Late

- infertility

urine, blood, faeces and vomit need to be treated with caution during treatment and for 72 hours after finishing treatment.

Other drugs used in conditioning therapy

ANTI-THYMOCYTE GLOBULIN (ATG/Atgam)

ATG is an immunosuppressive drug sometimes used in conditioning therapy to boost the effects on the immune system. ATG is prepared from the serum of animals, usually horses or rabbits, immunised with human thymocytes (the precursors of T lymphocyte cells). The serum contains antibodies against human T-cells, and helps kill any remaining lymphocytes in the patient's body (that could reject the donated stem cells). ATG can also eliminate donor T-cells that cause graft-versus-host disease.

ATG is usually given over 3 to 5 days during conditioning therapy, as an intravenous infusion lasting 4 to 6 hours. It may also be used to treat GvHD.

Possible side effects

Early

- allergic reactions during infusion (fever, rash, shortness of breath, dizziness due to low blood pressure)
- fever, chills
- low blood pressure (some patients experience low blood pressure without other signs of an allergic reaction)
- itchy rash (common)
- weakness, or feeling light headed
- swelling of the eyelids, hands and feet due to excess fluid retention
- diarrhoea
- dizziness or agitation (uncommon)

- nausea and vomiting (uncommon)
- bone and muscle pain (uncommon)

Delayed

- rash
- loss of protein in the urine
- reactivation of herpes simplex virus
- kidney damage
- blood clots
- pins and needles, numbness in fingers and toes

Special Instructions

Antihistamine, paracetamol and hydrocortisone will be given prior and during each dose of Atgam to lessen the infusion related side effects.

GRANULOCYTE COLONY STIMULATING FACTOR (G-CSF)

G-CSF stimulates the production of white blood cells. This medication is used to shorten the time that the patient has low blood cell counts (myelosuppression), which commonly follows chemotherapy. G-CSF can also be given to increase stem cell collections. G-CSF is usually injected subcutaneously (under the skin) or it can be given by intravenous infusion.

Possible side effects

Early

- pain, redness or itchiness around the injection site
- skin rash (uncommon)
- low grade fever (uncommon)

Delayed

- mild to moderate bone pain
- flare up of pre-existing eczema (uncommon)

Total body irradiation

Total body irradiation (TBI) is a form of radiation treatment that is used along with chemotherapy for some patients undergoing allogeneic transplant. In this treatment, radiation is delivered to the entire body by a machine called a linear accelerator. This machine is specially designed to allow treatment to be tailored to each individual patient, depending on his or her needs. Certain organs that are sensitive to radiation, such as the lungs, are shielded during part of the TBI.

TBI has two actions: it kills cancer cells and it also suppresses the immune system to allow transplanted cells to engraft. When a child has TBI, he or she sits or lies down,

and is kept still with the use of a special brace or sand bags. He or she will need to be alone in the treatment room, but is able to communicate with the radiation therapist who will be watching at all times.

usually, TBI is given twice daily for a total of six doses. However, this may vary depending on your child's individual treatment plan. Each treatment takes between 30 minutes and one hour. In most cases a drug called Lorazepam (Ativan) is given to help with relaxation and to reduce feelings of nausea. Children less than five years old usually require a general anaesthetic for each dose of TBI.

Possible short-term side effects

- nausea and vomiting
- hiccoughs (hiccups)
- swollen salivary glands (parotitis)
- skin redness
- mouth dryness, due to decreased saliva production
- mouth ulcers
- thickened saliva
- dry eyes, due to decreased tear formation
- diarrhoea
- bone marrow suppression

Graft-versus-host disease (GVHD)

Drugs used to prevent GVHD

CYCLOSPORIN A (CSA)

Cyclosporin A is an immunosuppressive drug used in patients receiving allogeneic stem cell or cord blood transplants. The drug helps prevent GvHD by slowing down the growth and development of the donor's T lymphocyte cells. This medication can be given by intravenous infusion or by mouth. The oral formulation is known as Neoral™ and is available in capsule or liquid. Cyclosporin is also used to treat chronic GvHD.

Possible side effects

Early

- mild nausea and vomiting
- diarrhoea
- burning feeling in the hands and feet (particularly during the first week of treatment and if infused too quickly)

Delayed

- increased susceptibility to infection

- impairment of kidney and liver function
- high blood pressure (hypertension)
- excessive facial and body hair (reversible when drug is stopped)
- tremor (shaking)
- weight gain
- swelling of eyelids, hands and feet due to excess fluid retention
- lethargy, headache, tiredness, depression, problems in vision, seizures
- itchiness, skin rash
- buzzing and ringing in the ears, difficulty hearing
- muscle cramps and weakness, feeling of pins and needles
- irregular or no menstrual periods in adolescent girls (reversible)
- acne in teenagers (this may develop or worsen while taking the medication)
- swollen and bleeding gums
- severe allergic reaction (rare)
- thrombotic thrombocytopenic purpura (a complication that results from changes in small blood vessels, causing clotting and blocking of blood flow; rare)

Late

- increased risk of skin cancer and lymphoma (rare)

Contact your BMT team if you notice:

- any signs of infection
- blood stained vomiting or dark stools
- severe nausea and vomiting and diarrhoea
- tremor (shaking/ trembling)
- oral thrush
- severe muscle weakness or tenderness
- numbness or pins and needles in the hands and feet
- severe headache
- buzzing or ringing in the ears, difficulty hearing
- swelling of the ankles, feet, eyelids and hands (due to excess fluid)
- severe itching or skin rash
- of the skin and or eyes (often accompanied by generally feeling unwell)

Special Instructions

- Neoral™ is taken twice a day, twelve hours apart. Neoral™ should be taken at the same time each day, and must be given either always on a full stomach, or always on an empty stomach i.e. this must be consistent.

- The capsules must be taken whole with a full glass of water. They must not be chewed.
- The dose of oral liquid should be measured with the syringe provided. The liquid should then be diluted in a glass cup with apple or orange juice or soft drink, and stirred well prior to taking. Rinse the container with more drink to ensure the whole dose is taken. Alternatively the dose can be taken undiluted followed by a drink. Wipe the outside of the syringe with a dry tissue; do not rinse it.
- DO NOT MIX WITH GRAPEFRUIT OR GRAPEFRUIT JUICE.
- restrict salt intake in order to avoid excessive water retention and high blood pressure.
- restrict eating large amounts of foods that are high in potassium. Your child's doctor can tell you which foods to avoid.
- If the medication is vomited within 30 minutes of taking it, the same dose should be repeated. If the medication is vomited again, call your doctor.
- If a dose is missed and it is almost time for the next dose, it is best to skip the dose that was missed and take the next dose when it is due. Otherwise the dose should be taken as soon as it is remembered and the patient should go back to taking it as he or she would normally. A DOUBLE DOSE SHOULD NOT BE TAKEN. If more than one dose is missed, contact the doctor as soon as possible.
- Good oral hygiene should be adhered to, to help prevent dental and mouth infections.
- The skin needs to be protected from over exposure to the sun. Your child should wear protective clothing and use a sunscreen when in the sun.
- If your child is to be started on any new medicines (including any bought at the supermarket, health food store or pharmacy), remind your doctor and pharmacist that he or she is taking Neoral™.
- Neoral™ can only be obtained through a hospital pharmacy, not your local pharmacy. Please ensure that you get a new supply before you run out.

Monitoring

- regular monitoring is required to check the level of Cyclosporin in the blood. This is done as a peripheral blood test (finger prick), or from the central line, using the lumen that has not been used to give the intravenous Cyclosporin (usually the red lumen). Monitoring is generally done twice weekly while in the hospital, and weekly or fortnightly once discharged. It is important that the morning dose of Cyclosporin is not taken until after the blood level is measured. Bring the medicine to clinic so that a dose can be taken after the blood sample is taken.
- Liver and kidney function will be tested regularly.
- Blood pressure will be tested regularly.

MYCOPHENOLATE MOFETIL

Mycophenolate is an immunosuppressive drug used to prevent and treat GvHD in patients receiving allogeneic stem cell or cord blood transplants. This drug is also used to prevent graft rejection after organ transplants (e.g. a kidney transplant). It can be given by intravenous infusion or by mouth. The oral formulation is available in capsule, tablet or syrup.

Possible side effects

Early

- mild nausea and or indigestion
- diarrhoea
- constipation

Delayed

- a drop in white blood counts
- impaired liver function
- stomach and or abdominal pain (less common)
- headache, tremor (shaking), dizziness, anxiety
- itchiness, skin rash (less common)
- oral thrush
- back pain (less common)
- mucositis
- a drop in red blood cell counts (less common)

Late

- increased risk of skin cancer and lymphoma (rare)

Contact your BMT team if you notice:

- blood stained vomiting or dark stools (rarely, bleeding into the gut can occur)
- any signs of infection
- severe nausea and vomiting and diarrhoea
- tremor (shaking)
- oral thrush
- severe itching or skin rash
- mouth ulcers

Special Instructions

- Mycophenolate is taken twice a day, twelve hours apart. It should be taken at the same time each day, and must be given either always on a full stomach, or always on an empty stomach i.e. this must be consistent.

- If the dose is vomited within 30 minutes of taking it, the same dose should be repeated. If the medication is vomited again, call your doctor.
- If a dose is missed and it is almost time for the next dose, it is best to skip the dose that was missed and take the next dose when it is due. Otherwise the dose should be taken as soon as it is remembered and the patient should go back to taking it as he or she would normally. A DOuBLE DOSE SHOuLD NOT BE TAKEN. If more then one dose is missed, contact the doctor as soon as possible.
- Do NOT open or crush the tablets. If tablets cannot be swallowed, there is a suspension available.
- The skin needs to be protected from over exposure to the sun. Your child should wear protective clothing and use a sunscreen when in the sun.
- The brand of Mycophenolate prescribed at Sydney Children's Hospital is known as CELLCEPT. This is not interchangeable with Myfortic (the other brand of Mycophenolate).
- This medication can only be obtained through a hospital pharmacy, not your local pharmacy. Please ensure you get a new supply before you run out.
- Any person administering the dose should wear rubber gloves for protection. Pregnant women should be particularly careful, as this medication can cause birth defects.

Monitoring

- regular tests of liver and kidney function will be done.

METHOTREXATE

This medication is abbreviated as MTx. Methotrexate, when used as a transplant medication, helps restrict the ability of donor T-cells to attack the recipient's organs and tissues (GvHD). It is a yellow coloured drug and is given intravenously.

Possible side effects

Early

- nausea, vomiting and loss of appetite
- diarrhoea

Delayed

- sores in the mouth and/or throat (mucositis)
- skin rash on different body areas when exposed to the sun (ultraviolet light)
- elevated liver function enzymes
- drowsiness, fatigue, dizziness and blurred vision
- liver damage (very rare)

- inflammation of the lung tissue (this is a very rare allergic reaction and is reversible on stopping the drug)

urine, blood, faeces and vomit need to be treated with caution during treatment and for 7 days after completing treatment.

TACROLIMUS (Prograf)

Tacrolimus is an immunosuppressive drug. It works by suppressing T-cell activation and B-cell growth, which are thought to play a major role in GvHD and transplant rejection.

Tacrolimus is usually given orally twice a day. If your child is unable to tolerate this, it may be given through a drip as a continuous infusion.

Possible side effects

Common

- tremor (shaking)
- headache
- diarrhoea
- nausea
- decreased kidney function
- increased blood pressure
- increased risk of infection

Less common

- allergic reactions
- high blood sugar (possibly requiring insulin)

Drugs used to treat GVHD

METHYLPREDNISOLONE(SOLU MEDROL)/ PREDNISONE (PREDNISOLONE)

Methylprednisolone and prednisone are synthetic steroid hormones. They work by suppressing the immune response of the donor cells to the patient's cells. Prednisone is used to treat grade 1 acute GvHD and chronic GvHD. Methylprednisolone is used to treat grades 2-4 GvHD.

Possible side effects

Early

- upset stomach
- bitter taste in the mouth

Delayed

- increase in appetite (may lead to weight gain)
- development of a 'moon face'
- fluid retention (leading to weight gain); swelling in hands and feet, increased blood pressure

- stomach ulceration/haemorrhage
- prolonged hiccoughs (hiccups)
- oral thrush
- increase in blood glucose level (leading to increased thirst or excessive urination)
- mood changes, including depression, irritability, euphoria (a feeling of well being), nervousness
- difficulty sleeping
- delayed wound healing and increased susceptibility to infection

After long-term therapy (more than 14 days)

- swelling and bloating of the face and abdomen, with thinning of the extremities
- loss of calcium from the bones
- inflammation of the stomach (stomach and intestinal tract bleeding)
- increased pressure within the eyes
- muscle weakness, especially in the shoulders and thighs
- acne in teenagers (this may develop or worsen while taking the medication, and will gradually subside after the medication is discontinued)

Late

- cataracts
- slowed growth
- **osteoporosis**
- erosion of the head of the femur or humerus (long bones in the legs arms)

Contact your BMT team if you notice:

- blood stained vomiting or dark stools (rarely, bleeding into the gut can occur)
- any signs of infection
- oral thrush
- severe muscle weakness or tenderness
- severe headache and or confusion
- increased thirst, or increased frequency of urination
- swelling of the ankles, feet, eyelids and hands (due to excess fluid)

Special Instructions

- The medication must be taken with food or milk.
- If the course over which the drugs are given is longer than 7 days, the dose will be gradually tapered (reduced) over a period of a few days. Your child should not stop taking the drug suddenly, or run out of the drug before treatment is completed.
- Salt intake should be restricted to avoid excessive water retention and high blood pressure.

DACLUZIMAB

Dacluzimab is a type of antibody that has an immunosuppressive effect. It is used when GvHD does not respond to Methylprednisolone, most frequently in the treatment of grades 2 - 4 GvHD of the skin. It is usually given through a drip on 5 days, spaced out over a 4-week period.

Possible side effects

Dacluzimab appears to have minimal side effects, apart from the following:

- rare allergic reactions
- increased risk of infection

INFLIXIMAB

Infliximab is a type of antibody used in conjunction with Dacluzimab to treat GvHD, as above.

Infections

Drugs used for bacterial infections

Initial treatment for bacterial infections consists of **broad-spectrum antibiotics** (usually a combination of a cephalosporin and a penicillin), plus one of the aminoglycosides (usually Gentamicin). vancomycin may be given up front, or added after about 48 hours of the initial combination therapy being given.

AMINOGLYCOSIDES (E.g. GENTAMICIN, TOBRAMYCIN)

The aminoglycosides are a group of antibiotics that kill certain bacteria by stopping them from forming certain proteins they need to survive. These antibiotics are effective against many 'Gram negative' bacteria such as *E. coli* and *Pseudomonas*, as well as some 'Gram positive' bacteria such as *Staphylococcus* species. These bacteria cause infections in many body systems including the respiratory, skin, blood, urinary and skeletal systems.

Gentamicin and Tobramycin are given through a drip, once daily.

Possible side effects

Common

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

Less common

- rash
- allergy
- gut disturbance (mainly diarrhoea)

Because some of the above side effects can have a long-term impact (particularly on kidney function and hearing), Gentamicin and Tobramycin levels are monitored regularly by taking blood samples, usually 2-3 times a week. Doses are altered according to the drug levels shown by testing.

CEPHALOSPORINS (E.g. CEFEPIME, CEFTRIAXONE, CLAFORAN, KEFLEX)

The cephalosporins are a group of antibiotics that kill certain bacteria by preventing them from making their cell walls. These drugs are effective against a variety of bacteria that cause respiratory, skin, blood, urinary and skeletal infections. These antibiotics are said to be 'broad spectrum' because they are effective against both the categories of bacteria (known as 'Gram positive' and 'Gram negative'). Bacteria that are susceptible to the cephalosporins include *Streptococcus* and *Staphylococcus* species and *E. coli*. These drugs should not be taken if the patient has a previous history of allergy to penicillin.

When used in transplant, the antibiotics are usually given through a drip once or twice daily, although in some cases they may be taken orally.

Possible side effects

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

PENICILLINS (E.g. TIMENTIN, TAZOCIN)

The penicillins are a group of antibiotics that kill bacteria by stopping them from forming their cell walls. The types of penicillins used in transplant are broad-spectrum and are used to treat infections caused by bacteria such as *E. coli*, *Pseudomonas* and *Staphylococcus* species.

Penicillins are usually given through a drip 3-4 times a day, each dose taking about 30 minutes.

Possible side effects

Common

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

Less common

- anaphylaxis (allergic reaction)
- nausea and vomiting
- decreased kidney or liver function

VANCOMYCIN

vancomycin is an antibiotic that kills bacteria by preventing them from forming cell walls and by damaging the cell membrane. This drug is effective against bacteria such as *Clostridium difficile*, *Streptococcus* species and *Staphylococcus* species.

vancomycin is given orally for *Clostridium* infections and through a drip for all other bacteria. It is given up to 4 times a day, with each dose lasting one hour or longer.

Possible side effects

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 (caused by rapid infusion)
- gut disturbances (nausea, vomiting or diarrhoea)
- hypersensitivity, indicated by chills, nausea, rash, fever

Note: Prolonged use may lead to antibiotic resistant bacteria, e.g. vancomycin-resistant *Enterococcus* (vRE).

regular monitoring of drug levels is carried out to reduce the risk of hearing loss or kidney damage. Doses are altered according to the drug level shown by testing.

Drugs used for fungal infections

AMPHOTERICIN

Amphotericin is the main drug used to treat proven or suspected infections caused by fungi such as *Candida* (*Monilia*), *Cryptococcus* or *Aspergillus*. The drug works by altering the membrane of the fungi's cells, causing some substances to flow out and ultimately resulting in the death of the cell.

Amphotericin is given intravenously. It is usually given daily and treatment may continue for many months, depending on the infection. Many patients are given another medication beforehand (called a premedication) to prevent or reduce the severity of infusion-related problems.

Other preparations of antifungal agents are available. These differ between hospitals and depend on the needs of the patient. Examples include Amphocil, Caspofungin, voriconazole and Ambisome.

Possible side effects

Common

- infusion related problems, including chills, rigors, fevers (leading to the nickname ‘Amphoterrible’)
- decreased kidney function
- nausea and vomiting
- decreased appetite, which may lead to 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 and dependent on dose)
- hypotension, cardiac arrest
- abnormal liver function
- kidney failure

Drugs used for viral infections

ACYCLOVIR

Acyclovir is an antiviral drug given to both treat and prevent viral infections, particularly those caused by *Herpes simplex* or *Varicella zoster*. It is given either orally or through a drip three times per day, depending on the patient's ability to swallow and retain the dose. Treatment with this drug begins on Day+1 and continues until Day+28.

Possible side effects

Common

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

Less common

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

GANCICLOVIR

Ganciclovir is an antiviral medication used to prevent or treat cytomegalovirus (CMV) infection. The drug works by interfering with the DNA of the viral cells and can be given either intravenously or by mouth. The oral form of this medication is called valganciclovir, but it is not always appropriate to use in children since there is no syrup available and the tablet cannot be crushed or broken.

Possible side effects

Early

- a drop in blood counts (especially neutrophils and platelets), which can increase susceptibility to infection
- mild nausea and vomiting
- loss of appetite
- diarrhoea
- weakness
- allergic rash (within 1-2 days after starting the medication)
- a drop in red blood cell count (anaemia)
- dizziness, confusion, seizures

Late

- infertility (dependent on the total dose given)
- secondary cancer (rare; dependent on the total dose given)

Special Instructions

- valganciclovir can be used in place of Ganciclovir.
- valganciclovir should be swallowed whole (not chewed or crushed) and taken after a meal.
- If your child is to be started on any new medicines (including any bought at the supermarket, health food store or pharmacy), remind your doctor and pharmacist that Ganciclovir is being taken.
- This medication can cause birth defects, so pregnant women should handle with caution.

urine, faeces and vomit need to be treated with caution during treatment and for 48 hours after completing treatment.

Drugs used for protozoal infections

COTRIMOXAZOLE (Bactrim DS)

Cotrimoxazole is an anti-infective agent made up of two drugs: trimethoprim and sulfamethoxazole. It is used in the prevention and treatment of *Pneumocystis carinii* pneumonia (PCP). Cotrimoxazole works by interfering with the building of cell walls, leading to cell death.

For the prevention of PCP, Bactrim DS is given twice daily two times a week. For the treatment of PCP, a higher dose of Bactrim is given more frequently, usually intravenously.

Possible side effects

Common

- nausea, vomiting
- lack of appetite
- rash
- bone marrow suppression (particularly when the drug is used to treat an infection, or is used long-term)
- increased likelihood 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 of the drug)
- electrolyte disturbances (particularly potassium)

Drugs used for veno-occlusive disease/sinusoidal obstructive syndrome

DEFIBROTIDE

Defibrotide has a number of complex actions that reduce clotting and blockage of small blood vessels in the liver. It therefore aids in the prevention and treatment of vOD.

It is administered twice daily through a drip. If being used for the treatment of vOD, it is usually given for at least two weeks.

Defibrotide does not usually cause side effects. Occasional side effects are listed below.

Possible side effects

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

URSODEOXYCHOLIC ACID (UDCA/URSO)

ursodeoxycholic acid is a naturally occurring bile salt that has been shown to help in the prevention and treatment of a number of liver problems, including vOD and GvHD. It is given orally in 2-4 doses from the start of conditioning therapy, for at least one month.

Possible side effects

Common

- diarrhoea
- itchy rash (in the first few weeks of treatment)

Less common

- allergic response
- nausea and vomiting
- sleep disturbances

Glossary

allogeneic transplant

A transplant that uses stem cells donated by another person.

apheresis

The process of using an apheresis machine, which spins blood and separates out the white blood cells, red cells, platelets and plasma. Stem cells are skimmed off for use in transplant, and the rest of the blood is returned to the donor.

Aspergillus

A common type of fungus that grows on decaying vegetation, such as compost heaps and fallen leaves. It can cause infection in the body.

autologous transplant

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

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.

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 usually keep it under control.

cataract

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

central line

Also known as a CvL or Hickman catheter. A catheter that is inserted under the skin of the 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 transplant 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 the body, made up of x-rays.

conditioning therapy

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

cord blood

Blood taken from the umbilical cord of a newborn baby. This is a rich source of stem cells.

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 an apheresis machine, which is used to collect peripheral blood stem cells.

dietitian

A health professional who specialises in nutrition.

engraftment

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

erythrocytes

See 'red blood cells'.

glomerular filtration rate (GFR)

A test of kidney function.

graft-versus-host disease (GVHD)

A common complication of allogeneic transplant, caused by the donor's immune cells killing the recipient's healthy cells. Acute GvHD occurs in the first 100 days after the transplant. Chronic GvHD develops more than 100 days after transplant.

graft-versus-leukaemia effect (GVL)

See 'graft-versus-tumour effect'

graft-versus-tumour effect (GVT)

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

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.

Hickman catheter

See central line.

HLA (human leukocyte antigen)

Proteins that are found on almost all the cells in the body. They are one of the main ways the 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 therapy

Therapy that suppresses the immune system. It kills the immune cells so that the donor's stem cells can become established in the body.

leukocytes

See 'white blood cells'

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 the 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 transplant treatment that causes mouth and throat pain.

mucous membranes

Moist surfaces of the eyes, mouth and gut.

myeloablative therapy

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

neutrophils

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

osteoporosis

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

peripheral blood

Blood that circulates around the body through the veins and arteries.

platelets

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

pluripotent stem cells

Early-stage cells in the bone marrow that are able to make copies of themselves. 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.

proteins

Essential nutrients that help the body build and repair connective tissue, cell membranes and muscle cells.

protozoa

Single-cell parasites, which need human cells to replicate (reproduce themselves).

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 blood cells, white blood cells and platelets.

T-cells

A class of lymphocyte (a type of white blood cell), which plays an important role in the immune response.

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 transplant.

tissue typing

A process to check how closely the cells from a potential donor match those of the person who will receive the transplant. 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.



This book has been produced as a guide for parents and other family members of children receiving blood and marrow transplants in Australia.

It has been written by doctors and nurses who care for children undergoing transplant, with contributions from psychologists, pharmacists, allied health professionals and the parents of children who have undergone a transplant.

Covered in the guide are the different phases of transplant and what to expect during each of these. Topics covered include:

- finding a suitable donor
- preparing for transplant
- life after transplant
- nutritional concerns
- emotional aspects
- common treatments
- side effects and possible complications

If a child in your family is undergoing a transplant, it is important that you have access to accurate, relevant and helpful information. This book has been written to provide that information in easy to understand language and includes a glossary of the most common medical terms related to transplant. read it at your own pace, and don't hesitate to ask your transplant team for more information about any of the topics covered.

This book contains contributions from:
Sydney Children's Hospital
The Children's Hospital at Westmead
Bone Marrow Transplant Network NSW

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