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THE SEVEN STEPS THE NEXT STEPS

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A handbook for long-term recovery after stem cell transplant

THE SEVEN STEPS – THE NEXT STEPS
A HANDBOOK FOR RECOVERY

Written by Michelle Kenyon
and Dr Bronwen Shaw

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Ordering more copies

If you would like to order more copies of The Next Steps, please get in touch with Anthony Nolan on **patientinfo@anthonynolan.org** and they will arrange for copies to be sent to you.

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INTRODUCTION

This book has been written to help you to understand more about the long-term recovery and effects of your transplant

It is important to bear in mind that for many patients, a stem cell transplant offers not only the chance of a cure, but also the chance of a normal quality of life. For some patients this goal may be achieved without too many problems. But for others, the journey to recovery can be very difficult and demanding, both physically and psychologically. Some patients find that relatively small problems and their effect on daily life are extremely difficult to manage, while others appear to cope well with difficult and complex problems. Both are normal and help is available for everyone, even those who may not appear to need it.

For a small group of patients, the long-term and late effects of the transplant can have a very serious impact on their general health and wellbeing. As a result good quality of life can be difficult to achieve.

Since some of the problems discussed in this book may be life-changing, life-threatening, or even lead to death, you may find some of the information upsetting and hard to read. However, many patients wish to know more about these problems so that they feel more prepared to cope with some of the challenges that may lie ahead.

You might recognise some of the topics from The Seven Steps. This book, The Next Steps hopes to address some of these in more detail to help you understand more about your transplant journey.

1 STEP ONE WHAT HAPPENS NEXT?

ISSUES DISCUSSED IN THIS STEP:

- Transition from inpatient to outpatient
- Appointments
- Transfusions
- Readmission to hospital
- High dependency and intensive care
  - Viral infections
  - Bacterial infections
  - Fungal infections
  - Kidney problems
  - Liver problems
  - Nausea and vomiting
  - Diarrhoea
  - Bleeding
  - Graft versus host disease
- Hickman line removal
- Medication

TRANSITION FROM INPATIENT TO OUTPATIENT

When you leave the hospital for the first time after your transplant, there is often a great sense of nervous excitement and anticipation. It can also be quite scary.

You have spent a number of weeks becoming a transplant recipient, learning the day-to-day routine of blood tests, observations and medications. All of this activity has been managed under the constant care and supervision of the team on the transplant unit.

You will have developed a basic understanding of the changes that can happen and an awareness of your own body that you may not have had before. However, the prospect of being 'let loose' on your own is often very daunting.

The reality is that you are never truly alone. The staff on the transplant unit will ensure that you leave the hospital with instructions of what to do if you become unwell. They will also give you the names and numbers of people to contact if you have any questions about your treatment and care.

Below is a list of items and information that you may need before you go home.

- List of contact numbers for the transplant centre
- Arrangements for Hickman line care or information about Hickman line care
- Nutrition and dietary advice
- Medication and information on how to take it
- Appointments for outpatient blood checks, outpatient clinic and investigations such as bone marrow tests

It is important to remember that although you are being sent home from the hospital, and an important phase of the transplant process is complete, it will be many months before you are fully recovered.

Although you are being sent home from the hospital, it will be many months before you are fully recovered

APPOINTMENTS

When you leave the hospital, you will be given a number of appointments. You may wish to keep a small diary just for these.

Following a transplant, very close monitoring and observation is usually needed. This involves regular blood tests as well as medical reviews. There are also a number of other tests that will be performed to assess the outcome of your transplant. These are discussed in the next section.

The frequency of your appointments depends upon how much time has passed since your transplant and how you are managing and progressing. At first, it is normal to see the doctor once a week, or once every two weeks and to have weekly blood tests. Sometimes, it is necessary to increase the frequency of your visits if you require extra monitoring, treatment, or the doctors are concerned about your progress.

Frequent visits to the hospital for repetitive tests can become very tiresome, particularly during the first weeks or over a prolonged period of time. It is likely that you will need to attend the clinic at your local hospital as well as at the transplant centre. In some cases, when other problems develop, you may also need to see other specialists.

The frequency of your visits will be continually reviewed and kept to a minimum where possible. However, regular and continuous monitoring is important so that any new problems can be identified early and treated promptly. This is essential for a successful outcome.

Below is a list of appointments that you may need. Please make sure that your next appointment is booked at each attendance.

- Outpatient appointment – local hospital
- Outpatient appointment – transplant centre
- Appointment for follow up investigations (such as bone marrow or scans)
- Appointment for pentamidine nebuliser if needed (usually given monthly until counts are 'normal' and then replaced with Septrin tablets)

TRANSFUSIONS

Some patients continue to need transfusions of blood and platelets after they go home. These can often be arranged with your local hospital or combined with other appointments at the transplant centre if needed.

There are a number of reasons why you may need transfusions. Please ask your doctor if you are concerned. Recipients of donor transplants must receive irradiated blood products for at least the first post-transplant year, although this usually continues lifelong. You can carry an

'irradiated blood product' card with you. Please ask your doctor or nurse for one of these.

READMISSION TO HOSPITAL

Readmission to hospital after a transplant is very common and can happen a number of times. The reasons for readmission are very varied and range from the simple and straightforward to the complex and serious. Some studies have shown that about a third of all patients (one in three) will need to be readmitted to hospital in the first few months after transplant. Whether you are admitted to the transplant centre or to your local hospital will depend on the local arrangements. This will be explained to you before you are discharged home following your transplant.

The length of your stay is dependent upon the problem that needs to be treated. Some patients come in with one problem and then develop others and end up staying in for longer than for the transplant, while others come in only for a few days.

Some common reasons for readmission are as follows:

- Infections
  - Viral
  - Bacterial
  - Fungal
- Kidney problems
- Liver problems
- Nausea and vomiting
- Diarrhoea
- Bleeding
- Poor nutrition/weight loss
- Graft versus host disease (discussed later)

Readmission to hospital after your transplant can be very challenging to your confidence and morale. Even knowing that this is a possibility does not make it any easier. It is often a period of great uncertainty and it is likely that you will need lots of support from your family, carers and the staff involved in your care.

It is often difficult to accept that you are going to feel unwell again after you have worked so hard and achieved so much during the first part of your transplant. Some of the problems that you can develop may leave you feeling well, but frustrated at having to spend more time in the hospital.

Other problems are serious complications that can arise after your transplant when your immune system is vulnerable or you are physically recovering from the demands of the treatment. This is an important time, since some problems can be very complex and difficult to treat and can lead to serious illness in a relatively short time.

Some problems can develop into life-threatening complications and may even lead to death. It is also possible that serious problems can develop at any time after your transplant, although the chances of that happening become less as the time since your transplant gets longer.

Readmission to hospital after your transplant can be very challenging to your confidence and morale

HIGH DEPENDENCY AND INTENSIVE CARE

There are times when you may need more specialist care on a high dependency or intensive care unit (ICU or ITU).

These units offer essential care and help for patients who need much closer observation and support. Occasionally, it is necessary to use special equipment and machines to monitor your condition and the staff on these units are specially trained in this area.

Sometimes, more lines are placed or inserted to monitor specific areas of the body. For example, a urinary catheter may be used to closely record the amount of urine that is being made, or a line may be inserted into an artery to closely monitor the amount of oxygen in your blood. There are also special drugs that may be used to either treat or support you, or make you feel more comfortable.

Some of these drugs also require special monitoring and this is often best done in a high dependency or intensive care area. The staff on these units have also been specially trained to use technical machines as part of your care. Some machines can help to take care of the kidneys if they are not working properly and others can help with breathing.

Being transferred to the high dependency or intensive care unit can be a very frightening and challenging time for you and your family. It seems strange that at such an important time, you are separated from the environment and staff that are familiar and moved to an area that looks, feels and sounds very different. The people who will be looking after you during your stay will work very hard to make sure that you settle in as quickly and smoothly as possible. Please talk to your team about any concerns you might have.

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You may be very unwell and in some cases breathing for yourself may not be possible. If that happens, a breathing machine or ventilator may need to be used.

Some patients will need to be unconscious while on ITU and may not be able to talk to or communicate with family members and loved ones. This can be distressing and it is not always possible to have enough time to talk to your family before being transferred to ITU.

If this is the case, the doctors will discuss this with you or your family and try to answer any questions as fully as they can.

Recovery from serious problems often takes a long time and means an extended stay in hospital. This is so that your progress can continue to be monitored closely by your team.

Do remember that only a few patients develop such serious problems. Although it is important to be aware that these situations can arise, for most patients, readmission means little more than an inconvenience or an interruption to progress and improvement.

This time, although unpredictable and sometimes frightening, is part of your recovery after your transplant. The doctors and nurses who are looking after you will keep you as informed as possible about your progress.

INFECTIONS

Viral infections

These types of infections are a common reason for admission and readmission following a transplant.

CMV

CMV (cytomegalovirus) is a virus that can be present with, or even without, any symptoms and can be detected by blood tests. CMV can cause infection almost anywhere in the body. When your immune system is poor, exposure to or reactivation of CMV can be serious and, in some cases, life-threatening. Significant progress has been made in preventing CMV infections, especially in patients who carry the virus or are at risk of reactivating the virus.

Many hospitals carry out weekly blood tests for CMV as this virus can be detected at very low levels. This is often referred to as CMV

reactivation and if it is detected, it needs to be treated.

A number of treatments are available and given either as a tablet or a drip, twice a day for at least two weeks. Sometimes, patients need to be in hospital for this treatment even though they usually feel well.

Most CMV reactivations occur during the first few months after the transplant, although some can occur later. Occasionally, patients experience repeated reactivations and may require treatment on and off for a number of months. This can be extremely frustrating, since despite feeling well, treatment must be given.

Other viruses

Some viruses can present like a common cold or flu-like illness and can cause inflammation of the airways and even lead to pneumonia. It is important to contact the hospital if you develop any of these symptoms and they will tell you if you need to have any tests done. One common test is a nose and throat swab which is taken to detect the presence of respiratory viruses which may cause a runny nose or sore throat.

It is important to contact the hospital if you develop any of these symptoms

The treatment of these viruses depends upon which one (if any) is identified. Some of the treatments can be given via a nebuliser (a device used to administer medication in the form of a mist inhaled into the lungs), while others can be given via an intravenous drip.

EBV (the virus causing glandular fever) can also be dormant in the body and then reactivate after a transplant. This is often picked up on a screening blood test when you feel quite well. In many cases treatment is not needed at all. For some, an antibody treatment (Rituximab) is needed which can be given as an infusion in the outpatient setting. Occasionally, the EBV can cause a more serious illness, with swelling

of the lymph nodes, and additional treatment, sometimes in the form of chemotherapy, may be required.

BK virus is another virus which can be problematic after transplant. It usually causes cystitis, which is inflammation of the wall of the bladder. This inflammation usually results in painful and frequent urination. In some patients the urine will contain blood.

Investigations to identify this problem will usually include urine testing in the laboratory and, if the virus is detected, it will often be present for many weeks. If the symptoms and discomfort remain or become worse, then the doctors may ask you to see another specialist who will carry out further investigations.

Bacterial infections

Bacterial infections are also a common reason for readmission after a transplant and one of the most common bacterial infections can come from the Hickman line. Hickman line infections are often, although not always, associated with chills and/or fever after the line has been used. In some instances, this happens almost immediately; at other times there can be a delay of a few hours.

Whatever the cause, bacterial infections can make you very unwell very quickly. It is vital that you contact the hospital immediately if you have a temperature above 38˚C, or if you suddenly feel unwell even without a temperature**.

There is always someone at the other end of the phone who will be able to give you advice.

***You do not always develop a temperature with infections and some drugs in particular, such as steroids or paracetamol, can reduce your body's ability to mount a temperature in response to infection.*

Fungal infections

Fungal infections tend to arise when blood counts are low following chemotherapy or a transplant. These infections most commonly occur in the chest or sinuses but can also be present elsewhere.

Fungal infections cannot be fully diagnosed on a normal X-ray. If your doctor thinks that you might have a fungal infection, then they might arrange for you to have a CT scan. A CT scan produces very detailed images which can be used to diagnose and monitor a variety of conditions. For some patients, fungal infections can appear later after the blood counts have recovered. To reduce the risk of them arising, most patients are given preventative medication when they go home.

Many patients will stop this medication a few months after the transplant. Those patients who need to continue immuno-suppression, or who have graft versus host disease, remain at risk of fungal infections and may need to continue with the medication for longer.

KIDNEY PROBLEMS

After your transplant, as part of your regular follow-up, the function of your kidneys will be monitored. This is done by performing a blood test and observing your weight at least once a week. The kidneys do a number of important jobs such as regulating calcium, water and other important substances as well as removing waste from the body. It is very important they remain healthy.

There are a number of reasons why the function of the kidneys can become abnormal. Sometimes this can be related to your medication, an infection or simply dehydration. Mild kidney problems are common, but occasionally, it is necessary to admit you for treatment until the blood levels become normal again.

In very rare instances, the kidneys can become damaged and may not work properly for quite some time. It is not always necessary to stay in hospital until the kidneys improve, but you may need extra visits to the hospital for monitoring.

TTP

Thrombotic thrombocytopenic purpura (TTP) is a rare condition which can occur after a transplant, where small clots (thrombi) can form within the circulation. This causes platelets to be used up, leading to a low platelet count (thrombocytopenia).

The exact cause of TTP is uncertain but is thought to involve a protein in the plasma called von Willebrand factor (vWF) which malfunctions and becomes very sticky. This causes the platelets to clump together, particularly in the small vessels supplying the brain and the kidney.

Some drugs, such as ciclosporin, are linked to TTP although very few patients who are taking this drug actually develop this problem. TTP has also been associated with certain infections and total body irradiation (TBI) treatment.

The symptoms associated with TTP can include fever, headaches and sometimes diarrhoea and easy bruising. If the vessels of the kidney become affected then high blood pressure may also develop.

The treatment of TTP requires specialist care and the doctors are likely to review all your medications and may even stop the ciclosporin.

There are a number of possible treatments including plasma exchange, which involves removing the patient's plasma and replacing it with donor plasma. This helps to remove the sticky vWF protein and replace it with normal vWF protein. The procedure usually needs to be performed daily for at least five days to be

effective and sometimes many more procedures are required to improve the condition.

LIVER PROBLEMS

The function of the liver also needs to be monitored after your transplant and occasionally it stops working properly. There are a number of reasons why the liver function might become abnormal. Sometimes this can be related to your medication, an infection, graft versus host disease (discussed later) or veno-occlusive disease (VOD).

VOD is a specific disease where the blood flow through the small veins of the liver is partially blocked. VOD can be life-threatening and cause symptoms such as yellowing of the eyes and skin (known as jaundice), swelling or distension of the abdomen and fluid accumulation. VOD usually occurs during the first few weeks after the transplant. In some cases it can occur later and is generally more common in patients who have had very high doses of chemotherapy for their transplant. It is usually very mild, disappears very quickly and you are often not even aware of it.

However, VOD can be a very serious problem and treatment is aimed at minimising its effects. New treatments are available which have improved the outcome for patients with severe VOD, and life-threatening disease is rarer than it used to be. Recovery is aided by the liver's own great ability to recover and regenerate from the effects of diseases such as this.

NAUSEA AND VOMITING

It is not unusual for nausea with or without vomiting to persist for a number of weeks and, in some cases, months after the transplant. There are several possible causes for this which might include infections and GvHD.

As nausea often interferes with other functions, such as appetite and diet, it is important to discuss

this with your team so that they can organise appropriate treatment and investigations.

DIARRHOEA

Diarrhoea after the transplant can be a troublesome symptom and, when persistent can cause significant weight loss and malnutrition. Again, there are several potential causes and it is even possible that the diarrhoea is caused by more than one problem at the same time. You must report new and persistent diarrhoea to your team so that they can take appropriate and prompt action.

BLEEDING

You may still need to have platelet transfusions after you go home. You should contact the hospital immediately if you develop any new bruising, bleeding (for example, blood in your urine or stools), or a persistent nosebleed. Although bleeding can occur later on after your transplant, this is generally not considered to be normal and must be reported to your team immediately so that they can investigatethe cause.

There can be many possible reasons for bleeding. Do remember that these effects do not mean that the transplant hasn't worked and it is usually necessary to make many adjustments to your treatment as you progress through your recovery.

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GvHD

(please see Step 3 for further information)

HICKMAN LINE REMOVAL

The Hickman line or any other venous access device is a potential source of infection at any stage of your treatment.

Your Hickman line will usually be removed as soon as it is no longer required, or if it becomes infected after the transplant. Removing the line is a simple procedure and is usually done in the

outpatient or day unit. You will be given an injection of local anaesthetic around the site of the line so that you won't be able to feel the sensations of the procedure. You will usually need a suture to help the site to heal, which can then be taken out around a week after.

Although it can be a little daunting to think about having the line removed, especially if you have had one for a long time, it is an important step towards independence.

MEDICATION

You will need to continue with all your prescribed medicines, including creams, lotions and mouthwashes, until your team advise you to stop. Some of the medication will need to continue for at least a year and certain drugs such as penicillin, which help to protect you from infections, need to be taken lifelong.

This in itself can be difficult for some patients, especially when their transplant was several years before. There is also a tendency to think that these drugs are no longer needed when you are well, but this is incorrect. Some of the damaging effects of your treatment are permanent and these drugs play an important part in protecting you from unnecessary life-threatening complications.

You may still need to continue taking immunosuppressive drugs such as ciclosporin (or tacrolimus). You need to remember that these drugs should be taken regularly as instructed and that the levels need to be monitored so that you benefit with minimal side effects. This is very important because if the drug levels are too low, they won't be able to work properly. If the levels run too high, they can cause damage to your kidneys or may result in more infections.

2 STEP TWO GETTING BACK TO 'NORMAL' AND LOOKING AFTER YOURSELF

ISSUES DISCUSSED IN THIS STEP:

- The new you
- Getting out and about
- Appetite and taste changes
- Managing fatigue
- Managing anxiety and emotions
- Talking to people
- Relationships with family, friends and socialising
- Reintegrating in the community
- Managing finances
- Return to work...
- ...or doing something different
- Quality of life
- Complimentary therapies
- Diet and lifestyle
- Insurance for travel
- Support groups
- Keeping in touch
- Finding the right information
- Contact with your donor
- Helping others

THE NEW YOU

Having reached this stage of your recovery, you might be starting to take stock. You may be thinking about the experience you have had and the journey you have made to get to this point. You may also be starting to think about what happens next.

Some patients start thinking about the way things were, others think about the opportunities that may now lie ahead. One thing is for certain – having a transplant is a life-changing event, either in the short term, long term or both. Even when life returns to 'normal', many transplant recipients say that their values have changed or their approach to life is different.

Some patients look and feel different from before. This may be a temporary change caused by losing weight or hair. This new 'identity' and the changes that are occurring can take a bit of getting used to. It is quite normal to need a little help and support in making the necessary adjustments.

GETTING OUT AND ABOUT

It is an important part of your recovery to start going out again as soon as you are able. This may mean walking to the end of your garden or

street to begin with. At first this will be daunting and you may even feel uncomfortable with the noise and stimulation of the world. You will have been told about the risks of going into crowded places and will have been advised to avoid contact with people with infections.

You may want to go shopping, and this is fine as long as you go at quiet times, or you may visit friends. The more normal the things are that you do, the better you will feel. Start slowly and build up your strength and stamina and your confidence will also soon start to improve.

If you are unsure whether your plans are suitable, please ask your team for advice. It is better to adjust your goals rather than take risks, or end up doing nothing at all.

One thing is for certain – having a transplant is a life-changing event

APPETITE AND TASTE CHANGES

Your appetite may still not be as good as it was before the transplant, although it will get better with time.

Try and eat small meals – little and often. If you are having problems managing meals, then try having your food served on a small plate. Large meals often look too difficult to manage and you can be put off as soon as you see it.

It is common for partners and carers to devote a great deal of time to preparing your favourite meals for you. You may still be quite fussy about your food and this can be frustrating for you as well as those around you.

You may have grand ideas about meals that you would like, but by the time they are cooked and served, you may have gone off the idea altogether. Try and choose food that can be prepared quickly, is tasty and easy to eat.

Go for things that you really fancy. Maybe you've been craving something while you've

been in hospital – now's your chance. It is easy to fall into the trap of becoming obsessed about your food particularly when eating can be difficult. Try to have fun and experiment with different flavours and you will eventually find something you enjoy. You don't need to stick to the dietary advice quite as strictly at this stage, but please be sensible.

You may continue to experience taste changes for some time after your transplant. Sweet tastes often return to normal first – a good excuse to treat yourself and add extra sugar!

You may also continue to experience some changes in your sense of smell. Cold foods tend to smell less than hot foods, so if smells make you feel nauseous or put you off eating, try it cold. Even if you are not eating as much as usual, make sure that you drink a lot – aim for six to eight glasses of water a day.

It is important to remember that if you are still taking the drug ciclosporin, you should continue to avoid grapefruit and any products that contain grapefruit.

MANAGING FATIGUE

It is common to feel very tired for a long time after your transplant. In fact fatigue is one of the most common problems that people report.

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Some people still experience fatigue beyond the first year after their transplant, so don't worry – you are not alone. People in this situation often find that they have lots of energy one minute and are exhausted the next. It is important to try and use this energy wisely so that you rebuild your stamina.

Studies have shown that patients who follow an exercise program adjusted to their individual needs feel better physically and emotionally, and cope better, too.

If you were sick and not very active during treatment, it is normal for your fitness, endurance, and muscle strength to decline. Your plans for physical activity should fit your situation. An older person who has never exercised will not be able to perform the same amount of exercise as a 20-year-old who plays tennis twice a week. If you haven't exercised for a few years, you will have to start slowly, maybe just by taking short walks.

There are many things that you can do to help to improve fatigue:

- Make sure that you are getting exercise and rest in balanced amounts
- Eat a balanced and healthy diet
- Drink plenty of fluids
- Try not to overdo it
- Have a rest during the day if you need it
- Try and get a good night's sleep (going to bed and getting up at a sensible time)

If you are concerned about fatigue, please discuss it with your team. Some centres organise or may be able to refer you to an exercise group which many people find helpful.

Exercise can improve your physical and emotional health in a number of ways:

- It improves your cardiovascular (heart and circulation) fitness
- Combined with a good diet, it will help you get to, and stay at, a healthy weight
- It makes your muscles stronger
- It reduces fatigue and helps you have more energy
- It can help lower anxiety and depression

- It can make you feel happier
- It helps you feel better about yourself

Long term, regular physical activity plays a role in helping to lower the risk of some cancers, as well as having other health benefits.

MANAGING ANXIETY AND EMOTIONS

Recovery after a transplant often feels like a very long rollercoaster ride that doesn't seem to stop. It can be difficult to cope with the feelings of uncertainty which can make it difficult to plan from day to day. Please be reassured that this does get better with time for most people, although some may find they need help.

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Please talk to your team if you are feeling anxious. It can often help to talk about your concerns, particularly if there is a certain aspect of your treatment that is troubling you. It is also common to feel low or depressed at times and while some patients feel emotional, they may find it hard to talk about their feelings with loved ones. Again this can be quite normal, and your team will be able to offer advice and help for you in dealing with this.

It is likely that those around you are also feeling anxious, worried or even frightened. Please encourage them to talk. It can be difficult for them to support you in your recovery when they too are feeling very uncertain. You may find it helpful to bring your carer to your appointments so that they can be involved in your recovery. It also helps to have another pair of ears to take in the information that is given to you, and to help think of questions that may be relevant.

Many centres have a counsellor or people that that they can refer you to for further help and support. Please ask your team if you think that this would be useful for you.

TALKING TO PEOPLE

Going through a transplant can take over your life at times. Some people can find it very difficult to keep telling their story or talking about the treatment even to those around them. Others find that it helps to talk about the experiences that they have had. Whichever sort of person you are, there is really no right and wrong.

Many patients find that looking for more information from other people or the internet helps. Others may find that attending support groups is a very useful way of sharing information. This is an opportunity to talk to 'like-minded' people who can relate to your experiences and provide you with reassurance by talking about their own. Support groups are not the answer for everyone but are a good way of bringing patients, and often carers, together. Please ask your team about available support groups in your area.

RELATIONSHIPS WITH FAMILY, FRIENDS AND SOCIALISING

Having a transplant can be an intense and stressful time for everyone involved. Some patients find that after spending several weeks in hospital and then dealing with the challenges of the treatment and recovering, there are a lot of changes in their lives.

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As you start to put the treatment behind you, you may feel you don't need to depend on your carers as much. You may even experience changes in your relationship with your partner and family. You may feel ready to reassert your role in the family and to take back some of the responsibilities that go with that role. This is rarely achieved overnight and you really need to set yourself attainable goals.

You may find that you soon feel ready to start going out again, either with friends or even

meeting new people. Again, this can be daunting to start with. If it is, begin with something familiar and comfortable – and remember to have fun!

REINTEGRATING IN THE COMMUNITY

Regaining your confidence in social situations is just another part of your recovery. Sometimes it's good to start with something familiar like the school run or going round to the corner shop. Be prepared that you may meet people who haven't seen you for a while and sometimes it can be difficult to know what to say. It may be helpful to take someone along with you on your first outings. It's often nice to have the company and it's reassuring to have someone there if you feel uncertain. At this stage, it's good to have the flexibility to be able to do things as and when you feel ready, rather than being committed to things before you feel you are really up to it. Use your common sense to guide you in making decisions.

Regaining your confidence in social situations is just another part of your recovery

You will need to be cautious about crowds, but this does not mean that you can't go out. If you want to go to public places, such as restaurants and shops, you may want to avoid them during peak hours to start with.

Touching people and physical contact are not discouraged, but you should initially limit this to family and others that are close to you.

MANAGING FINANCES

Having and recovering from a transplant can take a long time. This may mean many weeks and months of being unable to work, even on a part-time basis. You may need someone at home to look after you some of the time and this might be a further source of financial pressure. Patients who have undergone a transplant sometimes find it difficult to access appropriate mortgage or insurance advice. Your team will be able to point you in the right direction for help and advice.

There are ways of claiming financial support or grants from charities to assist with fares or equipment for your home. Please ask your team for information about financial assistance or if you can speak to a financial advisor about your situation.

RETURNING TO WORK...

There are no hard and fast rules about when you should return to work. This applies if you go out to work, or if you are a full-time housewife, or mother or father. As a rough guide, if you have had an autologous transplant, then you would normally need about three months off work. For donor transplants, this extends to four to six months but can be as long as a year.

You should not consider committing yourself to the pressures of work until you feel fully able to cope. If you are able to go back part-time initially, that is best. Generally, it is fine to return to work whenever you feel ready, but you should discuss it with your doctor first.

You might want to discuss your employment rights and your entitlement as an employee with your human resources department or your team may be able to help you access information about this.

...OR DOING SOMETHING DIFFERENT

It is not uncommon for people to take stock and think about doing something different in life, post-transplant. Sometimes people decide that they don't want to return to the way things were before. It is important to take time to make these decisions and discuss your thoughts and feelings with your family. This can be a time of enormous change and uncertainty and while it might be tempting to be impulsive, try not to change everything at once. It's important to have some stability and constancy for yourself as well as those around you.

It is important to take time to make these decisions and discuss your thoughts and feelings with your family

Please speak to your team about sources of advice and information.

QUALITY OF LIFE

As it takes time to recover after transplant, it also takes time for your overall quality of life to improve. Many patients report a good quality of life after transplant although for many it may not be the same as it was before the transplant.

Many factors are known to affect a person's quality of life. These can be measured by using questionnaires looking at physical (how you feel), social (you and the people around you), functional (what you can do) and emotional (worries and concerns) wellbeing. Whether you use a questionnaire or not, you are the person who is best placed to judge whether you have a reasonable quality of life. If this is something that you are concerned about, please discuss with your team.

COMPLEMENTARY THERAPIES

An important part of your recovery is about taking time for yourself to help the healing process. We often think about physical recovery, but we should be thinking about recovery of the 'whole' person. Complementary therapies can provide a holistic approach to treating some of the side effects of your treatment and can improve your overall sense of wellbeing.

Complementary therapies can be used alongside conventional treatments although it is always best to check with your team that your chosen therapy is safe for you.

Types of complementary therapies include:

- acupuncture
- aromatherapy
- healing and reiki
- homeopathy

- herbal medicine
- massage
- reflexology
- yoga
- relaxation and meditation

Complementary therapies are sometimes offered free or are subsidised by hospitals, support centres and charities. If there are no suitable free or low-cost therapies available, you may consider paying although the cost can vary greatly depending on the therapist and type of therapy you choose.

It can be difficult to judge how effective complementary therapies are because there is less reliable research about them compared to conventional treatments. Your doctors may advise you to avoid some therapies especially if they could interact with your treatment.

DIET AND LIFESTYLE

You may have reached a point in your recovery where you are starting to make choices to help you stay healthy and feel as well as you can. You might try to eat better or get more exercise or you might reduce alcohol or cut out tobacco. It's a good time to think about making changes that can have a positive impact on the rest of your life. You might start by working on those things that worry you most and ask for help with those that are harder for you.

It's a good time to think about making changes that can have a positive impact on the rest of your life

Eating a healthy, well-balanced diet is key to maintaining wellbeing. You may not feel like eating and lose weight when you don't want to. It can be hard to break habits that you acquire during your recovery. And once you start to regain the weight you might have lost during your transplant, it can be difficult to control or lose.

All these things can be very frustrating but bear in mind that these problems usually get better over time.

You may also want to ask your team about seeing a dietician who can give you ideas on how to deal with these concerns.

Once you put healthy eating habits in place, you may be surprised at the benefits. Reaching and maintaining a healthy weight, eating a healthy diet and limiting alcohol intake may lower the risk of a number of types of cancer, and create many other health benefits.

INSURANCE FOR TRAVEL

While it may be many months before you feel ready to plan a holiday, you should discuss any travel plans with your doctor.

You will almost certainly need to get special travel insurance cover and there are several companies that can provide this. Insurance for travel after transplant may be more expensive than your regular insurance. If you travel without appropriate insurance and then become unwell, you run the risk of having difficulties accessing lifesaving treatment, or generating expensive hospital bills. Please ask your team for details.

KEEPING IN TOUCH

Your transplant centre will monitor you life-long. As you recover, your appointments will become less frequent, and often a yearly check is all that is required. Please bear in mind that the door is always open. If you have any questions, or concerns in between your appointments, do not hesitate to contact your team at the transplant centre who will happily advise you.

FINDING THE RIGHT INFORMATION

It is now possible to access information about anything using the internet, through blogs and social networks. It is important to remember

If you have any questions or concerns and are finding it hard to access the right information, remember that the team at your transplant centre is always there

that this information is not always reliable or may represent a personal view or experience that may not always be relevant to others.

If you have any questions or concerns and are finding it hard to access the right information, remember that the team at your transplant centre is always there. Contact them and they will be happy to point you in the right direction.

CONTACT WITH YOUR DONOR

A number of patients start to correspond with their donors anonymously soon after their transplant. Often this is an exchange of letters or cards which naturally ceases after a year or so. For some donor-recipient pairs, this correspondence continues over many years and sometimes both parties express a wish to meet in person. It is important to know that the different registries have different guidance on donor-recipient contact and it doesn't always follow that both parties will wish to exchange letters or cards. Please ask the team at your centre for further information.

HELPING OTHERS

As you travel on your post-transplant journey, many patients feel a desire to 'give something back' and help others on their transplant journeys. You may wish to pass on your experience to help others in a similar position. Talking to other patients about your treatment and recovery can help them to overcome some of their anxieties. It also helps them to know some of the things about having a transplant that are difficult to understand from information books.

Other ways of helping might be working as a volunteer. Email **volunteering@anthonynolan.org** to find out about opportunities to volunteer at Anthony Nolan.

3 STEP THREE GRAFT VERSUS HOST DISEASE (GvHD)

ISSUES DISCUSSED IN THIS STEP:

- What it is
- Incidence
- Risk factors for GvHD
- Types of GvHD
- Assessment and diagnosis
- GvHD by organ and top tips
- Treatments
- GvL
- Living with GvHD

This step explains in more detail graft versus host disease (GvHD) - a complex illness that can occur as a consequence of stem cell transplantation. Every patient's experience of GvHD is different and this information should be used together with the care provided by your medical and nursing team. If you have any questions about the information in this booklet, please ask the team looking after you.

WHAT IT IS

GvHD can happen following a bone marrow or stem cell transplant using donated cells from another person. This is referred to as an allogeneic transplant and the donor can be related or unrelated to the recipient. GvHD is a term used to broadly describe the reaction that can happen when cells from the donor (graft) are attacking your own body (host). During this reaction, donor cells recognise that the recipient's body is 'foreign' and mount an attack against it.

The cells responsible for causing GvHD are called t-cells. They are a type of white blood cell from the immune system whose job is to help us to fight infections. T-cells recognise, attack and destroy cells that they see as foreign and potentially harmful, such as bacteria and viruses.

Normally, your own t-cells do not attack your own body cells. This is because they are able to recognise proteins on the surface of the cells called HLA (human leukocyte antigens) as 'self' (ie you). HLA is one part of your DNA which can be matched to other people. However, lots of other parts of your DNA ('DNA fingerprint') are unique to you, unless you are an identical twin where the DNA is also identical.

Before a stem cell transplant, donors have blood tests done to identify their HLA or tissue type and this is compared to yours to see how closely the HLA matches. When bone marrow donors are chosen, although the closest HLA match is often selected, there are still differences in the proteins on the surface of the cells. Generally, the closer the HLA match, the less chance of GvHD.

T-cells are able to tell the difference between 'self' and 'non-self'. When the donor bone marrow starts to make new blood cells after the transplant, the new t-cells see that the HLA proteins on the host's cells are not exactly the same. This might make the t-cells attack your body's cells, and this is called GvHD.

GvHD can cause a wide range of symptoms with varying degrees of severity. Patients with moderate to severe GvHD will often need much closer monitoring through blood tests and clinic visits. They may also experience frequent and prolonged readmissions to hospital as a result of further GvHD related complications.

In a small number of patients GvHD can be life-threatening and possibly even fatal, although most patients recover without any long-term disabling side effects.

Every patient's experience of GVHD is different and this information should be used together with the care provided by your medical and nursing team

INCIDENCE

Approximately 50% of patients who undergo an allogeneic transplant will develop GvHD.

Fortunately, for the majority of patients GvHD is mild, causing very few problems. However, in a small minority, GvHD is a serious and sometimes life-threatening illness that can have a detrimental effect on physical and psychological well being. GvHD can affect your quality of life and may mean that you are not able to do the things that you used to, such as going back to work, holidays or exercising.

RISK FACTORS FOR GvHD

There are a number of factors which increase the chance of GvHD developing after a transplant which including:

- unrelated donor
- HLA mismatch
- recipient age (risk of GvHD increases with older age)
- gender mismatch
- testing positive for cytomegalovirus (CMV)

Sibling donors (brothers or sisters) inherit their tissue type from their parents. The chance of developing GvHD is generally lower in siblings than when an unrelated donor is used. This is because the genes (DNA) between the HLA molecules may be different, even if the HLA type is the same in unrelated donors.

Where possible, HLA matched donors are chosen. When a matched donor is not available, donors who are mismatched may be considered although this often increases the chance of developing GvHD.

When the donor is a different gender from you, there is an increased chance of GvHD. This is especially true when a male recipient has a female donor who has experienced one or more pregnancies.

GvHD can affect your quality of life and may mean that you are not able to do the things that you used to, such as going back to work, holidays or exercising

Cytomegalovirus (CMV) has already been mentioned as a cause of infections post transplant. It is a very common and usually harmless virus with over 50% of people testing positive for it. This means that they have had CMV in the past and have detectable CMV antibodies in their blood. If either you or your donor is CMV positive, there is a risk of a CMV reactivation or infection after transplant. In this case there is a high chance of you needing treatment for CMV which can be very complicated and problematic when you also have GvHD. Some studies have shown the risk of GvHD to be increased in patients with CMV reactivation/infection.

TYPES OF GvHD

Generally, GvHD is referred to as acute or chronic. This relates to the time after the transplant when GvHD starts.

Acute GvHD	onset usually within 100 days of the transplant or when the immunosuppression is being withdrawn/stopped
Chronic GvHD	onset usually later after the transplant and may follow acute GvHD

ACUTE GvHD

Acute GvHD can be mild or severe and can begin around the time that the new bone marrow starts to produce blood cells. This is usually about 2-3 weeks after the transplant, but can also occur when the immunosuppressive drugs (such as cyclosporine) are tapered or withdrawn. Acute GvHD often affects the cells of the skin and may start with a rash on the palms of the hands and soles of the feet but can be more widespread. For some the skin can be itchy and red, for others the skin may be dry, scaly or may even, in severe acute skin GvHD, blister and peel.

Acute GvHD may also affect your gut and liver. This causes diarrhoea which can be mild or excessive, nausea and yellowing of the skin and eyes (jaundice) and swelling or pain in the abdomen.

Acute GvHD can be quite frightening as the symptoms can change rather quickly. It is important that you report any new problems or worsening problems to your medical team as soon as possible.

CHRONIC GvHD

Chronic GvHD can follow on from acute GvHD or can happen without warning many months after your transplant even if you never had acute GvHD.

Like acute GvHD, it can affect your skin, gut and liver, but it can also affect other parts of your body such as your mouth, eyes, lungs, genital system and joints. Chronic GvHD may be mild or severe and life-threatening. For some the symptoms can be present for many months, or even years.

It is important that you report any new problems or worsening problems to your medical team as soon as possible

ASSESSMENT AND DIAGNOSIS OF GvHD

During your follow-up after the transplant, you will be monitored for signs of GvHD. This is routinely done by asking you about your general wellbeing, blood tests and examination. If your team suspect that you have GvHD then they may decide to arrange for additional tests or ask other specialists for their opinions and advice to confirm this. The tests that are performed and the additional specialists involved will depend upon the area(s) of the body where the GvHD is suspected.

Biopsy

One of the ways of diagnosing GvHD is by taking a small sample of the affected tissue. This is called a biopsy. The biopsied tissue is sent to the laboratory so that it can be examined under

a microscope. The results are usually available after a few days. Other tests might also be done on the tissue sample to check for other causes such as infections.

Endoscopy
If you have symptoms of gut GvHD then the doctor may wish to arrange for you to have an endoscopy. An endoscopy is a procedure where the inside of your body is examined internally using an endoscope. An endoscopy is usually carried out while a person is awake. Before the procedure, a sedative (medication that has a calming effect) may be given to help you relax.

An endoscope is a thin, long, flexible tube that has a light source and a video camera at one end. Images of the inside of your body are relayed to an external television screen.

Examination of the digestive system and stomach by endoscopy is called a gastroscopy. For this, the endoscope is passed via the throat. Examination of the bowel is called a sigmoidoscopy or colonoscopy and the tube is inserted into your back passage (anus). Biopsies can be taken during the endoscopy and looked at under the microscope or tested for infections.

It is usually necessary to prepare the gut for this examination. You may be required to be 'nil by mouth' for a number of hours before the procedure to make sure that the stomach is empty. If the bowel is being examined, you may need to take a medicine which helps to purge or clear the bowel of faeces before the test takes place. It is common for the doctors to ask for both ends of the digestive tract to be examined by endoscope.

Scan
It may be necessary to perform a CT scan of the lungs so that the structure can be examined in better detail and other causes such as

infection can be excluded. It may be necessary to have a number of scans as part of the assessment for GvHD. The scans are usually looked at by specialists within a couple of days.

Pulmonary function tests

Another way of assessing GvHD of the lungs is to test the function and this is done in exactly the same way as the lung function before the transplant. It helps the doctors to see if the function has changed and how effectively your lungs work in terms of their capacity, elasticity and ability to exchange gas.

GRADES OF GvHD

Grade of GvHD is determined by the results of the doctor's assessment and can improve and worsen. Grading systems are often used so that the doctors have a standard way of describing the level of GvHD and recommending treatment. There are a number of grading systems used which are based upon assessing GvHD type symptoms in the main affected organs as described below.

TYPES OF GvHD BY ORGAN

Skin GvHD

In acute skin GvHD, you may develop a rash on the palms of the hands and soles of the feet. It can become widespread and may be painful and itchy or prickly. If the skin is very red, you may lose a lot of heat and find it difficult to keep warm. In severe skin GvHD, the skin may blister and peel.

In chronic skin GvHD, a rash may also develop and the skin may feel tight and dry. Sometimes the skin can look like you have eczema or even psoriasis-type rashes. The skin may also appear darker or in some cases may lose pigmentation, developing lighter patches. The skin may become thicker and lose its elasticity, which some times makes it difficult to move the joints.

Your nails and hair may also be affected and become thin or brittle. Some patients experience hair loss or find that the hair does not grow back properly or is even grey or white in colour.

Gut GvHD
Gut GvHD can affect the whole of the digestive system such as the mouth, oesophagus, stomach and bowel. It does not usually affect the whole system at one time, and acute gut GvHD usually affects the bowel.

Most patients who experience GvHD of the gut or bowel will have diarrhoea. The stool often looks green and watery and may have a 'bitty', possibly porridge-like appearance. You may see undigested food in the stool and occasionally it may contain mucous or blood. You may experience cramping or bloating in the abdomen and some patients describe a 'sense of urgency' to open their bowels. If the diarrhoea is very severe, you may find it difficult to control when and where you open your bowels. Other symptoms that may be associated with gut GvHD are indigestion, loss of appetite, nausea and occasional vomiting.

Oral GvHD can be painful and it can be difficult to enjoy certain foods and tastes

Because the lining of the gut becomes inflamed, it doesn't absorb the nutrients from food in the usual way and you might lose weight and become malnourished.

When the mouth is affected (oral GvHD), it can become sore and dry and you may find you are not producing enough or any saliva. The way that food tastes can become altered and blisters or ulcers can sometimes develop particularly when certain foods are in contact with the mouth. Oral GvHD can be painful and it can be difficult to enjoy certain foods and tastes.

Liver GvHD
When the liver is affected by GvHD, the first sign is often an increase to the levels of the

liver enzymes. This is detected through the routine blood tests that are done after your transplant. The tests can reveal early changes in the way your liver is working before any symptoms develop.

If the liver function becomes worse, you may become jaundiced where the skin and whites of the eyes can become yellow and the skin may itch. If the size of the liver becomes increased, your abdomen can also become swollen, uncomfortable and even painful.

The liver has lots of important functions such as cleaning the blood by removing certain toxins. When chronic GvHD affects the liver, it can become damaged and scarred to the extent that it might stop working properly and the toxins build up.

Lung GvHD
GvHD affecting the lungs can result in the lung tissue losing some of its flexibility and elasticity. You might experience shortness of breath or a wheezy sensation. You might find it more difficult to take exercise and may notice an increase in chest infections and coughs. In severe lung GvHD you might even require oxygen therapy to relieve symptoms.

Ocular (eye) GvHD
Patients with GvHD of the eye often describe a gritty sensation in the eyes. The eyes may feel dry or they may water almost continuously. They can become sore and uncomfortable and sometimes sensitive to bright lights. In severe cases the vision may become impaired.

Musculoskeletal GvHD
GvHD can affect almost any area of the body. In some patients this can include the tendons. When these are affected, they become inflamed and lose their ability to stretch. It can affect the range of possible movements of certain joints,

for example making it difficult to bend and straighten your arms and legs. It might affect the way you move around and impact such things as driving and climbing stairs.

Genital GvHD

GvHD of the genital tract may be problematic for female patients after transplant. In mild cases, they may experience symptoms of vaginal dryness but with otherwise normal sexual function. On examination there may be visible signs of GvHD and in extreme cases, there may be advanced signs of GvHD with vaginal strictures and ulceration. Patients may experience severe pain during sexual intercourse or difficulty or inability to insert a vaginal speculum for smear tests.

Treatment is often provided under the close guidance of a gynaecologist and often includes using lubricants possibly with hormone or steroid creams or pessaries. There is good evidence to suggest that sexual function is generally improved if regular intimacy resumes during the first year post-transplant. People generally find it difficult to talk about sexual problems after transplant. However, they are very common, so if you are having difficulties, please ask for help.

People generally find it difficult to talk about sexual problems after BMT. However, they are very common, so if you are having difficulties, please ask for help

TREATMENT FOR GvHD

A variety of treatments are available for GvHD and the type of treatment will depend upon the grade, type and area of GvHD.

Skin GvHD

Sometimes mild skin GvHD requires no treatment at all and will get better on its own.

Alternatively, you may need to apply moisturisers or a steroid cream either to affected patches or possibly all over if required. Steroids may also be given orally by tablet or intravenously by drip if the GvHD is moderate or severe or

isn't getting better with the other treatments. Other treatments for skin GvHD include immunosuppressive drugs, PUVA and extracorporeal photopheresis (ECP).

Your haematology doctor will often ask a skin specialist (dermatologist) for their opinion. They will often perform a skin biopsy and provide advice on the best course of treatment. You may need to continue visits to see the dermatologist particularly if the treatment for skin GvHD is ongoing.

Chronic skin GvHD can last for many months, or even years, and the treatment can be challenging and tiring.

Top tips

- Wear cotton clothes
- Try to avoid extremes of temperature such as hot or cold
- Use plain, unperfumed soaps
- Try not to rub your skin dry after bathing
- Use the moisturisers as advised
- Ask for help with putting on the moisturisers and lotions
- Try wearing cotton gloves at night to prevent scratch marks
- Cover the skin well even in spring and autumnal sunshine – exposure may worsen or stimulate skin GvHD

Gut GvHD

Again, mild gut GvHD sometimes requires no treatment at all, but the symptoms may make you feel nauseous and give you diarrhoea. You will need to make sure that you do not become dehydrated and so will need to drink more than usual. It may be difficult to take in enough fluid particularly if the diarrhoea is very severe, and so you may need fluids intravenously.

It may also be necessary to replace some of the salts and electrolytes.

You may experience pain in the abdomen and uncomfortable cramping sensations. Your doctor will be able to give you painkillers to help with this as well as anti-sickness drugs for nausea.

If you are unable to eat and are losing weight, it might be necessary to feed you through either your Hickman line if you still have it or a tube inserted into the stomach. This will help to stabilise the weight loss and prevent you from becoming very malnourished as a result of the GvHD.

There are a range of treatments used for gut GvHD which include steroids (general and targeted), immunosuppressive drugs and antibodies.

Top tips

- Monitor your fluid intake and increase if you are able to
- Use barrier creams to prevent the area around your bottom from becoming sore with diarrhoea
- Try to take small amounts of food if possible
- Tell your doctors and nurses if you are unable to take your tablets and if you notice an increase in the frequency or consistency of the diarrhoea

Liver GvHD

Often you will be unaware if you have liver GvHD as it is usually detected from abnormalities in the routine blood tests. The liver function tests can remain abnormal for quite a long time after the liver has started to recover. Sometimes, you may have symptoms which can include jaundice, itchy skin and discomfort in the abdomen.

There are a number of treatments used for liver GvHD which include steroids, immunosuppressive

drugs and anti-bodies. ECP is another treatment which has been shown to be of some benefit to some patients with liver GvHD.

Top tips

- Take anti-histamines to help reduce the itching if you have it
- Try to avoid extremes of temperature as the itching may be worse if you are very hot or cold
- Inform your doctor if you are prescribed any new medicines which may affect the function of the liver
- Minimise your intake of any other toxins such as alcohol which may worsen the liver function

OTHER TREATMENTS FOR GvHD

Most of the treatments for GvHD are aimed at suppressing the donor t-cells to reduce the attack on your body. Most of the treatments that are given to suppress the GvHD will weaken your immune system and make you more vulnerable to infections. Added to this, GvHD itself suppresses the immune system and so usually people with GvHD will experience more infections than those without.

Immunosuppressive drugs

Drugs that work to suppress the numbers or activity of the t-cells include ciclosporin, tacrolimus and mycophenolate mofetil. These drugs can be given alone or in combination with steroids. You should avoid grapefruit juice or products which contain grapefruit when taking ciclosporin as it affects the way that the drug works. The doses of these drugs may need to be changed to make sure that you are not taking too much or too little. Regular blood tests are usually done to check the levels of some of these drugs and also to check the liver and kidneys for unwanted side effects.

Steroids

Steroids can be administered in a variety of ways depending upon the grade and type of GvHD. They can be applied topically to the skin to treat limited or extensive skin GvHD. They can be used as a mouthwash for oral GvHD, given orally by tablet or even by intravenous drip if the GvHD is severe or extensive.

For some people, steroids can give you a sense of wellbeing; you might have more energy, a better appetite and a better mood while you are on treatment with steroids.

Some people find that they don't sleep very well while they are on steroids. Others find that they might be drinking much more fluid and passing much more urine than usual. If this happens, talk to your nurse or doctor.

When the GvHD is under control, the dose of steroids may be reduced. Some people find that the sense of wellbeing also lessens and they may feel a little lower in mood. It may be necessary to have numerous courses of steroids or even stay on a small dose of steroids for a period of time.

Monoclonal antibodies

Monoclonal antibodies tend to work by targeting specific proteins on the surface of certain cells and then attacking and destroying them. There are a number of different monoclonal antibodies that can be useful in the treatment of GvHD. However, many of them have quite a severe effect on the immune system, making you vulnerable to infections. They are usually given intravenously by drip sometimes as a single infusion or as a course. Please talk to your doctor about the effects and side effects of monoclonal antibodies as each one works differently.

PUVA

Psoralen plus ultraviolet A is a treatment that combines exposure to ultraviolet A (UVA) light with a medicine called psoralen. It can be used to help treat GvHD particularly of the skin. The psoralen makes the donor t-cells attacking the skin more sensitive to the UVA light which then helps to clear the skin of the GvHD. As your eyes and skin will be more sensitive to sunlight after each treatment, you will be advised to wear sunglasses and protect your skin.

Treatment is usually given twice a week, for a period of weeks to months. You will need to stand in the UVA cabinet for a period of a few seconds to several minutes and it can take several months to see any real improvement. It is often used alongside other immunosuppressive drugs which can then be reduced once the PUVA starts to take effect.

ECP

Extracorporeal photopheresis (ECP) can be used for skin, liver or oral GvHD. It is usually undertaken when other forms of treatment have not resolved the GvHD. It is a complicated treatment often delivered in specialist dermatological centres, but is usually very well tolerated by the patient and has minimal side effects. ECP consists of an infusion of UV-A irradiated mononuclear cells. These are collected from your blood using apheresis techniques similar to the way in which the stem cells were harvested for your transplant.

The cells are then treated with a drug called 8-methoxypsoralen (8-MOP) and then exposed to ultraviolet light. The light activates the drug so that it destroys the mononuclear cells. These cells are then returned to you as an infusion. Each treatment takes several hours to complete and is usually undertaken every two weeks. Recently, ECP has been used in the treatment of severe chronic and acute GVHD.

Other medications

Other treatments for GvHD might include 'topical' treatments that are applied or used directly on the affected area. This can include creams for the skin, eye drops and mouthwashes. These treatments can be just as important in controlling the symptoms and should be used as often as directed by your team to achieve the best effect.

The treatments described in this booklet are those that are most commonly used. However, there are a number of other treatments that can also be employed in the treatment of GvHD and which can also be effective for some. Please ask for more information from your team.

GvL

Graft versus leukaemia (GvL) or graft versus tumour effect is a beneficial part of GvHD. Patients with acute or chronic GvHD after allogeneic transplant tend to have a lower risk of disease relapse. This is because the t-cells of the donor immune system can also cause a beneficial immune reaction against your diseased bone marrow.

If your disease does return after transplant, there are a number of strategies that can be used to exploit the potential of the donor immune system to help fight the disease. These can include infusing additional donor t-cells and performing a second transplant, possibly even using a different donor. While both of these strategies may help to harness the GvL effect, they may also increase the likelihood of developing GvHD.

LIVING WITH GvHD

GvHD often feels like an unexpected and devastating effect of allogeneic BMT, not only for you but also your family. GvHD can have a detrimental effect on your quality of life and also your expectation of life after transplant.

GvHD often feels like an unexpected and devastating effect of allogeneic BMT, not only for you but also your family

However, despite the impact that GvHD can have, most patients do report a relatively good quality of life and very few actually regret having their transplant.

Regardless of GvHD, life after transplant can be difficult and there is help available to enable you and your family to cope with your ongoing treatment and recovery. If you would like more help, please ask.

Share your experiences and get support from others on our online community **anthonynolan.org/transplantcommunity** or contact the Patient Experience team for more support at **patientinfo@anthonynolan.org** or **0303 303 0303**.

4 STEP FOUR OTHER EFFECTS OF THE TREATMENT

ISSUES DISCUSSED IN THIS STEP:

- Long-term effects:
  - Infertility
  - Premature menopause
  - Sexual function and dysfunction
  - Skin changes
  - Joints and muscles
  - Eyes
  - Mouth
  - Teeth
  - Bone changes
  - Thyroid and other glands
  - Bowel
  - Kidneys and bladder
  - Liver
  - Chest
  - Heart
- Memory and other psychological changes
- Immune system and late infections
- Second cancers

As you already know from talking to the transplant team, reading information booklets and possibly talking to other patients there are a number of side effects that you might expect during and after the transplant. It is also true that although some of these effects may not occur during the transplant, they can still happen months or years later. Referred to as 'late effects', some are more common than others. It is important that you know what to look out for, and also how we monitor, screen for or prevent these effects from happening. Unfortunately some late effects cannot be predicted, but regular monitoring may mean that they are picked up sooner and can be more easily treated.

During the months leading up to the transplant, it is common for people to focus mainly on what will happen immediately and the chance that the transplant will cure you of your disease. It is very difficult at this time to concentrate on problems that might occur months or years after the transplant. We think it is important for you and your family to understand what will happen after the transplant, so that you can consider all the factors when making up your mind. You might also find it helpful to have another look at this booklet after you have recovered

from the transplant and are starting to return to normal.

The following section describes the different late effects that may occur in the main organs of your body. The most common problems are described first, with the rarer problems at the end.

Remember that the chances of developing these effects depends on many factors. These can include the type of transplant you had, other drugs or radiation that you received, your age and gender. You should discuss this with the transplant team.

GvHD, a common effect of donor transplant, can affect any organ in the body. Although some of those symptoms will be mentioned below, it is also important to read the GvHD chapter to understand what may happen and what to look out for.

The following pages explain what to look out for and the various treatments. The next section (Step 5) explains the tests and investigations that are likely to be suggested by your transplant team as part of your routine, the reasons for them, and long term follow-up care.

Unfortunately some late effects cannot be predicted, but regular monitoring may mean that they are picked up sooner and can be more easily treated

LONG TERM EFFECTS:

INFERTILITY

Many of the issues related to infertility have already been discussed in The Seven Steps and you will have talked about this with the team before starting your therapy. Now that you are recovering and thinking about life after transplant, you may want to find out for certain whether you are infertile. You may then want to explore what options are available to you should you wish to consider having a child.

Your transplant team may be able to give you some general advice about this but it is likely

that they will need to refer you to a specialist in order to assess your fertility and/or to discuss the options that are available to you. Please ask your team to refer you if you have questions about this.

If you are considering adopting a child, bear in mind that many adoption agencies will want to know that you have been well for several years. This could be as many as two to five years after the transplant before they will be able to help you to find a child. However, you may wish to find out more information before then in which case most agencies will be happy to answer any questions you have about the process. If you do eventually decide to adopt, the agency will want to ensure that you are well and in remission from your original disease. They will also most probably ask for a report from your transplant doctor. It may be reassuring to know that many patients have successfully adopted children after their transplant.

PREMATURE MENOPAUSE

Once again this topic has been covered in some detail in The Seven Steps, both in the main booklet and in appendix B. Your transplant team will discuss the implications of premature menopause with you (effects on the heart, bones and genital organs) and the different treatments (eg HRT, bone protecting agents) that are available. In many cases you may be referred to a gynaecology service for a full assessment before initiating any treatment if it is needed.

SEXUAL FUNCTION AND DYSFUNCTION

Almost everyone - men and women - who has a transplant will notice some changes in their sexual feelings or function following a transplant. This is nothing to be ashamed of or embarrassed about and it is important to talk to your transplant team about anything that is bothering you at any time after the transplant.

Many patients will only start to notice or become concerned about this once they are feeling better. In many cases, sexual desire and function will return naturally after a period of time. However, for many patients who feel that they have otherwise reasonable or good quality of life, sexual issues remain.

There are many different reasons why sexual problems can occur after the transplant, ranging from the physical, changes in body image, complications or medications and fatigue. In reality the cause is often a combination of some or all of these factors.

- **Fatigue**
  Tiredness, or fatigue, is a very common and often debilitating issue and for many patients it may persist for months or even years after treatment. It is often difficult to feel enthusiastic about having sex when everything else takes such a lot of effort!

- **Physical changes**
  You will often look and feel quite different in the early months after the transplant. Some of the changes may be caused by things such as hair loss, weight loss or scarring from previous Hickman lines. Some patients may develop GvHD which itself can cause some physical changes, as can some of the treatments for it. Some patients may also develop GvHD involving the sexual organs (the vagina and the penis can be affected) and this will require specific treatment (see Step 3).

- **Hormone deficiencies**
  It is extremely common to have low levels of the main sex hormones (testosterone in men, oestrogen in women) after your transplant.

  In men the symptoms of a low testosterone include lack of libido (desire) and erectile dysfunction (difficulties getting or maintaining

an erection). Testosterone levels may increase with time, but testosterone replacement is straightforward (by various means such as injections, patches or gels).

In women the symptoms are those associated with the menopause and can include loss of desire and painful intercourse. These symptoms are often improved by hormone replacement therapy and/or topical oestrogen creams or lubricants.

- **Body image**
  Alterations in body image frequently occur as your weight may have increased or decreased, your physical fitness level may have reduced, and complications (such as GvHD) may have changed your looks.

- **Emotions**
  Many relationships change during a serious illness – sometimes they become stronger, while in other cases a serious stress may be placed on them. In addition the nature of the relationship may change, becoming, for example, closer emotionally but less physical.

  In some cases your partner may be the one who is reluctant to reinitiate sexual contact, often due to concerns about how you are physically. Fear about the future often contributes to these feelings and may be very challenging for people who are single when they consider starting a new relationship.

  Good, honest and open communication about your feelings will help. Many patients find it helpful to talk to someone with their partner, and relationship or psycho-sexual counselling is often available. Viagra and other similar drugs can be used for both women and men to increase desire and may help to build confidence once again. There are several treatments for erectile dysfunction and many

centres have a specialised clinic that they can refer you to.

Simply talking these issues through with your transplant team is often enough to start on the road to recovery. Understanding that these are common issues and that there are solutions is often a relief. Many of the solutions are simple (eg hormone replacement), but some may require referral to another specialist in this area.

SKIN CHANGES

Your skin is a very large and sensitive organ and there are often changes to the skin after transplant. GvHD most frequently affects the skin and may need particular treatment (see GvHD chapter). Even without GvHD, your skin is likely to be drier and more sensitive (eg to sunshine) for a long time after the transplant. This is an effect of the chemo and radiotherapy, but certain drugs (such as antifungals) could also add to this.

Understanding that these are common issues and that there are solutions is often a relief

Thinning of the skin and loss of hair follicles can also result in you feeling the cold much more than usual, although this usually does get better with time.

It is very important for you to protect your skin. The use of high factor sun creams or sunblock and avoidance of direct sun (long sleeves, wearing a hat) is recommended in the long-term. This is particularly important as there is an increase in the risk of developing skin cancers after the transplant.

JOINTS AND MUSCLES

As discussed earlier, GvHD can affect joints and muscles. Steroids (used for treatment of GvHD) can cause muscle wasting (thinning and lack of strength). Muscle strength can also decrease through lack of activity and being unwell for long periods of time. Poor nutrition can contribute to this too.

It is common to have some joint aches and pains following the transplant, but these will often settle down with time. If they are very troublesome you might be referred to a specialist to investigate this further.

Muscle cramps, especially in the calves and hands, may occur for months or even years after the transplant. There are many possible causes including dietary or vitamin deficiencies and medication. In some cases supplements may help and taking quinine tablets can be helpful, but unfortunately in some cases the cramps will continue to occur from time to time. Numbness and tingling can also happen, usually in the hands and feet. In some cases this may be due to nerve damage following certain types of chemotherapy, and in most patients this improves over time.

Exercise, and in some cases physiotherapy, are very important to build up muscle strength and stability. Walking is one of the best ways of starting to increase your strength and stamina – starting small and gradually increasing the distance and maybe pace as you become stronger and more confident.

Walking is one of the best ways of starting to increase your strength and stamina - starting small and gradually increasing the distance

It is unlikely that you will reach the same level of fitness as before the transplant for several months, but many people will get back to their full fitness. This is highly individual and when you do start exercising you should always start slowly and gradually build it up.

EYES

There are a number of ways that your eyes can be affected after the transplant. However, remember that even without a transplant your vision may deteriorate with time and it is important to have regular checks. GvHD frequently affects the eyes (see Step 3) but even if there are no other signs of GvHD, people often complain of dry or gritty eyes.

Simple eye drops such as hypromellose or liquid tears may help to lubricate the surface of the eye and reduce the irritation. More specific problems include cataracts, which are more common following the transplant, especially if you have had TBI or steroids during the treatment. Cataracts occur in 40-70% of those having TBI, but only 15-20% in those without. They usually occur within the first 2-4 years, but could develop as late as 10 years after the transplant. The symptom is blurring of vision and it may be more difficult to see at night. People often notice that they have difficulty when driving. Cataracts can generally be easily treated providing that your eyes are otherwise healthy.

MOUTH

Even without GvHD your mouth can cause you symptoms for several months after the transplant. Your mouth may be very dry and the taste of food and drink may be altered. This might be due to particular medication, but in many cases a specific cause is not found. The dryness can be treated with artificial saliva although many people do not find this very helpful. Frequent sips of water are recommended and can be helpful. In most people these symptoms will resolve in time.

TEETH

Care of your teeth and gums is very important. Both can be badly affected by chemotherapy, drugs, radiation and malnutrition. Dryness of the mouth also encourages cavities. Just as it was during your transplant, mouth care and fluid intake remain important.

BONE CHANGES

There are two major problems which can involve your bones. The first, and most common, is osteoporosis or thinning of the bones. This is a common problem in the normal population, especially in post-menopausal women.

However it is more likely to happen after the transplant as the menopause (see Step 4) often occurs earlier as a result of the treatment. Men can also be at risk, as a lack of exercise, steroids, and other drugs or radiation may also make osteoporosis more likely. Although osteoporosis is generally not painful, the bones are much weaker and, as a result, fractures are more common. A simple scan (DEXA) can be done to look at the density of your bones and tell whether you are at risk of osteoporosis.

The good news is that osteoporosis is often reversible. Your bone density can return to normal by relatively simple means such as increasing exercise, hormone replacement (HRT) or 'bone-sparing' medicines which can be taken just once a week.

The second problem, avascular necrosis, is when the bone breaks down, usually in one joint. This problem is most common in those who have had a lot of steroids. Avascular necrosis can be very painful and result in difficulty walking (the hip is the most common joint affected) and other daily activities. Some simple treatments are possible; however, surgery is often needed to solve the problem. Many people will return to good mobility with no pain following surgery.

THYROID AND OTHER GLANDS

Up to 20% of people can develop an underactive thyroid gland after the transplant and this is more common after TBI. The symptoms include fatigue, constipation, hair loss, weight gain and others. This can be easily diagnosed by a blood test, and also easily treated by a tablet replacement of the hormone. The glands producing sex hormones (oestrogen/testosterone) are also very commonly affected. It is far less common for other glands or hormones to be affected.

BOWEL

Bowel function may take quite some time to get back to normal. Some patients find that their bowel habits are altered and remain different compared to before the transplant, either more loose or with a tendency to constipation. If, however, you have a new change in bowel habit you should definitely report this to the team as soon as possible.

KIDNEYS AND BLADDER

Your kidneys and bladder may have been affected by drugs or infections during the transplant and in some cases this may be long lasting. In many cases this will be noted as a slightly abnormal blood test, but you will not feel any symptoms.

LIVER

Long-term damage to the liver is relatively rare, especially in those without GvHD. There can be persistent damage from drugs or from iron deposition as iron from many blood transfusions can build up in the body. Yellow jaundice or pain under the ribs on the right side can be a symptom of a problem with the liver.

CHEST

Lung problems can cause breathlessness or a persistent cough. Sometimes this is because of GvHD and will need treatment and referral to a specialist. It can also occur if you have had a lot of chest infections during or after your treatment. Smoking is very strongly discouraged in all patients, due to the added risk of chronic lung problems, but also of lung cancer. If you would like information about getting help to stop smoking, please ask your team.

HEART

Heart problems, especially hardening of the arteries or ‘atherosclerosis’ is common in the general population and in particular as you get older. Heart disease is also increased after a

transplant. This can result in chest pain, an abnormal heartbeat or symptoms related to a 'floppy' heart such as swollen ankles and breathlessness. You can help to reduce the risks of developing heart disease by looking after the health of your heart and doing exercise, eating the right foods (reduced salt and cholesterol) and not smoking. Other family members who have not had a transplant may already be doing the same!

MEMORY AND OTHER PSYCHOLOGICAL CHANGES

Short-term memory loss and difficulties concentrating are common after the transplant. Usually these would not be bad enough to affect your ability to work, but some people are more troubled than others (the crossword often takes longer!). Making notes and lists often helps with this and for most people these symptoms improve with time.

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Depression and anxiety are also common. Some patients are frustrated as they feel that they are not getting better quickly enough, or that their activity is restricted. Fear about the future and money concerns can cause anxiety too. Some patients suffer from nightmares or panic attacks (similar to post traumatic stress disorder) after the transplant. This does not mean that there is anything permanently wrong with you or your mind – these are normal responses to the difficult or stressful situation that you have been through. Usually successful treatment with counselling and/or antidepressants or anti-anxiety medications can be given. The first step is recognising the symptoms and talking to the transplant team about them.

IMMUNE SYSTEM AND LATE INFECTIONS

Even though your blood counts are back to normal, your immune system may take up to two years to return to normal. In some ways it may never be as effective as before. Often this is

a result of damage that the radiation and chemotherapy have done to your spleen. This is the reason that you may be asked to take an antibiotic such as penicillin for the rest of your life. You will also be asked to have your childhood vaccinations again.

SECOND CANCERS

Unfortunately, even though you may be cured of the disease for which you had the transplant, there is an increased risk of developing a second cancer after a transplant. This may occur in any organ, although it is more common in some organs such as skin. The most important way to deal with this is by education (knowing what to look out for), avoidance (eg using sun creams, not smoking), screening (see Step 6) and early intervention if a cancer is discovered. In many cases second cancers can be successfully treated, although it depends on the specific type of cancer. The risk of developing a second cancer can also depend on other risk factors, such as the type of conditioning (TBI or not), age, family history, GvHD and personal behaviour. Remember that this is one of the reasons that we recommend life-long follow up for all patients and why you will be having regular assessments.

Remember that this is one of the reasons that we recommend life-long follow -up for all patients and why you will be having regular assessments

In some cases a different blood cancer can actually develop. The most common form is called PTLD - (post-transplant lymphoproliferative disorder) - and is usually caused by EBV, a very common virus. This can be treated with combinations of chemotherapy, steroids and antibodies. Developing this (or any other) cancer in the donor cells does not mean that the donor has cancer or will develop a cancer. The changes will usually happen to the donor's cells after they are already transplanted and it is most likely an effect of some of the medications.

5 STEP FIVE LONG-TERM INVESTIGATIONS

ISSUES DISCUSSED IN THIS STEP:

- Blood tests and investigations and surveillance
  - Immune system and infections screening
  - Liver tests
  - Respiratory tests
  - Endocrine tests
  - Skeletal investigations
  - Renal tests
  - Vascular screening
  - General screening and preventative health
  - Screening for second cancers
- Other health professionals that may be involved in your long-term care and monitoring
- Other interventions that may be performed after the transplant
  - Immunisations
  - Venesections

Many patients will feel completely well and 'back to normal' with a good quality of life at about a year after the transplant. As with all aspects of the treatment, though, this varies a lot for different people. It is important even at this stage for the transplant team to continue to review you in clinic and you will still need to have a number of tests and investigations. As explained in Step 4, there are side effects that can occur months or even years after the transplant. For many of these, early detection means that we can treat these problems promptly before they affect your health and quality of life. Therefore, even if you feel completely well, you should have follow-up visits long-term. These appointments may not always be in the transplant centre, and in that case it is especially important that you understand what to expect and look out for.

For some patients, the thought of ongoing monitoring and tests can be daunting and may raise concerns or questions that you can discuss with your team.

There is an international guideline used by transplant centres worldwide which lists all of the tests and examinations recommended, and how often these should be performed.

BLOOD TESTS OR INVESTIGATIONS FOR LONG-TERM FOLLOW-UP AND MONITORING

Immune system and infections

- Your blood count will be checked at each clinic visit
- Immunoglobulin levels are tested at one year and are repeated if they are abnormal

Liver tests

- Liver functions (bilirubin, ALT or AST, alkaline phosphatase) should be checked at six months and then annually if normal (but more frequently if abnormal)
- Ferritin, a marker of the iron level in the body, should be measured at one year and repeated if abnormal or for patients being treated for a high or low level (see below)

Respiratory tests

- Pulmonary function tests and chest X rays must be done if previously abnormal, or new symptoms develop, or the patient has ongoing GvHD

Endocrine tests

- Thyroid function should be checked between six months and one year after transplant and then annually
- An endocrinological gonadal assessment should be done six months and one year after transplant for men and women. After one year, assessments will based on symptoms or need

Skeletal investigations

- DEXA (bone density) scanning should be performed at one year in all woman and men with prolonged steroid use
- If abnormal, this should be repeated following therapy (eg vitamin D and calcium, bisphosphonates) or a monitoring period

Renal tests

- Renal function should be performed at six months, one year and then annually. Deteriorating renal function should be investigated with a GFR and patients referred if appropriate
- Children should have a GFR routinely at one year and repeated if abnormal

Vascular screening

- BP and weight measurements should be done at every clinic visit
- Lipid profiles (you will be asked for a fasting blood sample for cholesterol and other fats to be tested) should be performed at one year and then as appropriate

General screening and preventative health

- Vitamin B12, folate and vitamin D should be measured at one year and repeated if they were abnormal

Screening for second cancer

- The age at which breast screening starts depends on whether you had TBI or not. This will usually be a mammogram, but might be an MRI or ultrasound
- Cervical smears should be performed every 1-3 years in women older than 21 or within three years of onset of sexual activity
- Patients should be screened in line with population guidelines for other malignancies (eg colorectal, prostate)
- Patients should also be educated about self-examination of breast, testes and skin and should contact their team if they have any concerns

OTHER HEALTH CARE PROFESSIONALS THAT MAY BE INVOLVED IN YOUR LONG-TERM CARE AND MONITORING

All patients

- GP or other primary care physician: your GP will be asked to be involved in many aspects of your care, including normal population screening such as smear tests and immunisations
- Dentist: you should see your dentist at least once a year. For patients with GvHD this may be six-monthly. They should actively examine your mouth for oral cancer
- Gynaecology service: most women will need to see a gynaecologist for advice on HRT or other treatment for menopausal symptoms
- Opthalmologist/optician: patients should be seen annually

Selected patients

- Endocrinologist: all paediatric patients should see an endocrinologist due to the fact that they are still growing, but it is not necessary for every adult patient to be referred
- Chest specialist
- Liver specialist
- Kidney specialist
- Nerve specialist
- Physiotherapist
- Dietician
- Psychiatrist or other mental health professional
- Urologist
- Assisted conception unit/fertility service: please let your team know if you would like to speak to someone about fertility issues or having a family after transplant.

A referral to the ACU or fertility service can be made so that you can benefit from expert advice on the options that may be available to you

OTHER INTERVENTIONS THAT MAY BE PERFORMED AFTER THE TRANSPLANT

Immunisations

During the transplant your own immune system is destroyed or damaged. This is replaced with the donor cells. However, because of some of the drugs such as cyclosporine which you have had after you receive the cells, the immunity in the donor cells against all infections will not be perfect. For this reason we will recommend that you have all of your childhood vaccinations again.

This will usually be several months after the transplant. Some of the vaccines need to be given more than once. Live vaccines such as MMR are not recommended until at least two years after the transplant, or longer for patients with GvHD.

Your transplant team will have a schedule that they can give you, and often your GP will be asked to give you the vaccinations. There are international guidelines which make basic recommendations, although these may differ depending on where you live and your age.

Here is a brief summary:

- The influenza ('flu') vaccine is usually given in the autumn starting six months after transplant. However this might be earlier if advised by national or local policy during, for example, an outbreak.
- General immunisations are usually commenced at 6-12 months post allograft, although may be delayed if you are still taking immunosuppressive drugs

- Pneumovax can be started earlier (3-6 months)
- Vaccination against human papilloma virus may be considered for certain patients based on national guidelines

Venesections

Iron levels can build up during your treatment as you get a lot of iron from blood transfusions. In general the body is not very good at getting rid of iron. If the levels remain high for long periods of time (usually years), iron can settle in many of the organs and cause damage and symptoms. For this reason if you have a high ferritin (usually more than 1,000) the team will recommend venesections.

This is essentially exactly the same as being a blood donor, as a pint of blood is removed from your vein using a large needle. The blood is then discarded. Venesections will not usually be started until your haemoglobin is normal as we do not want you to become anaemic. Some people feel faint after or during a venesection, but usually they are very well tolerated. They can be done periodically until your ferritin is below 1,000.

6 STEP SIX DISEASE MONITORING AND FURTHER TREATMENT

ISSUES DISCUSSED IN THIS STEP:

- Disease assessment
- Chimerism analysis
- Donor lymphocyte infusion (DLI)
- Further treatment for disease recurrence
  - Chemotherapy
  - DLI
  - Second transplant
  - Other drugs
- Palliative care

DISEASE ASSESSMENT

Although each time you come to clinic you will have blood tests and a clinical assessment, there will be several time points when a 'formal' assessment of your remission status is done. This may include a bone marrow test and/or CT, PET or other scans.

The frequency and type of test will depend on what your disease was and on the local policy. Most patients will have a disease assessment at one year, but not 'formally' thereafter unless something else happens, such as your blood counts drop or you become unwell.

CHIMERISM ANALYSIS

Chimerism means that two different 'types' live together in one body. After the transplant your bone marrow and blood changes to that of the donor. Because there are genetic differences (like a DNA fingerprint) between you and the donor, tests can be done on your blood or bone marrow which can tell what proportion of your blood or marrow is donor and what proportion is your blood. In many cases it is expected that you will 'become' 100% donor in your blood and marrow, but in some cases 'mixed chimerism' will occur.

Mixed chimerism does not mean that the disease has returned, it just means that some of your blood cells have survived the transplant. Mixed chimerism does not always need particular treatment; sometimes it will improve spontaneously over time. If you are still on immunosuppression such as cyclosporine this might be stopped or cut down. If treatment is required this is usually with donor lymphocyte infusions (DLI).

DLI FOR MIXED CHIMERISM

A donor lymphocyte infusion is when more cells from your original donor are given to 'strengthen' the donor cells and push their levels up to 100%. Often these cells will have been stored since the time of your transplant if there were cells 'left over'. If not, the donor will need to be contacted to ask if they are willing to donate again. In general donors are very committed once they have made a donation and it is extremely unusual that they would say no.

Collecting DLI is also easier for the donor as they do not need to have any injections before the cells are collected on the apheresis machine. These cells cannot be collected directly from the bone marrow. Once we have the cells, these can be given to you as a short infusion in the outpatients department through a cannula. You will not need any special lines like the Hickman line, but if you do still have one the cells can be given through that. You usually do not need any chemotherapy or other drugs.

The main risk of DLI is that you might develop GvHD and your doctor will talk to you about the risk in your case. Usually a very small dose of cells is given to lower the chances of GvHD. If a single dose of cells does not increase the chimerism, further doses can be given.

FURTHER TREATMENT FOR DISEASE RECURRENCE

Unfortunately, despite having a transplant, some patients will have a relapse of their original disease. This is a devastating thing to happen to you and your family, particularly if a long time has passed since the transplant. In general the risk of relapse is highest in the early post-transplant period, and reduces after about two years. It is much more unusual for the disease to come back after five years, but unfortunately this can sometimes happen too. The relapse may be noticed at your clinic visit, for example by an abnormal blood test or a swollen gland, or you might become unwell and seek medical advice. Further tests such as a bone marrow scan will often need to be done to confirm the relapse.

In general the risk of relapse is highest in the early post-transplant period and reduces after about two years

In many cases more treatment will be available if you want it. However this will depend on the time since the transplant, your general health, whether you have GvHD or not and other factors related to the disease. You should have an honest discussion with your doctor and your family and loved ones about whether further treatment (and what type of treatment) is the right thing for you.

Chemotherapy
Chemotherapy can be very effective to get the disease into remission again, but chemotherapy alone will rarely work to keep the disease away in the long term. If chemotherapy is given it will often be combined with DLI or a second transplant (see below) as the best chance of curing the disease. You are familiar with the risks and side effects of chemotherapy, but you should talk these through with the team and your family and friends again before making your decision.

DLI for relapsed disease

DLI can be given for relapsed disease, and the procedure is very much as described above for mixed chimerism. There are two main differences. One is that the DLI is often given after chemotherapy or other types of drugs to help it work better. The other is that the dose of cells is also usually higher and this means that the risk of getting GvHD is increased. DLI can be very effective in some diseases such as CML, but works less well in others such as ALL.

Second transplant

For many patients the only chance of a cure in this situation is having a second transplant. In most cases the same donor as before will be used, but the transplant will be done in a different way. You know about the graft versus leukaemia (malignancy) effect and this must be maximised after a second transplant. GvL often goes along with GvHD and therefore you will be at a much greater risk of developing GvHD after the second transplant. In fact your doctor may explain that they will try to cause GvHD in order to keep the disease away. The amount of GvHD is unpredictable and unfortunately some patients may have very bad or life-threatening GvHD after a second transplant. You should talk to the team very carefully about these risks.

Other drugs

For some diseases specific drugs such as imatinib for CML can be given after the transplant, either with or without DLI, to treat relapse. These can be extremely effective with low side effects. In some cases drugs such as these may even be used as 'maintenance'. For instance, the drug will be continued after transplant even if there is no sign of disease.

PALLIATIVE CARE

In some cases it may not be advisable or possible to have further active treatment. This could be because the risk to you is too high

or without an obvious benefit, or that you do not want to have further treatment. Discussions between all members of the team, with you and your family or friends, is very important to make sure that everyone understands the options and agrees the best approach.

During the palliative phase of your care, you may still receive transfusions and antibiotics. You may also require analgesia or drugs for pain. The palliative care team are specialists in this area and a referral to them will enable you and your family to access their support and care during this time.

7 STEP SEVEN LOOKING AHEAD

Having a transplant is a difficult and complex treatment and there may be numerous complications during your recovery.

Life after transplant may not be the same as it was before. However, as life regains some sense of normality, it is important to keep looking ahead and at the same time be proud of the journey you have travelled. After all, you have come a long way.

The further you are from the transplant, the more confident you will feel and hopefully life will begin to settle into a familiar pattern and routine.

There are lots of positive things that can happen after transplant. Many patients feel renewed and with a greater sense of purpose and ambition, although this rarely happens quickly. Many patients tell us that they feel as though they have a new life and a new beginning. Although it can take time to really feel comfortable with the 'new you', it can be an opportunity to look at life differently and take on new challenges or just enjoy the way things are.

It is still possible to experience bouts of uncertainty and some patients will naturally still have many questions or concerns.

Please discuss any concerns you have with your transplant team, who will always be happy to help you, or get in touch with the Patient Experience Team for more information and support at **patientinfo@anthonynolan.org** or **0303 303 0303**.

Share your experiences and get support from others on our online community at **anthonynolan.org/transplantcommunity**.

Although it can take time to feel really comfortable with 'the new you' it can be an opportunity to look at life differently and take on new challenges or just enjoy the way things are

FINAL COMMENTS

Now that you have reached the end of this book we hope that you have found it useful. This book was developed in response to feedback from many patients over many years who felt that they were not able to find enough information about the long-term recovery and effects of their treatment.

During its development, we learned a lot about the needs of patients and individuals and their experiences after the transplant. We have included their comments and feedback in this book and we hope the information helps to make your journey to recovery a little easier.

Use this book as you wish. You might want to read it all the way through, or look at the steps you think will answer your questions. You might also want your family to read it so that they can learn a little more about your recovery.

Michelle Kenyon and Dr. Bronwen Shaw

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