Myeloma Australia

Autologous Stem Cell Transplant

A guide for people with myeloma

Autologous Stem Cell Transplant – a guide for people with myeloma

This book is written for people who have been diagnosed with myeloma. It will also be helpful for their families, friends and health professionals.

Myeloma Australia is a national non profit organisation dedicated to providing information and support for those affected by myeloma. Founded in Victoria in 1998 by three families living with myeloma, the organisation has grown to become a significant provider of services and support for the myeloma community.

Myeloma Australia:

- provides information and support to people living with myeloma, their family, friends and health professionals through its specialist Myeloma Support Nurse led programs
- raises awareness of myeloma
- provides funding for research projects
- advocates to state and federal government for support regarding access to new therapies

To talk to someone about any aspect of myeloma, its treatment and management, call the Myeloma Australia toll free Telephone Support Line on 1800 MYELOMA (1800 693 566). The Telephone Support Line is available 9am to 5pm (AEST) Monday to Friday and an experienced Myeloma Support Nurse will answer the call in confidence.

Acknowledgements

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Disclaimer

Introduction

This book has been written for people with myeloma, their families, friends and health professionals. It provides information about high-dose therapy and autologous stem cell transplantation (HDT-AuSCT), one of the treatment options for myeloma. It aims to:

- Explain more about HDT-AuSCT
- Describe the autologous stem cell transplantation procedure and what it involves
- Explain what to expect from this treatment and its potential advantages and disadvantages
- Help to make informed treatment decisions about treatment and care

Some of the more technical or unusual words appear in bold the first time they are used and are described in the Medical terms explained section on page 49

What is myeloma?

Myeloma, also known as multiple myeloma, is a type of cancer arising from plasma cells that are normally found in the bone marrow. Plasma cells are a type of white blood cell which form part of the immune system.

Normal plasma cells produce different types of **antibodies** (also called **immunoglobulins**) to help fight infection. In myeloma, the plasma cells become **malignant** and release a large amount of a single type of antibody, known as **paraprotein**, which has no useful function. It is often through the measurement of paraprotein that myeloma is diagnosed and monitored.

Bone marrow is the 'spongy' material found in the centre of the larger bones in the body. As well as being home to plasma cells, the bone marrow is where blood cells (such as **red blood cells**, **white blood cells** and **platelets**) are made. These all originate from blood **stem cells**. Plasma cells normally make up less than 5% of the total blood cells in the bone marrow.

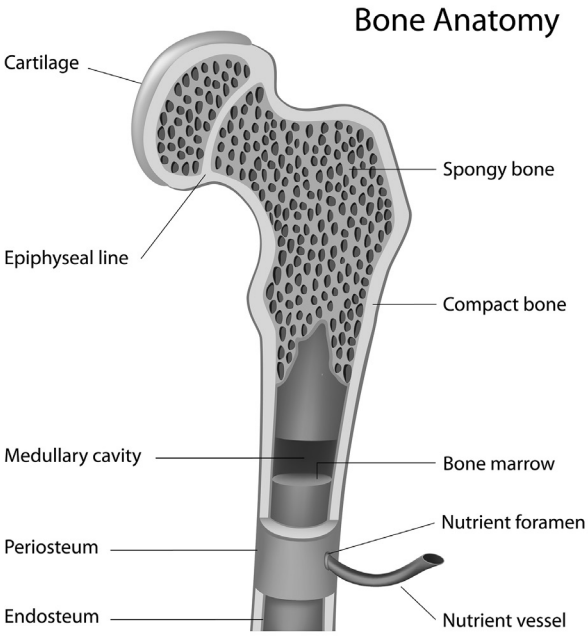


Figure 1. Bone marrow diagram

Myeloma affects multiple places in the body where bone marrow is normally active (hence why it is sometimes referred to as 'multiple myeloma'), i.e., within the bones of the spine, pelvis, rib cage and the areas around the shoulders and hips. The areas usually not affected are the extremities – the hands and feet – as the bones here do not contain bone marrow.

Most of the complications and symptoms of myeloma are caused by a build-up of the abnormal plasma cells (often called myeloma cells) in the bone marrow and the presence of paraprotein in the body. Common problems include bone pain, bone fractures, tiredness due to **anaemia**, frequent or recurrent infections (such as chest infections, urinary tract infections and shingles), kidney damage and **hypercalcaemia**.

Myeloma most commonly occurs in people later in life, i.e., over the age of 65. However, sometimes it can be diagnosed much earlier. It is also slightly more common in men than in women. The causes of myeloma are not fully understood but it is believed to be caused by an interaction of both genetic and environmental factors. There are thought to be multiple environmental factors which may increase the risk of developing myeloma. Exposure to specific chemicals, radiation, viruses and a weakened immune system are considered possible contributing factors. It is likely that myeloma develops when a susceptible (at risk) individual has been exposed to one or more of these factors.

There is a slight tendency for myeloma to occur in families. Although rare, this suggests there may be inherited factors in myeloma. This alone is not enough to cause myeloma but may make an individual at a slightly higher risk of developing myeloma – other environmental factors also need to have an impact before it develops. To date there is no way to predict if an individual will develop myeloma later in life.

In the majority of cases, however, the causes of myeloma are unclear and are likely to be unique to each person. Research is ongoing into the biology and genetics of myeloma to determine the factors responsible for its onset and progression.

Treatment for myeloma – the basics

Thankfully we now have many different types of very effective treatment for myeloma that can gain good control of the disease. Survival rates have increased exponentially in recent years however, unfortunately myeloma remains incurable.

In general, treatment is given to:

- Reduce the amount of myeloma in the body
- Control the myeloma for as long as possible
- Control the myeloma when it returns (**relapse**)
- Relieve the symptoms and reduce the complications the myeloma is causing
- Improve quality of life
- Prolong life

Before embarking on treatment, important decisions need to be made about which treatment is best or most appropriate and when to receive it. Not everyone diagnosed with myeloma will need to start treatment immediately. The timing of when to start will depend on several factors including how quickly myeloma markers are rising, overall health, age, fitness, any previous treatments and individual preferences. Each option must be considered carefully so that the benefits of treatment are considered against the possible risks and **side effects**.

Treatment for myeloma is often most effective when two or more drugs, with different but complementary mechanisms of action, are given together over a duration of several months. Supportive care treatments are also prescribed concurrently to help prevent or manage side effects of treatment, prevent infection and provide relief from myeloma related symptoms.

Read more about myeloma and its treatments in our book
Myeloma a Comprehensive Guide
www.myeloma.org.au or call **1800 MYELOMA (693 566)**

Basic facts

There are approximately 2000 new cases of myeloma per year in the Australia

Incidence is slightly higher in males than females

Myeloma accounts for just over 1% of all new cancer cases

Myeloma mostly affects people aged 65 and over

The Principle behind Transplantation

Initial treatments provide an effective way of treating myeloma however, in order to achieve a deeper, and hopefully longer response, more intensive treatment is required.

Unfortunately, we cannot give the initial treatments, otherwise known as **induction treatment**, in higher more intensive doses or schedules. This is because high doses of **chemotherapy** are very toxic to the blood forming stem cells in the bone marrow and they severely affect blood cell production. This results in blood counts falling to dangerously low levels, causing potentially life-threatening complications.

High-dose therapy and autologous stem cell transplantation (HDT-AuSCT) provides a solution to this problem. It involves giving high-doses of chemo-therapy to destroy myeloma cells, followed by returning previously collected stem cells to 'rescue' the bone marrow allowing the bone marrow to recover and blood cell production to continue. Because the stem cells belong to the individual the procedure is referred to as an autologous stem cell transplant, this type of transplant is by far the most common type of transplant used to treat myeloma.

The process of HDT-AuSCT will be discussed in more detail later in this chapter, the following is a summary of the process.

HDT-AuSCT involves a course of induction treatment to remove as much of the myeloma as possible. This is followed by the **mobilisation** and collection of stem cells before a high dose of chemotherapy, usually **melphalan** is given with the aim of destroying the remaining myeloma cells.

The stem cells are then returned to the blood, where they find their way back to the bone marrow and start to make new blood cells, through a process called

engraftment. A successful engraftment effectively 'rescues' the bone marrow, enabling it to recover and re-establish blood cell production.

HDT-AuSCT following induction treatment therefore can destroy more myeloma cells than would be possible with induction treatment alone. This increases the likelihood of a longer **remission** or **plateau** and a better quality of life. However, it is worth noting that myeloma is a very individual cancer and each person's myeloma has its own distinct characteristics, which may affect treatment outcomes.

Read more about the different characteristics of myeloma in our book
Myeloma a Comprehensive Guide
www.myeloma.org.au or call **1800 MYELOMA (693 566)**

What is the aim of HDT-AuSCT?

The aim of stem cell transplantation is to consolidate the response to the induction treatment, helping to achieve a deeper more durable response and ultimately improve the quality and duration of life. HDT-AuSCT is an intensive treatment option that is not suitable for everyone. It is generally limited to younger and/or fitter people. There are no rigid age cut offs but generally people over 70 years old with unfavourable general health (i.e. other illnesses/or less fit), would not usually be a candidate for this treatment. This is mainly because the possible advantages are almost certainly outweighed by the possible disadvantages of the treatment in this group.

What are stem cells?

There are various types of stem cells, but when talking about stem cell transplantation in myeloma, we are referring to blood stem cells (also called **haematopoietic stem cells**).

Blood stem cells exist in the bone marrow and have the ability to divide and develop into the three main types of cells found in the blood: red blood cells, white blood cells and platelets.

Each of these cells perform essential functions in the body:

- Red blood cells carry oxygen from the lungs to the entire body
- White blood cells fight infection by combating bacteria and viruses
- Platelets form clots and help control bleeding from injuries

It is the unique ability of haematopoietic stem cells to divide into blood cells and be collected safely that makes HDT-AuSCT a treatment option.

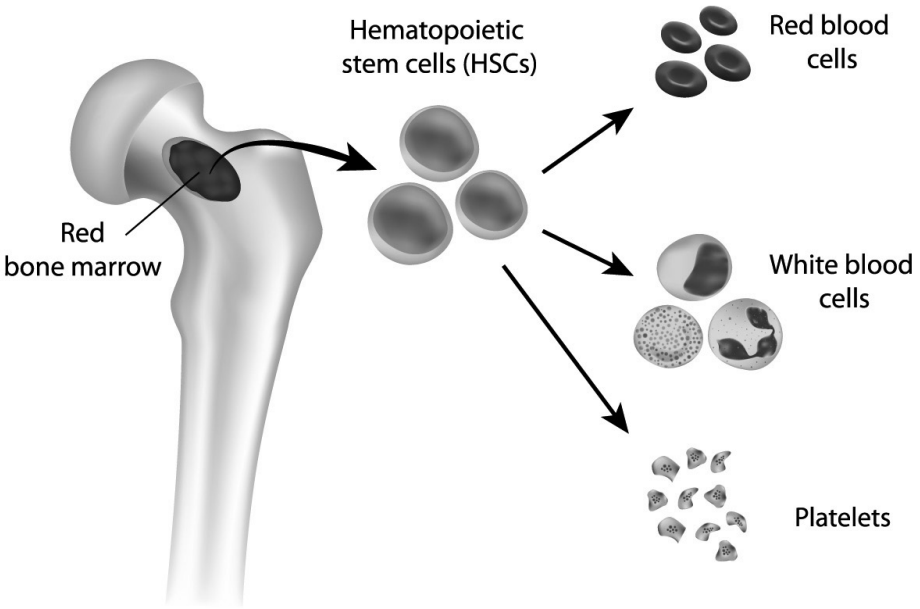


Figure 4. Blood stem cell diagram

What are the possible advantages and disadvantages of HDT-AuSCT?

Understanding the possible advantages and disadvantages of any treatment option is important in making decisions about the management of myeloma.

The possible advantages of HDT-AuSCT include:

- Evidence from clinical trials show that the use of HDT-AuSCT can improve the duration, depth and quality of response and extend life compared with standard-dose anti myeloma treatment
- The relative safety of HDT-AuSCT means that it can be considered as an option for many people if they are fit enough
- The potential for improvement in quality of life after the transplant as fewer residual myeloma cells may mean fewer ongoing complications, such as myeloma bone disease

However, HDT-AuSCT may not benefit everyone and there are some possible disadvantages:

- High-dose therapy is more toxic than standard doses of chemotherapy and therefore there is a risk of more side effects
- There is a longer recovery period following HDT-AuSCT compared with standard chemotherapy
- The success of this or any other treatment cannot be guaranteed. Not everyone will achieve the desired response, and unfortunately HDT-AuSCT is not a cure for myeloma
- The effects of HDT-AuSCT may affect fertility. Options such as sperm banking or egg storage should be discussed with a specialist doctor prior to starting anti myeloma treatment.
- As with all procedures, there is a very small risk of death

Considering the options and making a decision

The whole process, from the initial discussion with a specialist to recovery after the transplant, can take several months and may seem like a daunting prospect.

The process begins by looking at all the available options. The option of HDT-AuSCT may be raised soon after a myeloma diagnosis or it could be discussed a little later when initial anti myeloma treatment is underway. Deciding to go ahead with a recommended transplant can be stressful and it is important to have enough information to make an informed decision

Information on advantages, disadvantages, risks and potential side effects should be provided. Everyone is unique and will have differing priorities, concerns and lifestyle preferences – all of which can play a significant part in the decision making process.

HDT-AuSCT is only performed in approved specialist transplant centres within larger hospitals. A pre- transplant consultation with a transplant expert will take place where more information will be provided. A provisional date may be discussed but this will likely not be confirmed until stem cells are collected. This consultation is a great opportunity to ask questions.

Read more about communicating with the medical team in our book
Myeloma a Comprehensive Guide
www.myeloma.org.au or call **1800 MYELOMA (693 566)**

The transplant specialist will make a recommendation on a person's suitability to proceed to transplant from a medical perspective, taking into consideration general fitness, mental health, and carer support. This treatment option does not suit everyone, and even suitable candidates may choose not to proceed. The timing of the HDT-AuSCT will be based on individual circumstances, such as a person's lifestyle, family situation, response after induction treatment and appropriate resource availability at the hospital. If the proposed timing of the transplant is not right, it may be an option to collect and store stem cells to have the transplant at a later date. Not all hospitals have the facilities to store stem cells and practice varies around the country. Therefore, a discussion about the options with a specialist should be undertaken.

An overview of the stages of the HDT-AuSCT process

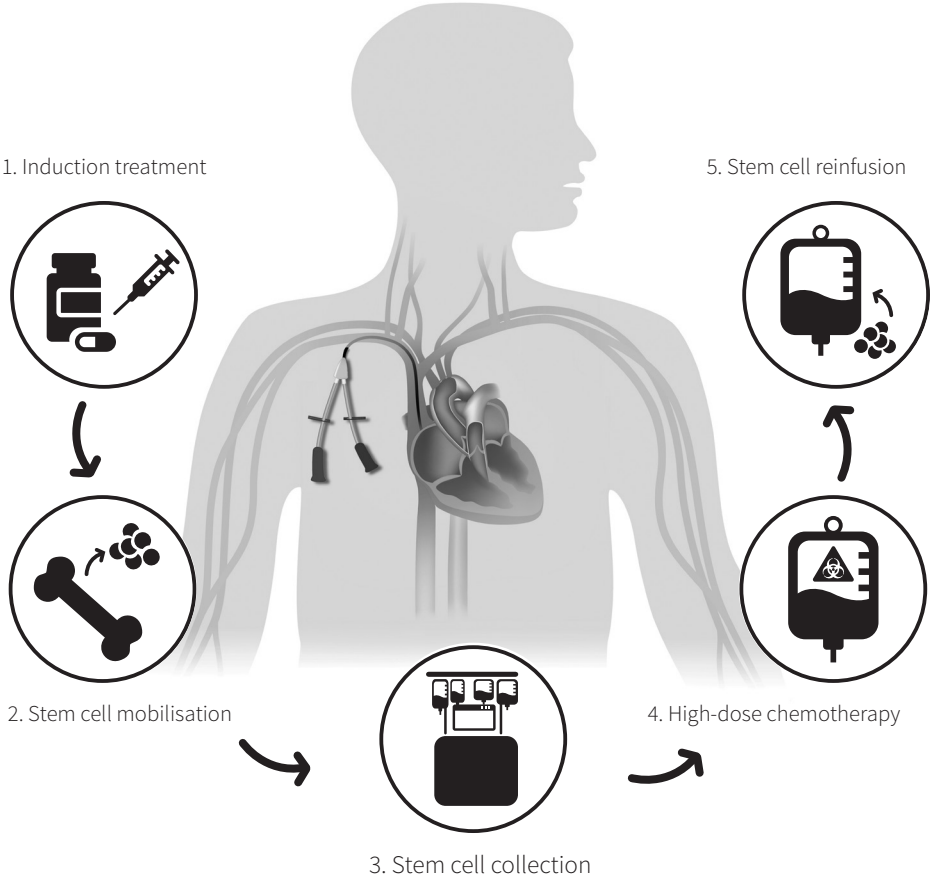


Figure 3. An overview of the stages of the HDT-ASCT process

Induction treatment

As described earlier, the initial treatment given before HDT-AuSCT is called induction treatment. Induction treatment aims to reduce the amount of myeloma in the bone marrow before the stem cells are collected.

Courses of induction treatment usually last for several months and are given in cycles. Induction treatment should ideally rapidly reduce the amount of myeloma and reverse disease symptoms. The number of cycles given will depend on various factors relating to the myeloma, the type of induction treatment and the response to treatment. Therefore, it is difficult to know exactly how long this induction treatment will last, but it is usually about four to six months.

Anti myeloma drugs can cause side effects such as nausea, diarrhoea, fatigue, peripheral neuropathy (nerve damage) and anaemia. An individual's risk of getting an infection or developing a blood clot is also increased while on treatment.

Each person is different, and these side effects can vary greatly between individuals, but can usually be prevented, treated or managed. Additional medications such as **antibiotics**, **antivirals** or **anticoagulants** may be needed to treat or prevent the onset of these side effects.

It is important to report side effects to the medical team as soon as possible so they can manage and monitor them accordingly and prevent them from causing lasting problems. In many instances, side effects can be reduced simply by lowering the dose of the medication and/or changing the treatment schedule. Side effects are usually short-term and often resolve once treatment has finished.

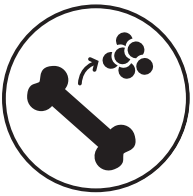
It is important that the induction treatment reduces the myeloma adequately to get the best outcome for the subsequent stem cell transplant. This generally means a 50% or better reduction in myeloma protein levels.

After each cycle, the doctor will request a series of routine blood tests. These will assess the myeloma protein levels and check to ensure the treatment isn't causing too much disruption to things like red blood cells, white blood cells, platelets and kidney and liver function.

After 3 – 4 cycles of treatment more thorough investigations, such as bone marrow tests or repeat imaging, may be required to confirm that there has been a good response to treatment.

If, after 3 – 4 cycles, a good response is not achieved, switching to an alternative induction treatment may be necessary. If there is still a limited response to the second induction treatment, it may not be beneficial to continue to HDT-AuSCT and the specialist will discuss other available options.

If undergoing the HDT-AuSCT process as part of a clinical trial, there may be differences to what is described above.



Stem cell mobilisation

In preparation for HDT-AuSCT, there must first be an adequate amount of stem cells collected from the blood. As stem cells live in the bone marrow, the number circulating in the blood is normally very low.

To collect an adequate number for a transplant the bone marrow needs to be stimulated to release the stem cells from the bone marrow into the blood. This process, known as stem cell mobilisation, can be achieved by a number of different methods.

The most common method of stem cell mobilisation is to give a synthetic form of a **growth factor** called **granulocyte-colony stimulating factor** (G-CSF). G-CSF is the main protein that controls the growth and development of blood stem cells in the bone marrow.

Treatment with G-CSF, such as filgrastim, increases the number of stem cells in the bone marrow, causing them to 'spill over' into the blood where they can be collected. It is given as an injection under the skin (subcutaneous) daily or twice daily depending on the transplant hospital's local policy, for approximately 5 – 7 days prior to the collection.

Nurses at the hospital will explain how to administer G-CSF injections at home. It is important to have the injection around the same time each day and to store the G-CSF as directed.

Side effects of G-CSF

G-CSF injections can cause side effects for some people. The most common side effects are flu-like symptoms (fever, aches and bone/joint pain). These symptoms are temporary and should disappear when the injections stop. The bone pain is usually a positive sign and indicates increased stem cell activity. The bone pain can be managed with pain-relieving medication such as paracetamol but occasionally stronger pain relief may be required during this period.

Mobilisation with a chemotherapy drug and growth factor

Although it is possible to mobilise stem cells using G-CSF alone, an infusion of a chemotherapy drug, usually **cyclophosphamide**, can be given before the G-CSF injections.

Cyclophosphamide temporarily reduces the number of stem cells in the bone marrow. When the bone marrow recovers, it goes into stem cell production 'over-drive'. With the addition of G-CSF, it is usually much easier to collect the required number of stem cells. Cyclophosphamide is given **intravenously** in the chemotherapy day unit.

When used after cyclophosphamide, the G-CSF is given for approximately 10 days, this may differ slightly between transplant hospitals. Please note the aim of using cyclophosphamide in this setting is not to treat myeloma, it does however, play an important role in mobilisation.

Side effects of cyclophosphamide

The most common side effects of cyclophosphamide include low blood counts and increased risk of infection, loss of appetite, hair thinning/loss, nausea and general weakness. Some may also experience symptoms associated with bladder irritation such as pain or burning during urination, urgency, blood in the urine or stomach or pelvic pain.

For some, the side effects of cyclophosphamide may be more intense than the induction chemotherapy, but usually resolve quickly.

What if the mobilisation is unsuccessful or inadequate?

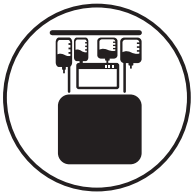
Although first attempts to mobilise stem cells with G-CSF and cyclophosphamide are successful for most people, it is possible that further intervention may be needed to collect the minimum amount of stem cells necessary for transplant.

In such cases, a drug called **plerixafor** (**Mozobil®**) can be added to the mobilisation regime. Plerixafor works by disrupting how stem cells are anchored to the bone marrow, resulting in the release of stem cells and in combination with G-CSF, greatly improves the amount that can be collected from the blood.

Plerixafor is reserved for people who prior to collection are found to be having difficulty releasing adequate numbers of stem cells into the blood stream. It can be added to the G-CSF or G-CSF and cyclophosphamide combination or alternatively can be used during subsequent attempts at mobilisation. G-CSF injections will be given for four to five consecutive days first, followed by the plerixafor, which is also a subcutaneous injection. In some cases, another injection of plerixafor may be used to reach the desired effect.

Side effects of plerixafor

The most common side effects associated with plerixafor include diarrhoea, nausea, dizziness, headache, joint pain and irritation or redness at the injection site. These are temporary and should disappear when the injections stop.



Stem cell collection and storage

After the mobilisation process the stem cells need to be collected. Stem cell collection and transplantation takes place in hospitals with specialist transplant centres. Some people will already be managed at these centres, others will need to be referred by their primary haematologist after receiving induction treatment

Collecting stem cells from the blood is done as an outpatient. To ensure there are enough stem cells in the blood for collection to take place, a blood test is required. This is called a **CD34+ blood test** and is performed on the day the stem cell collection is predicted to begin.

CD34+ is the technical name given to a protein found on the surface of stem cells. Measuring CD34+ provides a useful way of 'tagging' stem cells which enables the number of stem cells in the blood to be counted. If the CD34+ count is high enough, stem cell collection will begin. This procedure is referred to as **apheresis**.

Apheresis is the technique through which stem cells are collected from the blood using a cell separator machine. Collecting the stem cells takes about four hours but may take longer. A needle attached to a line is inserted into a vein in each arm. Blood is taken from one arm and sent through the line into the cell separator machine. The machine separates the stem cells from other blood components and is collected into a bag. The remaining blood is returned through a line into the other arm. For people whose veins are not robust/large enough for collecting stem cells, a central venous catheter otherwise known as a **central line** is required. A central line is a flexible plastic tube inserted into a large vein, either in the chest area underneath the collar bone or in the upper thigh/groin area.

Stem cells being collected via apheresis
(image credit: Peter MacCallum Cancer Centre)

Apheresis needle
(image credit: Peter MacCallum Cancer Centre, Melbourne)

It is a common concern that the stem cell collection might contain some myeloma cells that will then be re-infused with their stem cells following the high-dose therapy. The apheresis machine is programmed to 'skim off' stem cells, separating them out from other blood cells based on their specific gravity. Any remaining myeloma cells – a different cell type entirely from stem cells – should therefore not be collected in the apheresis process. Studies have shown that, if myeloma cells do 'contaminate' the stem cell collection, this does not appear to affect the success of the transplant.

The minimum number of stem cells needed for a successful transplant is two million stem cells per kilogram of body weight. However, as a contingency, it is desirable to collect a higher number of stem cells. It is almost always the aim to collect enough for two transplants (over four million stem cells per kilogram of body weight), even though most people will only receive one. In this case the remaining stem cells may be stored and only used if a second transplant is a suitable treatment option in the future. Stored stem cells are thought to remain viable for about ten years.

A small number of people will be recommended a tandem HDT-AuSCT, which means having a second transplant just 3 – 6 months after the first. In this instance, over 6 million cells may need to be collected.

Sometimes an adequate number of stem cells will be collected in just one session. However, two or three sessions over consecutive days may be needed to obtain the desired number of stem cells.

Unfortunately, for a very small number of people, it is not possible to collect enough stem cells even after additional mobilisation treatments such as cyclophosphamide or plerixafor. In this situation, it is not possible to proceed safely to HDT-AuSCT and other treatment options for the future should be discussed.

Side effects of stem cell collection

During the stem cell collection process, the most common side effect is a cramp-like or tingling sensation in the hands, feet or around the mouth.

This happens because the blood is mixed with citrate, an anticoagulant drug that stops the blood from clotting in the machine. When the blood is returned, this drug can cause a decrease the body's calcium levels. This can be managed with calcium tablets prior to the collection or an intravenous calcium infusion during the procedure.

Storage of stem cells

After collection, the stem cells are carefully labelled and taken to the processing laboratory in the hospital. The stem cells are then frozen and placed in special bags before being stored in liquid nitrogen until the transplant.

A chemical called **dimethyl sulphoxide** (DMSO) is mixed with the stem cells before freezing. DMSO prevents the water in the cells from forming ice crystals, which would permanently damage the stem cells during the freezing process.

As mentioned earlier, it is common practice to collect enough stem cells to have the option of a second transplant in the future, even though most people only receive one.

In some hospitals stem cells can be stored for many years. However, not all hospitals have the facilities to store stem cells. Local hospital policy will dictate if stem cells can be stored and if so, for how long.

Central line insertion

A large number of intravenous infusions and regular blood tests will be required during the transplant. Therefore, it is necessary to use a central line to create a more permanent way to safely and frequently administer medications and withdraw blood without inserting a needle each time.

The central line will be put in prior to the transplant and will likely remain in place and be regularly accessed during recovery.

The central line consists of a venous catheter, a flexible, hollow tube, which is inserted into a large vein in the chest. The most common type of catheters used during HDT-AuSCT are known as a Hickman catheter or a Permacath.

The central line is usually inserted into one of the large veins through a small cut in the upper chest. An injection of local anaesthetic will be given first into the skin to numb the area around the collar bone and chest.

The central line is placed under the skin from the chest to the neck and once in the neck, is inserted into a large vein which leads to the heart. The part of the central line outside the body is stitched or taped to the chest and dressed to ensure it does not come out and that it remains clean and dry. The insertion procedure usually lasts between 30 – 60 minutes but may occasionally take longer.

During the transplant, a nurse will care for the central line. If it is necessary to care for the central line at home, education will be provided.

It is very important to try to prevent infections while a central line is in place.

Below are some things to remember about having a central line:

- Always wash hands thoroughly before and after touching the central line
- Inspect the area of skin around the central line site daily, checking for any signs of infection such as tenderness, redness, pus or bleeding
- If experiencing a temperature of 38°C or higher, present to the nearest emergency department immediately for intravenous antibiotics
- The dressing will need to be changed weekly to reduce the risk of infection
- Seek advice from the nurse if the dressing irritates the skin

- Do not leave a wet dressing on the central line site
- Do not bathe or swim with a central line. It cannot be immersed in water

The majority of people having HDT-AuSCT will have a central line but some hospitals may recommend a PICC (peripherally inserted central catheter) line instead. A PICC line is inserted in a vein on the inside of the elbow and slowly advanced until the end of the catheter sits in one of the large veins that lead to the heart. The principles of caring for a PICC line are the same as for a central line.

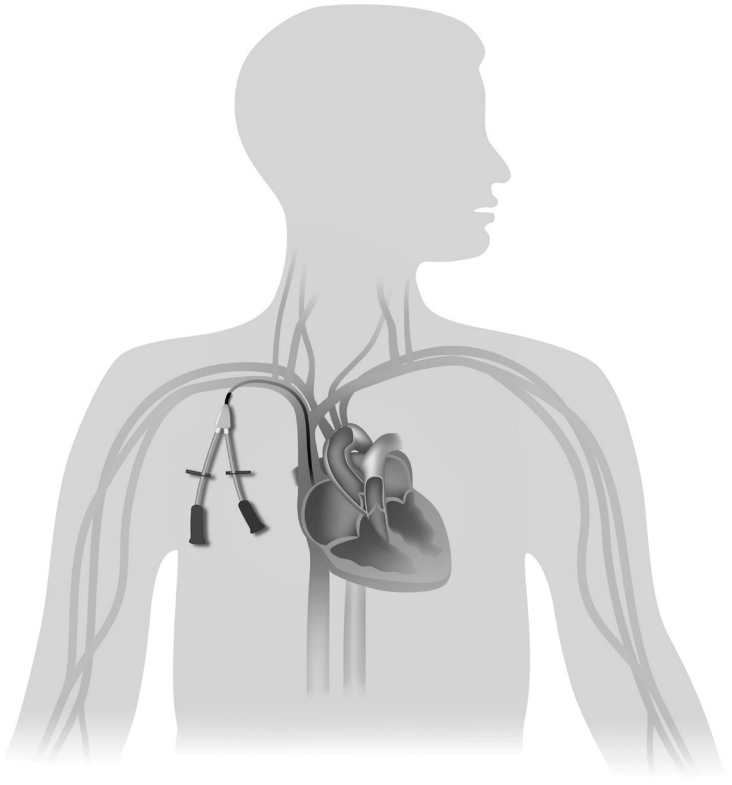


Figure 4. Central line diagram

Pre-transplant tests and investigations

There are a number of tests and investigations carried out before a stem cell transplant. These tests are preformed to determine general health and fitness and to ensure vital organs are working well enough to proceed. These tests include checking heart, lung and kidney function. The results of these tests also act as a baseline to compare to after transplant to ensure the body has recovered well. Not all investigations described may be needed for everyone.

Blood tests

Blood tests provide information on general health and the myeloma itself. Tests may include: paraprotein level; full blood count; blood group; kidney, liver and thyroid function; blood clotting; beta 2 microglobulin; lactate dehydrogenase; hormone screen; iron and glucose levels.

An infection screen will be completed prior to the stem cell collection and repeated if there is a long gap between the stem cell collection and transplant. A blood sample will be sent to screen for viruses and other infections. Tests may include: HIV (type 1+2); Hepatitis B+C; Cytomegalovirus (CMV); Epstein-Barr virus (EBV). This will ensure there is opportunity for infections to be treated prior to transplant or highlight whether any additional medications are required during transplant to prevent infection.

The Serum **Free Light Chain** assay measures the amount of free light chains in the blood and/or urine. This can be done at the same time as other routine blood tests and is particularly important for those with **light chain myeloma**.

Read more about myeloma and these blood tests in our book
Myeloma a Comprehensive Guide
www.myeloma.org.au or call **1800 MYELOMA (693 566)**

Bone marrow aspirate and trephine (BMAT)

A BMAT involves putting a needle into bone (usually the back of the pelvic bone) to get a small sample of the bone marrow. A local **anaesthetic** is used to numb the pain and sometimes a light sedative is given to help the person relax. There are two parts to this test, taking a sample of the liquid bone marrow (aspirate) and taking a small core of bone along with the marrow inside (trephine). Both are used to establish the presence and amount of myeloma cells in the bone marrow. The BMAT is routinely used at diagnosis and any time a complete assessment of the myeloma is required. This test is particularly important for people with **non-secretory myeloma** to monitor the disease.

24-hour urine collection

This test accurately measures kidney function and Bence Jones proteins (the light chain part of paraprotein). A portion of people with myeloma will make enough Bence Jones proteins to be measurable in the urine. A large bottle is supplied or can picked up from any pathology centre to collect all the urine passed for 24 hours. The first void of the day is passed into the toilet, taking note of the time. Each void for the following 24 hours is then collected into the bottle. It is important to catch all urine produced during this time and if staying at home is not possible, the bottle needs to be taken along. The collection is then returned to the hospital the day of completion. For the results to be accurately calculated a blood sample will also need to be taken.

Imaging or scans

A chest x-ray may be ordered as a simple way to screen the health of the heart, lungs and bones of the rib cage.

A skeletal survey is a series of plain x-rays of the spine, skull, chest, pelvis and long bones which can detect myeloma bone lesions.

Whole body low dose computerised tomography (WBLDCT) scan may be ordered to assess bone health. A WBLDCT is a more sensitive test for assessing myeloma bone disease using x-ray technology to create a three-dimension digital image.

Although not routine other imaging could include Magnetic Resonance Imaging (MRI) or Positron emission tomography (PET) scans.

MRI is a non-invasive way to produce a detailed two or three dimensional imagine of structures inside the body using magnetism and radio waves. An MRI can detect focal lesions (early abnormal areas in the bone) and obtain imagines of plasmacytomas and spinal cord compression.

A PET scan uses a mildly radioactive drug called Fluoro-deoxyglucose (FDG) to show up areas in the body where cells are more active than normal, such as actively growing myeloma cells. A PET can detect extramedullary disease, which is myeloma that grows outside the bone marrow. Useful for disease monitoring in non-secretory disease.

Heart Function

There are a few ways in which heart function will be tested.

An Electrocardiogram (ECG) is a simple test which records the rhythm and electrical activity of the heart. A series of electrodes (sticky dots) are placed on the chest, ankles and wrists. These are connected to an ECG recording machine which picks up the electrical signals that make the heart beat. The electrical signals are drawn as a graph and any problems with the heart rhythm can be picked up by a change in the shape of the graph. The test itself is not painful, but it is necessary to sit or lie still for a few minutes.

Cardiac gated blood pool scan (CGBPS) is an imaging test used to assess heart function, performed by the nuclear medicine department. This scan involves an injection of radioactive dye which 'labels' the blood by attaching to the red blood cells. It is then possible to see how much blood is being pumped through the heart with each beat and how well the heart muscle contracts.

Alternatively, or in addition to a CGBPS, an echocardiogram may be ordered to comprehensively determine heart health. This test involves an ultrasound of the heart and provides more detailed information about the structure and function of the heart chambers, valves and related vessels.

Dental check-up

A dental check-up is necessary to ensure good health of the teeth and gums prior to high-dose chemotherapy as it is important to identify and eliminate sources of existing infection. It is also a good opportunity for the dentist to promote the importance of good dental hygiene during and after transplant.

Getting fit for transplant

Exercise plays an important role when preparing for HDT-AuSCT. Improving fitness may help a person to physically and mentally cope with treatment. Also, maintaining fitness before and during transplant can reduce recovery time. Exercise physiologists (EP) and physiotherapists are trained to design exercise programs to suit the current level of fitness and goals set. Some transplant centres provide access to an EP or physiotherapist or they can be accessed in the community. The costs involved can be subsidised through Medicare Australia's Chronic Disease Management plan which is accessed through the GP.

For information about exercise and Medicare Australia's Chronic Disease Management Plan
Myeloma a Comprehensive Guide
www.myeloma.org.au or call **1800 MYELOMA (693 566)**

Outpatient HDT-AuSCT

The majority of HDT-AuSCTs will be facilitated as an inpatient in a major tertiary hospital with a transplant centre. A hospital stay of approximately 2 to 3 weeks is standard for an inpatient transplant, but this can vary.

There are some hospitals in Australia that have programs allowing for some or all of the HDT-AuSCT to be facilitated as an outpatient. Outpatient transplants are only offered to those who fit the following criteria:

- Live close to the transplant centre or can arrange accommodation close by
- Are physically and emotionally fit
- Have no additional complexities involved in their care
- Have a willing and able carer available to them 24 hours a day
- Feel confident with the reduced contact with the hospital

Individuals who are managed completely as an outpatient will be required to attend the hospital as an outpatient regularly (possibly daily) for assessment

and blood tests. If the person lives far from the hospital, some centres may offer accommodation close to the hospital during this time.

Many transplant centres have a hospital in the home (HITH) medical team comprised of doctors and nurses who do home visits providing the necessary care in the home and removing the need for daily visits to the hospital.

Being treated as an outpatient for some or all of the HDT-AuSCT process is becoming more common in Australia, although it is by no means the norm for every transplant centre and it is dictated by many factors.

Receiving high-dose therapy

In most cases, high-dose therapy (HDT) followed by a stem cell transplant will be arranged 2-4 weeks after the stem cell collection.

The high-dose therapy is almost always a chemotherapy drug called melphalan which is given intravenously, usually via the central line. The dose of melphalan that is given is aimed at removing any residual myeloma cells following induction treatment. The dose of melphalan may be adjusted based on the person's kidney, heart and lung function. Other anti-myeloma treatments may be added to the high-dose treatment.

Immediately before receiving the high-dose therapy, extra fluid will be given through a drip, which aims to prevent any dehydration and kidney damage the melphalan can potentially cause. If kidney function is already poor, the dose of melphalan may be adjusted.

The dose of melphalan given will affect the blood cells and stem cells within the bone marrow and within a few days of receiving the melphalan, blood counts will start to drop. All other treatments such as **bisphosphonate** treatment, which helps protect the bones and prevent further bone damage, will usually be stopped during the transplant process.

Side effects of high-dose therapy

The most common side effects of high-dose therapy include:

Nausea and vomiting

High-dose chemotherapy can result in nausea and vomiting. Anti nausea medication is used to help prevent and minimise the risk of this happening. Anti nausea medications are given both intravenously (through the drip) and taken orally. There are many different anti nausea medications available and while a standard combination is used for high-dose therapy this can be adjusted if needed to optimise the control of nausea and vomiting. It is important to let the nurse and doctor know if the nausea is not well controlled.

Sore mouth

It is common to have a sore mouth, called oral **mucositis**, for a short time after receiving high-dose therapy. Chemotherapy drugs attack rapidly dividing cells, which includes the myeloma cells in the bone marrow, but also the cells lining the mouth and digestive system. This can lead to inflammation which can vary from mild soreness of the mouth and taste changes, to being more painful with ulcerations, perhaps causing difficulty in eating and drinking.

Mouth care is necessary to prevent infection. This may include using mouth-washes, brushing teeth frequently with a soft toothbrush and inspecting the mouth for signs of infection. If the mucositis is painful, pain-relieving medication may be required. The medical and nursing team will frequently assess and review this.

> To help reduce the risk of mucositis, it is recommended to suck ice cubes 15 minutes before the high-dose therapy is administered and up to 1 hour after the infusion. This process is called cryotherapy. The ice constricts the blood vessels inside the mouth therefore reducing the amount of blood containing chemotherapy reaching and damaging the lining of mouth.

Diarrhoea

High-dose therapy as mentioned above can cause inflammation all the way down the digestive tract. This can lead to cramps, gas, bloating and diarrhoea. Diarrhoea is very common, and the nurse should be informed straight away so a sample can be collected to test for infection. Once infection has been ruled out, then medication can be given to relieve the diarrhoea and relieve discomfort. Keeping the area clean and applying a barrier cream can help protect the skin.

Altered taste and smell

Taste and sense of smell can be altered by the high-dose therapy. It is common to dislike the smell of some foods and have a reduced appetite. Sticking to cold foods with minimal odour, adding extra sugar to sweet food, and extra salt to savoury may help. If taste changes make drinking water difficult, lemon juice

can be added. It can take some time, but taste sensation and smell will return to normal.

Weight loss

Weight loss can be common due to the side effects mentioned above. It may help to adjust eating habits to small frequent meals to be able to consume enough calories as appetite decreases. A dietitian will be involved to ensure adequate nutrition requirements are met. High protein drinks can be substituted if needed to improve nutritional intake and it may be necessary to receive nutrients intravenously. This is called Total Parenteral Nutrition (TPN) and will be given via the central line. Body weight will be measured regularly to monitor for weight loss and fluid balance.

Fatigue

Feeling tired and lethargic after high-dose therapy is common, as is sleeping more than usual and having trouble concentrating. It may be some time before energy levels return to normal. In hospital, even if fatigued, it is advised to sit out of bed as often as possible when awake, particularly for meals and attempt a small walk each day. This can significantly help with physical and mental recovery and side effect management. Fatigue may persist longer than the other side effects noted above and can last months to a year after the HDT-AuSCT. Maintaining an exercise routine during and after the transplant will be important.

Hair loss

Hair loss is an inevitable side effect of the high-dose therapy. It can take 2 – 3 weeks before the hair starts to fall out and it is a gradual process. During this time the scalp may feel mildly sore or itchy. Many people choose to have their hair cut short or shaved before receiving the high-dose therapy and/or have a wig fitted. There are a number of specialist suppliers and their details will be available at the transplant centre. It can take 3 – 6 months for hair to grow back.

The transplant – having stem cells returned

The stem cells will be reinfused the day after the high-dose therapy, this day is referred to as 'day zero'. The process of reinfusing the stem cells is very straight forward and on average takes approximately 30 minutes. The frozen bag (or bags) of stem cells are thawed in a warm water bath at the bedside and returned to the blood system via the central line.

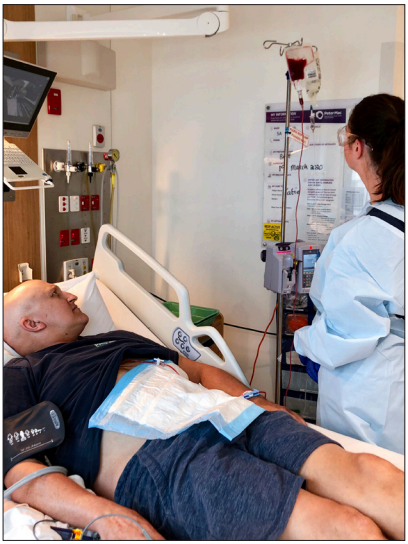
The most common temporary side effects of the infusion are usually very mild and are caused by the dimethyl sulphoxide (DMSO) preservative. They include, facial flushing, feeling chilled and a ticklish feeling in the throat that causes a cough. Most people experience a taste that some say resembles garlic or sweetcorn, but this is temporary and resolves very quickly. Visitors might notice an unusual odour but this will disappear.

In rare cases, the infusion may cause low blood pressure, a fast heart rate and shortness of breath. Medications are given before the infusion process to prevent or lessen some of the expected effects of the re-infusion.

Stem cells transported to bedside in dry ice
(image credit: Peter MacCallum Cancer Centre, Melbourne)

Frozen stem cells
(image credit: Peter MacCallum Cancer Centre, Melbourne)

Stem cells being thawed in water bath
(image credit: Peter MacCallum Cancer Centre, Melbourne)



Stem cells being reinfused
(image credit: Peter MacCallum Cancer Centre, Melbourne)

Engraftment

Once the stem cells are put back into the blood stream, they migrate to the bone marrow, where they settle and develop into new blood cells – a vital process known as engraftment.

The engraftment process signals the beginning of the bone marrow recovery period. It takes 10 – 14 days for adequate numbers of newly formed blood cells to be produced from the engrafted stem cells. Until this occurs the individual remains **immunocompromised**. This is the high-risk period for developing infection. During this time, regular blood tests will monitor the **blood counts**.

Very rarely, stem cells do not engraft well leading to prolonged low blood counts. Injections of growth factors (G-CSF) and in some cases a 'top-up' of stem cells may be given to help the blood counts recover if they are available. There are a number of reasons for stem cells may not engraft well, including certain viral infections and medication side effects.

Supportive care during recovery

The period of time waiting for the stem cells to engraft and start producing new blood cells is, for many people, the toughest part of the transplant process.

Until the new blood cells are produced and enter the bloodstream, there is a high risk of infection, anaemia and bleeding. Special precautions and supportive measures are necessary during this time. The most common precautions are described below.

Protection against infection

Until the white cell count rises, risk of infection is high. Infections that may not normally pose much bother can become very serious if not managed properly. Several precautions are taken to help reduce this risk including being observed and monitored very closely during this time to check for signs of infection.

The most common source of infection originates from the individual's own body, not from the environment or another individual. Commonly the bacteria in the gut can be a source of infection when the natural protective barriers are impaired as a result of the high-dose therapy. These 'opportunistic' infections occur at this time because the immune system is significantly weakened. It is recommended to bath or shower daily and wear clean clothes. Ensure towels and bedding are changed frequently.

Most transplant centres will recommend a '**neutropenic** diet' designed to minimise potential exposure to bacteria and other harmful organisms in food. This special diet will be discussed prior to the HDT-AuSCT process, but may include avoiding soft cheeses, raw meats, uncooked foods, blemished or unwashed produce etc. Most hospitals will have a booklet or fact sheet on the neutropenic diet and a dietitian to speak with.

To minimise mouth infections related to mucositis, regular mouth care is necessary. Clean teeth with a soft toothbrush after meals and use a mouthwash that does not contain alcohol as these can dry out the mouth. The transplant team will recommend the right product to use.

Antibiotics and other drugs may be prescribed to help prevent bacterial, fungal and viral infections, these are usually given in tablet form. It is quite common

to develop an infection at some point when the white cell count is low and a raised temperature is a typical sign of infection. In the case of an infection, intravenous antibiotics will need to be commenced promptly.

> If the temperature rises to 38°C and above, a trip to the nearest emergency department as quickly as possible is necessary for assessment and treatment. An infection can be very serious, sometimes life-threatening if not managed promptly.

It is important to inform family and friend of the infection risks. Visitors are allowed and encouraged during the transplant but only if they are well. All visitors will be asked to wash their hands prior to entry and to stay away if feeling unwell.

Protection against anaemia and bleeding

The high-dose therapy can also cause a period of a low red blood cell count (anaemia) and a low platelet count which may cause bleeding.

To reduce the risk of bleeding when platelets are low, take extra care when walking to avoid falls, use a soft toothbrush to protect the gums and avoid shaving. An electric razor can be used if desired. A tendency to bruise easily may also be noticed.

If experiencing any bleeding or symptoms of anaemia (fatigue, shortness of breath), a blood transfusion can provide relief. To help minimise reactions to blood transfusions when the immune system is low, the donated red blood cells and platelets are treated to destroy any white blood cells. This process is called irradiation. Only irradiated blood products will be used during and after a transplant.

General measures

Bring something into hospital to keep the mind occupied such as books, magazines and tablet devices – usually there is a TV and phone available at the bedside. It is common to feel a lack of concentration during this time, so it

is a good idea to do things that are relaxing and that can be picked up and put down easily. Exercise bikes may be available in some hospitals and using a bike or doing regular gentle exercises can help reduce the loss of muscle tone that can occur during this period of reduced activity.

Continuing recovery and follow up care

In order to begin the next phase of recovery, blood counts will have returned to a safe level, there will be no signs of infection and there will be no issues taking oral medications, eating and drinking. However, it will be some time until everything is fully recovered.

If the transplant was received as an inpatient in hospital, it is normal to have a mixture of emotions when getting discharged. The excitement of going home and relief that the transplant is over may be mixed with anxiety about coping at home and wondering how successful the treatment has been. Some people feel vulnerable and nervous about managing without nurses and doctors at hand.

Checklist before discharge:

- Know the signs and symptoms to look out for and how to report them
- Have a clear understanding of necessary precautions to reduce the risk of developing an infection
- Obtain a list of contact numbers for the transplant centre
- Gain advice about nutrition and diet
- Understand take home medications and know how to take them
- Receive information about appointments for the outpatient clinic, outpatient blood tests and any other investigations
- Ensure there are arrangements for central line care (e.g.Hickmans), or advice on managing it at home

The full recovery period may last for months but can vary greatly, depending on the individual. It can be a challenging time for people and their families. Attempts to get back to normal life are balanced against some possible physical and emotional difficulties that commonly occur during this time. The following sections provide some insight on what to expect to help manage the recovery period at home.

Treatment follow-up and appointments

For the vast majority of people, there is a gradual recovery following the transplant. Regular follow-up appointments as an outpatient at the transplant centre will be necessary in the first month after the transplant. These appointments may be once or twice a week to begin with. Frequency of appointments will lessen as the recovery continues. If distance from the hospital or travel is a concern it may be possible to get transport support or help towards travel costs. Speak with the transplant team for more information. It may also be possible to replace some trips to the hospital with the use of Telehealth (videoconferencing) at the GP clinic.

Blood counts will be monitored to ensure they continue to rise. Sometimes blood counts recover more slowly than expected and blood or platelet transfusion support may be needed. After a HDT-AuSCT only irradiated blood products should be used, as described earlier.

Medications to prevent bacterial, viral and fungal infections may continue for a period of 6-12 months after transplant. Other drugs that may be needed are anti-nausea drugs, supplements of electrolytes (such as potassium and magnesium) and drugs that protect the stomach. Report any new concerns to the doctor or nurses, they are there to help.

When the transplant team are satisfied that an adequate recovery has been achieved, care will likely be transferred back to the primary healthcare team for ongoing monitoring. Bisphosphonate (bone strengthening) treatment, normally stopped during the HDT-AuSCT process, is usually resumed at this time unless otherwise indicated by the specialist.

Living well at home

As mentioned before, it can take many months after the HDT-AuSCT for the immune system to fully recover. During this time, precautions may need to be taken at home and when out in the community, to reduce the risk of infection.

Diet and nutrition

The transplant team will advise when it is safe to eat ‘normally’ again, this coincides with white blood cell count recovery and an improved immune system. However, it is a good idea to continue to practice good common sense

with food handling, preparation and storage. For example, wash hands before eating and maintain a clean kitchen. Food should be cooked properly and eaten by the 'use by' dates. Buy from reputable stores and avoid foods that may have been left out for some time.

Personal hygiene

Continue to have a daily bath or shower, wash hands before eating, preparing food and after going to the toilet. Use a clean towel every day and allow the towel to dry before using it again. If a central line in still in place, make sure it is managed as instructed by the nurses. Continue to maintain oral hygiene and use any mouthwashes that are prescribed. It may take several weeks before the sense of taste returns to normal.

Vaccinations

After HDT-AuSCT, immunity gained from childhood vaccines is compromised. Therefore, it is necessary to be re-vaccinated against preventable diseases. There are two types of vaccines, 'live' or 'active' and 'inactive'. The re-vaccination schedule will be initiated around 6 months after transplant, starting with inactive vaccines such as whooping cough and tetanus. Two doses of the flu vaccine given 28 days apart are recommended for adequate protection from the flu in the first year after transplant.

The specialist will wait until such time as the immune system has fully recovered to give live vaccines such as measles, mumps and rubella. This is because, until then there is a risk the vaccine will not work and the person may become unwell with the illness being vaccinated against.

Shingles

A small percentage of people will develop shingles infection. This usually occurs 6 to 24 months after transplant. Shingles is an infection that results from the re-awakening of the chickenpox virus which lays asleep along a nerve ending. It can begin as a painful or itchy sensation followed by the appearance of a rash. Shingles can affect any part of the body but is often found on the chest or back. It can be treated with antiviral drugs which should be started as soon as possible following a shingles diagnosis. It is important to see the doctor as soon as symptoms begin. Pain and fatigue from shingles can sometimes go on

for quite a while which can be difficult to cope with after going through so much treatment.

Socialising and getting out and about

In the first few weeks following HDT-AuSCT it is advised to avoid crowded public areas at peak times for example buses, trains or cinemas to reduce the risk of infection. Visiting family and friends can be a good way to start getting out and about, so long as they are free from colds, flu or other infectious illnesses. Dust from building work or renovations may carry a fungus called 'aspergillus'. It is wise therefore to suspend or delay any building work planned for the house and avoid areas of construction until approved by the doctor.

Pets and gardening

Pets should never be allowed on the table or in areas where food is prepared. Do not handle cat litter trays or dog faeces, as they can be a source of infection. When gardening, wear gloves as soil can harbour organisms that could be harmful. Any cuts obtained from gardening must be cleaned thoroughly and dressed if necessary, please check vigilantly for signs of infection. If the cut does become infected, antibiotic treatment is likely to be required. Avoid working with organic manure and potting mixture for at least 3 months after the transplant and after this period wear a mask.

Coping with fatigue

Fatigue can be a major issue during the recovery period and this may continue for some time. It is a good idea to take it easy initially, get plenty of rest and participate in gentle exercises. Transplant related fatigue is not relieved by sleep or rest and presents both physically and mentally. Some people find it difficult to concentrate even on simple things such as watching television or holding a conversation. It is important to set realistic goals and manage expectations. Prolonged fatigue can sometimes be due to factors other than the impact of the HDT-AuSCT. There may be ways of improving energy levels. Seek advice on lifestyle changes such as diet and exercise from the transplant team.

Exercise

Keeping active is very important post-transplant, despite fatigue, to help prevent complications and speed up physical and mental recovery. It is normal for fitness, endurance and muscle strength to decline during the transplant period. Therefore, it is important to start slowly and gradually build up physical activity. If an exercise physiologist or physiotherapist has been involved in the pre-transplant preparation, arranging a follow-up appointment can be beneficial to assist with a recovery plan

Skin care

The skin can feel very dry following high-dose therapy. Moisturise skin regularly with a moisturising cream such as sorbolene. Bathing with soap can cause further dryness, speak with the transplant nurse about a more suitable product.

It is important to use adequate skin protection and avoid prolonged exposure to the sun, skin will be more sensitive to sun damage after high-dose therapy. Wear a hat, long sleeves and sunscreen to protect exposed skin. Alternatively go out in the early morning or later in the day when UV levels are lowest.

Work, driving and holidays

There are no set rules on when to return to work following a transplant – whether work be full time, part time or looking after the home and/or children. As a guide however, most people need at least three months before they are ready. It may be possible to go back sooner depending on the type of work or if the workplace is flexible. Again, talk to the transplant team about when it is advisable to return to work, or about any risks there may be within the workplace.

It is usually safe to start driving once recovered, but again, do check with the doctor.

It is important to stay reasonably close to the transplant centre when recovering from a transplant. Therefore, it is not advisable to plan a holiday outside Australia for six months after HDT-AuSCT. Always inform the doctor about any travel plans prior to booking a trip and discuss issues such as safety to fly and vaccinations. It is recommended to see a travel health doctor at least 4 weeks before travel for further advice. There may be additional vaccines needed depending on the destination.

Emotional support

Treatment with HDT-AuSCT from start to finish can put an enormous physical, emotional and financial strain on individuals and their families. For most people there is a huge sense of relief when it is over. Adjusting to life after having HDT-AuSCT, however, is not always easy and it is not unusual to feel quite low during parts of the recovery.

It is important to regain some 'normality', but it may not be possible to return to everything at full capacity initially. It will be necessary to modify some activities and focus on things that are achievable until more strength is gained. Some people see this period as an opportunity to make some beneficial lifestyle changes and it can be a positive turning point in their life.

For others, the changes are not so easy to come to terms with and it is not uncommon for individuals and family members to have feelings of anger, resentment, depression and anxiety over the unknown future. It can feel like there is a lack of control and a sense of grief about the fact that some things will not be the same as before. These feelings usually come at a time when the body has recovered well from the transplant and support from the health care team is decreasing. All these feelings are a completely normal part of the recovery process. Speak with the GP or treating team for advice on getting through this period. Alternatively, speak in confidence with a myeloma support nurse via the contact details below.

Support groups and telephone support

Support groups, either in person or via the telephone, are a great place to share transplant experiences with others who understand. It is easy to feel isolated once discharged and some people find peer support helpful.

Find the closest Information and Support Group via our website
www.myeloma.org.au or call our
toll-free Telephone Support Line – 1800 MYELOMA (693 566)
Monday – Friday 9am – 5pm AEST
There is also a Telephone Support Group available co-facilitated by
Cancer Council NSW and **Myeloma Australia**
– for more information call 1300 755 632

Assessing response to the transplant

The aim of all myeloma treatment is to destroy the myeloma cells in order to control the symptoms and complications they give rise to.

To assess response, several regular tests will be carried out. These tests may vary slightly but will generally include regular blood tests, a bone marrow biopsy usually around three months (100 days) post-transplant and occasional scans.

In general terms, the doctor will use the results of these tests to measure the response to HDT-AuSCT according to the criteria outlined in the table below.

Type of Response	Paraprotein	% Plasma Cells in the Bone Marrow	Skeletal Disease (on scan)
Stringent complete response (sCR)	No longer detectable in the blood and/ or urine; negative **immunofixation** test; normal free light chain ratio	<5%; no myeloma cells present	Stable
Complete response (CR)	No longer detectable in the blood +/- urine; negative immunofixation test	<5%	Stable
Very good partial response (VGPR)	No longer detectable in the blood +/- urine, but positive immunofixation test, or 90% decrease	N/A	Stable

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Partial response (PR)	≥50% decrease	N/A	Stable
Minimal response (MR)	25%-49% decrease	N/A	Stable
Stable disease (SD)	Not meeting the definition of minimal response or progressive disease		
Progressive disease (PD)	>25% increase	>25% increase	New bone lesions or increase in size of existing lesions

Tandem transplants

A single HDT-AuSCT is currently the gold standard of initial treatment for younger and/or fitter people with myeloma. However, further transplant approaches which aim to prolong the response to the first HDT-AuSCT may be recommended.

Having a 'tandem transplant' means having a second HDT-AuSCT shortly after the initial HDT-AuSCT (usually within six months of each other).

There is some evidence from clinical trials to suggest that tandem HDT-AuSCT may improve response rates for some people, such as those with **high-risk myeloma**. An alternative strategy is to collect enough stem cells to carry out two HDT-AuSCT but to delay the second HDT-AuSCT until the myeloma comes back.

Allogeneic stem cell transplant

An allogeneic transplant is a stem cell transplant using the stem cells from a matched donor, this may be a brother or sister or unrelated. Allogeneic transplants aim to use the immune system of the donor to help fight against the myeloma. This represents the main advantage of allogeneic SCTs compared to autologous SCTs – the donated stem cells have the potential to attack myeloma cells and prevent relapse. However, the risk of this procedure is that the donor's immune cells also attack the recipient's healthy cells, leading to **graft-versus-host disease**, which can be serious and potentially life-threatening.

Allogeneic transplants are not a part of routine treatment in myeloma and investigations are still ongoing to determine their benefit. An allogeneic transplant may be considered at the transplant specialist's discretion for a small number of people with 'high risk' myeloma if a matched donor is available.

In recent years this procedure has been refined and a non-myeloablative or less intensive allogeneic transplant is performed. This involves lower doses of chemotherapy which reduces the serious risks associated with the 'full intensity'.

Consolidation and maintenance treatment

Prolonging the period of response following HDT-AuSCT may also be achieved through further anti-myeloma treatment.

The two types of treatment are:

Consolidation treatment – a standard dose of anti-myeloma treatment that is given over several months, the aim of which is to further reduce any residual myeloma

Maintenance treatment – consists of a low dose of anti-myeloma treatment given over a period of many months or years with the aim of sustaining or enhancing the response already achieved.

There is evidence that certain groups may benefit from these treatment approaches, but any benefit must be balanced against side effects that may occur. In Australia, these treatments may be accessible through the Pharmaceutical Benefits Scheme or clinical trial. Ask the treating team if consolidation or maintenance treatment is an appropriate addition to the plan.

Treatment for myeloma that has relapsed after HDT-AuSCT

Despite the potential for an excellent response, like all myeloma treatment, HDT-AuSCT is not a cure and relapse almost always occurs. This is understandably a difficult time especially if the relapse occurs sooner than expected.

Why is HDT-AuSCT not a cure for myeloma?

While very effective, unfortunately, high-dose therapy is not able to destroy all the myeloma cells in the bone marrow. It can greatly reduce the amount of myeloma cells, but those that are resistant to the treatment will survive. Over time, these residual cells multiply and grow to numbers large enough to cause relapse.

When relapse occurs, the specialist will take into consideration many factors when recommending the next type of treatment. If it has been some time since the last treatment, there may be new options available. They will consider the length of time since last treatment, how well the myeloma responded to the previous treatment and the overall health of the individual.

Standard treatment with anti-myeloma drugs

There are a number of different types of treatment options available following relapse. Each new type of treatment attacks the myeloma in a different way. Therefore, if one type of drug isn't working as well as hoped, it is possible that another drug will. Each course of treatment will usually include a combination of anti-myeloma medication and a steroid with the possible addition of a chemotherapy agent.

A second transplant

Having a second HDT-AuSCT at the time of relapse is different to a tandem transplant, where two transplants are planned at the outset and occur usually within 6 months of each other. A second HDT-AuSCT may be offered if relapse occurs and there are enough stem cells stored that can be used.

The option of a second HDT-AuSCT will depend on the timing of the relapse, age, previous treatment and general health/fitness to be able to undergo the procedure again. Generally, a second HDT-AuSCT will only be offered to people who achieved at least 18 – 24 months remission or plateau from their first HDT-AuSCT.

Before a second HDT-AuSCT is performed, a course of anti-myeloma treatment is given in order to reduce the amount of the myeloma. This may be the same as the first induction treatment received, or a different combination might be given.

Clinical trials

Novel drugs under investigation in clinical trials may be available at the time of relapse. It is important to understand that not every person is suitable for every new treatment or clinical trial. Ask the doctor if there are any clinical trials available and appropriate.

Long-term and late effects of HDT-AuSCT

Evidence suggests people with myeloma who have received HDT-AuSCT, together with improved treatments and supportive care, are living longer and have a better quality of life.

However, as people are living longer, they are more likely to experience some long-term and late effects associated with HDT-AuSCT and other treatments they have received.

Broadly speaking long-term and late effects are side effects that continue long after transplant or develop later in life as a result of treatment.

Long-term and late effects may:

- be specific to a body organ or system (e.g. lungs, heart, reproductive, bones)
- affect a person's physical and psychological functioning (e.g. fatigue and cognitive problems)
- include an increased risk of other cancers occurring

There are many factors that contribute to the probability of someone experiencing a long-term or late effect. The type of issues and degree of seriousness will vary from person to person. Therefore, it is so important to

maintain regular follow up appointments and report any symptoms to the specialist. It is also important to have a good relationship with the GP and ensure any issues are investigated or referred on to the appropriate specialist. Sometimes it is necessary to have a number of different clinicians helping to manage and monitor long-term and late effects. Some hospitals may have specialist 'late effects' nurses and doctors that can be involved.

Future directions

Over the past two decades, HDT-AuSCT has evolved to become a safe and effective treatment providing newly diagnosed younger and/or fitter people with myeloma the best chance of obtaining a durable remission.

More recently, encouraging responses seen in individuals treated with novel treatment combinations – often including **bortezomib** and/or **lenalidomide** – have led to a growing interest in comparisons between the effectiveness of HDT-AuSCT and the novel drugs.

Various clinical trials have investigated the role of HDT-AuSCT and compared its effectiveness against different combinations of anti-myeloma treatments. The evidence continues to reinforce the important role that HDT-AuSCT has to play in the treatment of myeloma. It therefore remains the gold standard of treatment for younger and/or fitter people with myeloma.

Attention has now turned to finding the best sequence of anti-myeloma treatment combinations that can be used in conjunction with HDT-AuSCT.

Research is also taking place to determine who responds best to HDT-AuSCT. It is hoped that the results of ongoing genetic research will identify features of myeloma that can be used to predict the response to treatments such as HDT-AuSCT.

An increased understanding of how specific groups of people with myeloma may respond to treatment will allow doctors to prescribe a treatment plan suited to an individual's myeloma and may help improve outcomes.

Research is continually taking place to make all types of transplant as safe and effective as possible.

Many advances are also being made in supportive care, such as more effective antibiotics and anti-nausea medication, better fatigue management and multi-disciplinary support.

Multidisciplinary support may include input from health professionals such as dietitians, physiotherapists/exercise physiologists, social workers, psychologists and medical staff from other specialties. This may not only make transplants safer but may also improve quality of life both during and after the procedure.

Questions for the doctor/medical team

- What are the objectives of HDT-AuSCT?
- What exactly does HDT-AuSCT involve?
- How long will the entire process take (from referral to recovery)?
- Will I have to stay in hospital or will I be treated as an outpatient?
- Will I need a central venous line for my stem cell collection?
- Will I need a central venous line for the HDT-AuSCT?
- What are the alternatives to HDT-AuSCT?
- How ill might I feel during and after high-dose therapy?
- What are the potential side effects, how long might they last and are they serious?
- What is the likelihood of experiencing side effects and what can be done to treat them?
- Why is HDT-AuSCT being recommended?
- In the event of relapse, what might the options be?
- Which doctor will be responsible for my care whilst I am having HDT-AuSCT?
- Which nurse can I contact to ask questions about HDT-AuSCT?
- How can I best prepare myself for HDT-AuSCT?

Medical terms explained

Anaemia: A decrease in the normal number of red blood cells, or the haemoglobin that they contain, causing shortness of breath, weakness and tiredness.

Anaesthetic: A type of drug used to temporarily reduce or take away sensation so that otherwise painful procedures or surgery can be performed. A general anaesthetic makes the person unconscious and therefore unaware of what is happening. A local anaesthetic numbs the part of the body that would otherwise feel pain.

Antibiotics: Drugs used to prevent or treat an infection caused by bacteria.

Antivirals: Drugs used to prevent or treat an infection caused by a virus.

Antibodies (immunoglobulins): Also known as immunoglobulins, antibodies are proteins found in the blood which are produced by cells of the immune system, called plasma cells. Their function is to bind to substances in the body that are recognised as foreign such as bacteria and viruses. They enable other cells of the immune system to destroy and remove them, thereby helping to fight infection.

Anticoagulant: Drugs used to prevent blood clots from forming.

Apheresis: A procedure in which stem cells are collected from the blood using a machine that separates them out and returns the remainder of the blood components to the body.

Autologous stem cell transplantation: A procedure in which a person's own stem cells are collected, stored and then given back following high-dose chemotherapy.

Bisphosphonate: Drugs used to protect bone from being broken down. Commonly used bisphosphonates include Bonefos® (sodium clodronate), Aredia® (pamidronate) and Zometa® (zoledronic acid).

Blood count: The number of red blood cells, white blood cells and platelets in a sample of blood.

Bone marrow: The soft, spongy tissue in the centre of bones that produces white blood cells, red blood cells and platelets.

Bortezomib (Velcade®): A type of drug called a proteasome inhibitor

CD34+ blood test: A test which measures the amount of stem cells in the blood.

Central line: A catheter (tube) that is inserted or tunnelled under the skin in the chest into a large vein just above the heart. It can be kept in for several months and is used to administer treatments, like chemotherapy, and to take blood samples.

Chemotherapy: Treatment with potent drugs intended to destroy cancer cells. Chemotherapy drugs can be injected into a vein (intravenous or IV) or swallowed as tablets (orally).

Consolidation treatment: Treatment given over a short period of time after the main standard dose of treatment has finished. The aim is to prolong the period of response.

Cyclophosphamide: A type of chemotherapy drug which is given orally or intravenously.

Dexamethasone: A type of drug called a steroid. Often given alongside other drugs in the treatment of myeloma.

Dimethyl sulphoxide (DMSO): A chemical used to preserve and store collected stem cells.

DNA: Stands for deoxyribonucleic acid. It is the hereditary material in humans and almost all other organisms. DNA is in every cell of the body and directs their actions.

Engraftment: The process by which transplanted stem cells travel to the recipient's bone marrow, where they begin to grow and develop into new blood cells. During this time the number of red blood cells, white blood cells and platelets in the blood may be lower than normal.

Free light chain: Part of an antibody that circulates freely in the blood.

Graft-versus-host disease (GVHD): A complication that can occur after an allogeneic stem cell transplant in which the newly transplanted donor cells attack the recipient's own tissue.

Granulocyte-colony stimulating factor (G-CSF): A type of drug called a growth factor which is used to stimulate the growth of stem cells before collection.

Growth factor: A protein produced by the body that stimulates the development and growth of cells. Growth factors can also be made synthetically and given as a treatment in some circumstances.

Haematopoietic stem cell: an immature cell found in the bone marrow that can develop into all types of blood cells, including white blood cells, red blood cells, and platelets.

High-risk myeloma: a more active or more difficult to treat myeloma, often associated with certain genetic abnormalities.

Hypercalcaemia: A higher than normal level of calcium in the blood, which may cause loss of appetite, nausea, thirst, fatigue, muscle weakness, restlessness and confusion. Often associated with reduced kidney function since calcium can be toxic to the kidneys.

Immune system: The complex group of cells and organs that protect the body against infection and disease.

Immunocompromised: The term used to describe a person whose immune system is impaired and unable to fight infection or disease as normal.

Immunofixation: A technique used to identify the type of abnormal protein in the blood

Immunoglobulins (antibodies): Also known as antibodies, immunoglobulins are proteins found in the blood which are produced by cells of the immune system, called plasma cells. Their function is to bind to substances in the body that are recognised as foreign such as bacteria and viruses. They enable other cells of the immune system to destroy and remove them, thereby helping to fight infection.

Induction treatment: The initial standard-dose chemotherapy that is received as part of the stem cell transplant procedure. Induction treatment aims to reduce the amount of myeloma in the bone marrow before the stem cells are collected.

Intravenously (IV): Into a vein.

Lenalidomide (Revlimid®): A type of immunomodulatory drug.

Light chain myeloma: A type of myeloma where only the light chain portion of the immunoglobulin is produced. It occurs in approximately 20% of people with myeloma.

Low intensity allogeneic transplant: A type of allogeneic transplant that uses lower doses of chemotherapy than the standard allogeneic transplant.

Maintenance treatment: Treatment given over an extended period of time, often at a lower dose, after the main standard dose of treatment has finished. Maintenance treatment aims to reduce the risk of disease progression.

Malignant: Cancerous cells which have the ability to invade and destroy tissue.

Melphalan: A type of chemotherapy drug.

Mobilisation: The process of stimulating the bone marrow with medications to release stem cells into the blood stream to be collected.

Mozobil® (plerixafor): A drug used in combination with granulocyte-colony stimulating factor (G-CSF) to help move stem cells from the bone marrow into the blood for collection prior to transplantation.

Mucositis: Pain and inflammation of the lining of the mouth and/or gastro-intestinal tract.

Neutropenic: A low number of neutrophils (type of white cell) in the blood, which can lead to an increased risk of infection. Can be caused by the myeloma itself or as a side effect of treatment, particularly chemotherapy.

Non-secretory myeloma: A type of myeloma in which there is no detectable paraprotein or light chains in either the blood or urine.

Paraprotein: An abnormal antibody (immunoglobulin) produced in myeloma. Measurements of paraprotein in the blood can be used to diagnose and monitor the disease.

Pharmaceutical Benefits Scheme: A program of the Australian Government that provides subsidised prescription drugs to residents.

Plasma cells: Specialised white blood cells that produce antibodies (immuno-globulins) to fight infection.

Plateau: A period of time when the myeloma, and the paraprotein level, is relatively stable.

Platelets: Small blood cells which are involved in blood clotting.

Plerixafor (Mozobil®): A drug used in combination with granulocyte-colony stimulating factor (G-CSF) to help move stem cells from the bone marrow into the blood for collection prior to transplantation.

Quality of life: A term that refers to a person's level of comfort, enjoyment, and ability to pursue daily activities. It is a measure of an overall sense of wellbeing.

Red blood cells: Blood cells which transport oxygen around the body.

Relapse: The point where disease returns or becomes more active after a period of remission or plateau (often referred to as stable disease).

Remission: The period following treatment when myeloma cells and paraprotein are no longer detectable, and there are no clinical symptoms of myeloma.

Revlimid® (lenalidomide): A type of immunomodulatory drug.

Side effects: The undesired effects caused by a drug or treatment, for example fatigue or nausea.

Stem cells: The cells from which all blood cells develop. Stem cells give rise to red blood cells, white blood cells and platelets. Stem cells are normally located in the bone marrow and can be harvested from the blood for transplant.

Velcade® (bortezomib): A type of drug called a proteasome inhibitor.

White blood cells: Blood cells involved in the body's immune system, which help to fight infection.

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