



UNDERSTANDING MYELOYDYSPLASTIC SYNDROMES (MDS)

A guide for patients and
families



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INTRODUCTION

This booklet has been written to help you and your family understand more about myelodysplasia or the myelodysplastic syndromes (MDS).

Some of you may be feeling anxious or a little overwhelmed if you or someone you care for has been diagnosed with MDS. This is understandable. Perhaps you have already started treatment or you are discussing different treatment options with your doctor and your family. Whatever point you are at, we hope that the information contained in this booklet is useful in answering some of your questions. It may also raise others, which you should bring up with your doctor or specialist nurse.

You may not feel like reading this booklet from cover to cover. It might be more useful to look at the list of contents and read the parts that you think will be of most use at a particular point in time.

We have used some medical words and terms which you may not be familiar with. These are highlighted in *italics*. Their meaning is explained in the booklet or in the glossary of terms at the back of the booklet.

In some parts of the booklet we have provided additional information you may wish to read on selected topics. This information is presented in the shaded boxes. Some of you may require more information than is contained in this booklet. We have included some internet addresses that you might find useful. In addition, many of you will receive written information from the doctors and nurses at your treating hospital.

It is not the intention of this booklet to recommend any particular form of treatment to you. You need to discuss your particular circumstances at all times with your treating doctor.

Finally, we hope that you find this information useful and we would appreciate any feedback from you so that we can continue to serve you and your families better in the future.

THE LEUKAEMIA FOUNDATION

The Leukaemia Foundation is the only national not-for-profit organisation dedicated to the care and cure of patients and families living with leukaemias, lymphomas, myeloma and related blood disorders. Since 1975, the Foundation has been committed to improving survival for patients and providing much needed support. It does not receive direct ongoing government funding, relying instead on the continued and generous support of individuals and corporate supporters to develop and expand its services.

The Foundation provides a range of **free** support services to patients and their carers, family and friends. This support may be offered over the telephone, face to face at home, hospital or at the Foundation's accommodation centres, depending on the geographical and individual needs. Support may include providing information, patient education seminars and programs that provide a forum for peer support and consumer representation, practical assistance, accommodation, transport and emotional support/counselling.

The Leukaemia Foundation also funds leading research into better treatments and cures for leukaemias, lymphomas, myeloma and related blood disorders. Through its National Research Program, the Foundation has established the PwC Foundation Leukaemia and Lymphoma Tissue Bank and the Leukaemia Foundation Research Laboratory at the Queensland Institute for Medical Research.

In addition, the Foundation funds research grants, scholarships and fellowships for talented researchers and rural health professionals.

SUPPORT SERVICES



Foundation staff provide patients and their families with information and support at the Foundation's accommodation centres across Australia.

The Leukaemia Foundation has an extensive team of cancer nurses and allied health professionals working across the country. They offer personalised support and care to you and your family right throughout the journey – from diagnosis and treatment to recovery.

The support services provided include:

Information, Education and Support

Support is provided by telephone and through visits to hospitals, office or home, referral to specialist services and practical assistance.

The Foundation also offers you and your family free disease-specific or general education programs and workshops on subjects such as Taking Control, Caring for the Carer, survivorship issues and grief. We also coordinate patient and family support groups, and have established an on-line support group at www.talkbloodcancer.com

The Leukaemia Foundation has a range of booklets such as this one that are available free of charge. These can be ordered via the form at the back of this booklet or downloaded from the website. Translated versions (in languages other than English) of some booklets are also available from our website.

Accommodation

Accommodation and other housing arrangements close to hospitals are available if you have to relocate for treatment. The self contained modern units and houses are fully furnished, providing a 'home away from home' for you and your family.

Transport

Courtesy cars and other forms of transport support are available in many areas to transport patients and carers to and from hospital for treatment.

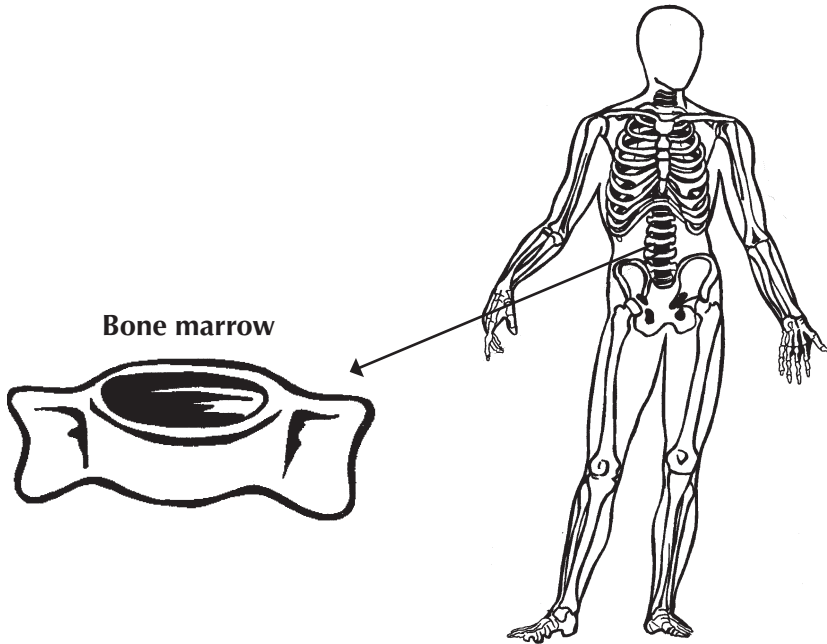
Practical Assistance

Leukaemias, lymphomas and myeloma can affect you and your family's normal way of life and there may be practical things the Foundation can do to help. By working with you, your doctors and social workers, the Foundation can find out the best way to care for you and your family. In special circumstances, the Leukaemia Foundation provides financial support for patients who are experiencing financial difficulties.

Contacting us

The Leukaemia Foundation provides services and support in every Australian state and territory. Every person's experience of living with these cancers and disorders is different. Living with leukaemias, lymphomas or myeloma is not easy, but you don't have to do it alone. Please call **1800 620 420** (freecall) to speak to a local support service staff member or to find out more about the services offered by the Foundation. Alternatively, contact us via email by sending a message to info@leukaemia.org.au or visit www.leukaemia.org.au

BONE MARROW, STEM CELLS AND BLOOD CELL FORMATION



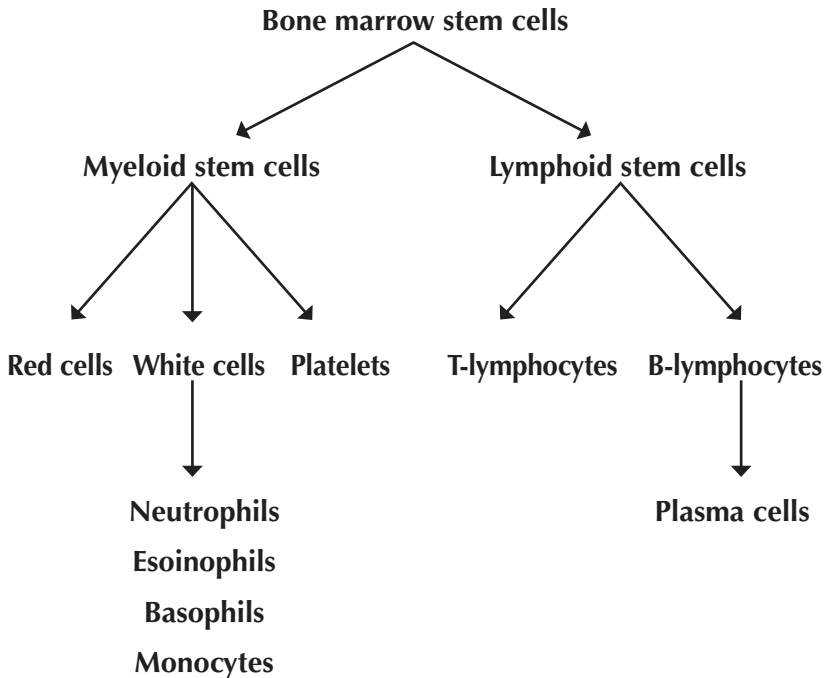
Bone marrow

Bone marrow is the spongy tissue that fills the cavities inside your bones. Most of your blood cells are made in your bone marrow. The process by which blood cells are made is called *haemopoiesis*. In infants, haemopoiesis takes place at the centre of all bones. In adults, it is limited to the hips, ribs, spine, skull and breastbone (*sternum*). Some of you may have had a *bone marrow* biopsy taken from the bone at the back of your hip (the *iliac crest*) or the breastbone.

You might like to think of the bone marrow as the blood cell factory. The main workers at the factory are the blood *stem cells*. They are relatively small in number but are able, when stimulated, not only to divide to replicate themselves, but to grow and divide into slightly more mature stem cells called *myeloid* stem cells and *lymphoid* stem cells. These cells multiply and mature further to produce all the circulating blood cells. There are three main types of blood cells: *red cells*, *white cells* and *platelets*.

Myeloid ('my-loid') stem cells develop into red cells, white cells (neutrophils, eosinophils, basophils and monocytes) and platelets.

Lymphoid ('lim-foid') stem cells develop into two other types of white cells called T-lymphocytes and B-lymphocytes.



Growth factors and cytokines

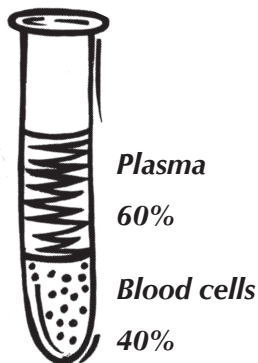
All normal blood cells have a limited survival in circulation and need to be replaced on a continual basis. This means that the bone marrow remains a very active tissue throughout your life. Natural chemicals in your blood called *growth factors* or *cytokines* control the process of blood cell formation. Different growth factors stimulate the blood stem cells in the bone marrow to produce different types of blood cells.

These days some growth factors can be made in the laboratory (synthesised) and are available for use in people with blood disorders. For example, *granulocyte-colony stimulating factor* (G-CSF) stimulates the production of white cells called neutrophils while *erythropoietin* (EPO) stimulates the production of red cells. Unfortunately, drugs to stimulate platelet production have been less successful, but research is continuing in this area.

BLOOD

Red cells and haemoglobin

Red cells contain haemoglobin (Hb), which gives the blood its red colour and transports oxygen from the lungs to all parts of the body. Haemoglobin also carries carbon dioxide to the lungs where it can be breathed out.



The normal haemoglobin range for a man is between 130 and 170 (130 - 170 g/L)

The normal haemoglobin range for a woman is between 120 and 160 (120 - 160 g/L)

Red cells are by far the most numerous blood cell and the proportion of the blood that is occupied by blood cells is called the haematocrit. A low *haematocrit* suggests that the number of red cells in the blood is lower than normal.

The normal range of the haematocrit in a man is between 40% and 52%

The normal range of the haematocrit in a woman is between 36% and 46%

Anaemia

Anaemia is a condition caused by a reduction in the number of red cells, which in turn results in a low haemoglobin. Measuring either the haematocrit or the haemoglobin will provide information regarding the degree of anaemia.

If you are anaemic you will feel run down and weak. You may be pale and short of breath or you may tire easily because your body is not getting enough oxygen. In this situation a red cell transfusion may be given to restore the red cell numbers and therefore the haemoglobin to more normal levels.

White cells

White cells fight infection. There are different types of white cells that fight infection together and in different ways.

<i>Neutrophils</i>	<i>kill bacteria and fungi</i>
<i>Eosinophils</i>	<i>kill parasites</i>
<i>Basophils</i>	<i>work with neutrophils to fight infection</i>
<i>Monocytes</i>	<i>work with neutrophils and lymphocytes to fight infection; they also help with antibody production and act as scavengers to remove dead tissue</i>
<i>T-lymphocytes</i>	<i>kill viruses, parasites and cancer cells; produce cytokines</i>
<i>B-lymphocytes</i>	<i>make antibodies which target microorganisms</i>

When your white cell count drops below normal you are at risk of infection.

The normal adult white cell count varies between 3.7 and 11 ($3.7 - 11 \times 10^9/L$)

Neutropenia

Neutropenia is the term given to describe a lower than normal neutrophil count. If you have a neutrophil count of less than 1 ($1 \times 10^9/L$) you are considered to be seriously neutropenic and at risk of developing frequent and sometimes severe infections.

The normal adult neutrophil count varies between 2.0 and 7.5 ($2.0 - 7.5 \times 10^9/L$)

Platelets

Platelets are disc-shaped cellular fragments that circulate in the blood and play an important role in clot formation. They help to prevent bleeding. If a blood vessel is damaged (e.g. by a cut) the platelets gather at the site of injury, stick together and form a plug to help stop the bleeding.

The normal adult platelet count varies between 150 and 400 ($150 - 400 \times 10^9/L$)

Thrombocytopenia

Thrombocytopenia is the term used to describe a reduction in the platelet count to below normal. If your platelet count drops below 20 ($20 \times 10^9/L$) you are at risk of bleeding and tend to bruise easily. Platelet transfusions are sometimes given to bring the platelet count back to a safe level.

The normal blood counts provided here may differ slightly from the ones used at your treatment center. You can ask for a copy of your blood results, which should include the normal values for each blood type.

WHAT IS MDS?

Myelodysplastic syndromes (MDS) are a group of diseases which *all* affect, to a greater or lesser extent, the production of normal blood cells in the bone marrow.

In MDS, abnormal bone marrow stem cells (called *blast* cells) produce increased numbers of immature blood cells. These cells do not grow properly and often die prematurely. This results in lower numbers of mature red blood cells, white blood cells and platelets being produced. The blood cells that do survive are often of poor quality, are abnormal in shape (*dysplastic*) and unable to function properly. The release of these abnormal cells from the bone marrow into the blood stream is also defective. This means that people with MDS often have a very active bone marrow but a low number of circulating blood cells. Without enough red blood cells, white blood cells and platelets you can become fatigued, more susceptible to infections, and to bleeding and bruising more easily.

In approximately 15 per cent of cases, people with MDS have very low numbers of cells in their bone marrow. This is referred to as '*hypoplastic myelodysplasia*'.

There are different types of MDS and the disease can vary in its severity and the degree to which normal blood cell production is affected. People with mild disease are often found to simply be anaemic, or they might have a lower than normal white blood cell or platelet count, but in many cases they have few, if any, troubling symptoms from their disease. In more severe cases, the lack of circulating blood cells is more pronounced, causing more symptoms.

Some cases of MDS, approximately 30 per cent overall, have the potential to progress to acute myeloid leukaemia, and MDS is therefore a pre-leukaemic disease.

WHO GETS MDS?

Over 90 per cent of cases occur in people over the age of 60, but MDS can occur at any age, including very occasionally in children.

HOW COMMON IS MDS?

Overall, MDS is relatively uncommon, with an incidence of between four and five per 100,000 of the population but in patients over the age of 60, this increases to anything from 20 to 50 per 100,000. It is therefore one of the more common haematological disorders in the elderly.

It's difficult to be sure of the exact number of people who have MDS. This is because in many cases the disease develops slowly and people don't have any symptoms for a long time. In these cases MDS may go undetected for several years, or it may be picked up accidentally during a routine blood test.



WHAT CAUSES MDS?

We understand how defects arise in the bone marrow stem cells which results in MDS. Why these defects arise in a particular person at a particular time is more difficult to understand, although the effects of ageing on cell growth appears to play a major role. There are also some recognised factors which may put some people at a higher risk of developing MDS. These are called risk factors or predisposing factors and they are described below.

How MDS occurs

MDS occurs as a result of a mutation (or change) in one or more of the genes that control blood cell development. This change or changes results in the abnormal growth of blood stem cells. The original mutation is preserved when the affected stem cell divides and produces a 'clone'; that is a group of identical cells all with the same defect. This is why MDS is sometimes described as a 'clonal blood stem cell disorder'.

Mutations in dividing cells occur all the time, and cells have clever ways of stopping these abnormalities persisting and causing problems within the body. The longer we live, however, the more chance we have of acquiring mutations that manage to escape these safe-guards. That is why MDS, like most leukaemias and other cancers, becomes more common as we get older. This naturally occurring or spontaneously-arising MDS is referred to as primary MDS. It is not contagious; you cannot 'catch' it by being in contact with someone who has the disease and it is not inherited or passed on within families.

Why MDS occurs – some known risk factors:

Any process which damages genes and leads to mutations may have a role in the development of MDS.

Ageing

As we mentioned above, ageing appears to be the most important risk factor for MDS because the risk of developing mutations increases with age.

Chemicals

Exposure to high levels of some environmental chemicals, especially benzene and petroleum products, is associated with the development of MDS.

Cigarette smoking

Exposure to chemicals in tobacco smoke may increase the risk of developing MDS.

Cytotoxic chemotherapy

People previously treated for cancer or other conditions with cytotoxic chemotherapy, are at an increased risk of developing what is called *secondary* or *treatment-related MDS*. This accounts for less than 10 per cent of all cases of MDS. Secondary MDS is associated with different mutations than those that occur in spontaneous MDS, and has a worse prognosis. The time between exposure to the drugs and development of MDS may be over 10 years.

Radiation

Previous radiation therapy, or accidental exposure to high levels of environmental irradiation, is associated with an increased risk of MDS, which in some cases may not be apparent for up to 40 years.

Rare congenital or familial causes

Certain congenital disorders such as Bloom's Syndrome, Down's Syndrome, Fanconi Anaemia and neurofibromatosis have unstable genes and are more at risk of developing mutations that cause MDS or cancer.

WHAT ARE THE SYMPTOMS OF MDS?

Many people in the early stages of MDS have no symptoms at all and it is picked up accidentally during a routine blood test. In other cases people go to see their general practitioner (GP) because they have some troubling symptoms from their disease. The types of symptoms that people experience depend on how severe their disease is and the type of blood cell which is most affected.

The most common symptoms are caused by a lack of red cells, or anaemia:

- persistent tiredness and fatigue
- weakness
- shortness of breath with minimal exercise
- looking pale

Abnormal white cell function, often with low white cell counts, causes:

- recurring infections, especially chest infections
- fevers
- sore mouth due to mouth ulcers

Abnormal platelet function, often with low platelet counts, causes:

- easy bruising
- purpura – a rash of small red dots, seen often on the lower limbs initially, due to small superficial capillary bleeds which are known as petechiae
- tendency to bleeding from the nose and gums

Many people with MDS have a combination of symptoms. This is because the production of all of the blood cell types may be affected by the disease.

WHICH DOCTOR?

If your GP suspects that you might have MDS you may be referred to another specialist doctor called a *haematologist* for further tests and treatment. A haematologist is a doctor who specialises in the care of people with diseases of the blood, bone marrow and immune system.

HOW IS MDS DIAGNOSED?

MDS is diagnosed by examining samples of your blood and bone marrow.

Diagnosis

- *full blood count*
- *bone marrow biopsy*
- *cytogenetic tests*

Full blood count

The first step in diagnosing MDS requires a simple blood test called a *full blood count* (FBC) or *complete blood count* (CBC). A sample of blood is drawn from a vein in your arm, sent to the laboratory where the blood cells are counted, and a blood film is examined under the microscope.

The number of red cells, white cells and platelets, and their size and shape, is noted as these can all be abnormal in MDS. Other blood tests will be done to exclude other causes of anaemia, for example; low iron, folate and vitamin B12 levels and tests of thyroid function to exclude another common cause of fatigue.

Bone marrow biopsy

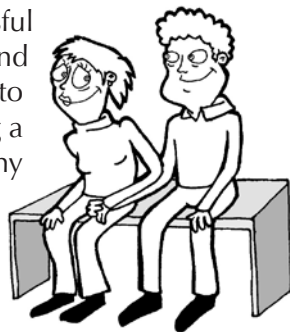
If the results of your blood tests suggest that you might have MDS, a bone marrow biopsy may be required to help confirm the diagnosis. A bone marrow biopsy involves taking a sample of bone marrow, usually from the back of the iliac crest (hip bone) and sending it to the laboratory for examination under the microscope.

The bone marrow biopsy may be done in the haematologist's rooms or clinic under local anaesthesia or, in selected cases, under a short general anaesthetic in a day procedure unit. A mild sedative and a pain-killer is given beforehand and the skin is numbed using a local anaesthetic. This is given as an injection under the skin. The injection takes a minute or two, and you should feel only a mild stinging sensation.

After allowing time for the local anaesthetic to work, a long thin needle is inserted through the skin and outer layer of bone into the bone marrow cavity. A syringe is attached to the end of the needle and a small sample of bone marrow fluid is drawn out - this is called a 'bone marrow aspirate'. Then a slightly larger needle is used to obtain a small core of bone marrow which will provide more detailed information about the structure of the bone marrow and bone - this is known as a 'bone marrow trephine'.

You might feel a bit drowsy afterwards, so you should take a family member or friend along who can take you home. A small dressing or plaster over the biopsy site can be removed the next day. There may be some mild bruising or discomfort, which usually is managed effectively by paracetamol. More serious complications such as bleeding or infection are very rare.

Waiting around for tests can be both stressful and boring. Remember to ask beforehand how long the test will take and what to expect afterwards. You might like to bring a book, some music or a friend for company and support.



The sample of bone marrow is examined in the laboratory to determine the number and type of cells present and the amount of (blood forming) activity taking place there. Although the blood counts are low, in the majority of cases of MDS, the bone marrow is very active (hypercellular) but with increased numbers of immature cells that are abnormal in both shape and size. In addition, blood cell production is usually found to be very inefficient; this is referred to as ineffective haematopoiesis. The percentage of blast cells (the abnormal stem cells) seen in the bone marrow (and sometimes in the blood) gives a guide to the severity of the myelodysplasia.

Cytogenetic tests

Cytogenetic tests provide information about the genetic make-up of the cells, in other words, the structure and number of chromosomes present. Chromosomes are the structures that carry genes. Genes are collections of DNA, our body's blueprint for life.

Certain genetic abnormalities, such as missing or extra chromosomes, are a clue to the underlying mutation in the DNA of the gene. Not all mutations cause obvious changes to the chromosomes, but abnormalities may be detected in over 60 per cent of cases. These may help to confirm the exact type of MDS you have and provide information about the likely course of your disease (prognosis) and the best way to treat it. One of the commonest cytogenetic abnormalities found in MDS is deletion of part of the long arm of chromosome 5 known as deletion 5q del(5q) or 5q minus (5q-). This is illustrated below.

Normal Chromosome 5



Chromosome del(5q)

TYPES OF MDS

The current World Health Organisation's classification system recognises several major subtypes of MDS (see below). These subtypes are distinguished from each other by the degree to which normal blood cell production is affected, the number of blast cells present and the likelihood of transformation to acute myeloid leukemia.

Knowing the exact type of MDS you have is important because it helps the doctor to decide on the best course of treatment to recommend for you.

Major Subtypes of MDS (based on the World Health Organisation (WHO) Classification)

Refractory anaemia (RA)

In this type of MDS, the red blood cells are most affected, causing anaemia. The bone marrow contains less than 5% abnormal blast cells and there are none found in the circulating blood. This type of MDS rarely transforms to leukaemia and treatment is regular observation or blood transfusion only.

Myelodysplastic syndrome with del (5q) chromosome

Red blood cells are affected, causing anaemia. There is usually less than 5% blast cells in the bone marrow and circulating blood. The developing blood cells in the bone marrow display the unique chromosome abnormality del (5q), described above. This is an example of a chromosome abnormality associated with a good prognosis.

Refractory anaemia with ringed sideroblasts (RARS)

Similar to RA, but in this case the red blood cells are unable to process the iron that normally goes into making haemoglobin, the oxygen carrying component of the red cell. Instead the iron granules are deposited in a way that forms a ring around the nucleus of a developing red blood cell. These are called 'ringed sideroblasts', and can be seen under the microscope.

Refractory anaemia with excess blasts – type 1 (RAEB-1)

One or more blood cell types are affected. The bone marrow contains between 5% and 9% blast cells and there are only a small number of blast cells (less than 5%) found in the circulating blood.

Refractory anaemia with excess blasts – type 2 (RAEB-2)

One or more blood cell types are affected, but this time the bone marrow contains between 10% and 19% blast cells and the number also increases (between 5% and 19%) in the circulating blood. The number of red cells, white cells and platelets in the circulating blood is reduced and there is a greater likelihood of transforming to acute myeloid leukemia.

Refractory cytopenia with multilineage dysphasia (RCMD)

Two or more blood cell types are usually affected here but again the bone marrow contains less than 5% blast cells and there are usually none found in the circulating blood.

Refractory cytopenia with multilineage dysphasia and ringed sideroblasts (RCMDRS)

Similar to RCMD, but with ringed sideroblasts found in the red blood cells.

Myelodysplastic/myeloproliferative diseases (MDS/MPD)

These are a group of diseases that have characteristics of both myelodysplastic (abnormal bone marrow cells producing too few blood cells) and myeloproliferative (abnormal bone marrow cells producing too many blood cells) diseases. These include chronic myelomonocytic leukemia (CMML), juvenile myelomonocytic leukemia (JMML), atypical chronic myeloid leukemia (aCML) and myelodysplastic/myeloproliferative diseases unclassifiable (MDS/MPD-U).

Chronic myelomonocytic leukaemia (CMML) is an example of MDS with higher than normal white counts in the blood, mainly due to abnormal monocytes and myelocytes (immature white cells). Chemotherapy drugs given orally, or sometimes by injection, may be used to control the level of the white counts.

PROGNOSIS

A prognosis is an estimate of the likely course of a disease and the chances of curing or controlling it for a given time.

Your doctor is the best person to give you an accurate prognosis regarding your MDS as he or she has the most information to make this assessment.

If you have MDS your overall prognosis depends on many factors and a scoring system known as the International Prognostic Scoring System (IPSS) has been developed to provide an estimate of how your disease might progress.

The International Prognostic Scoring System (IPSS)

*The severity of your disease is determined using the **International Prognostic Scoring System (IPSS)**. This system is used to help predict the risk of your disease transforming to acute myeloid leukaemia and how long you are expected to survive, once you have been diagnosed with MDS.*

Using this system, different factors including your blood cell count at diagnosis, the percentage blast cells seen in your bone marrow and the types of chromosomal abnormalities detected are given individual scores, which are then tallied to give your overall score.

*Depending on your score, you will be regarded as being in one of the following four risk categories: **low, intermediate-1, intermediate-2 or high risk**. Those in the low risk category are less likely to transform to leukaemia and they are expected to survive longer. Those in higher risk categories are at greater risk of developing leukaemia and are generally expected to have a reduced survival time.*

For some people MDS remains stable for many years causing few symptoms. Unfortunately for others, it can progress rapidly, transforming into leukaemia. Signs that the disease is progressing include more frequent infections, spontaneous skin bruises and other bleeds (usually gums and nose) and the need for more frequent blood transfusions.

TREATMENT FOR MDS

The treatment chosen for your disease depends on several factors including the exact type of MDS you have, your age, other prognostic factors, and your general health.

Information gathered from hundreds of other people around the world who have had the same disease helps to guide the doctor in recommending the best treatment for you.

Remember however that no two people are the same. In helping you to make the best treatment decision, your doctor will consider all the information available including the details of your particular situation.

Standard therapy

Standard therapy refers to a type of treatment which is commonly used in particular types and stages of disease. It has been tried and tested (in clinical trials) and has proven to be safe and effective in a given situation.

Clinical trials

These trials (also called research studies) test new treatments or 'old' treatments given in new ways to see if they work better. Clinical trials are important because they provide vital information about how to improve treatment by achieving better results with fewer side effects. Clinical trials often give people access to new therapies not yet funded by governments.

If you are considering taking part in a clinical trial make sure that you understand the reasons for the trial and what it involves for you. You also need to understand the benefits and risks of the trial before you can give your informed consent. Talk to your doctor who can guide you in making the best decision for you.

Informed consent

Giving an informed consent means that you understand and accept the risks and benefits of a proposed procedure or treatment. It means that you are happy that you have adequate information to make such a decision.

Your informed consent is also required if you agree to take part in a clinical trial, or if information is being collected about you or some aspect of your care (data collection).

If you have any doubts or questions regarding any proposed procedure or treatment please do not hesitate to talk to the doctor or nurse again

Regular observation only

Many people, particularly in the early stage of disease remain very well, living a relatively normal life for a long time without any treatment. At this stage the bone marrow is still relatively healthy. If you are at this stage, your doctor may simply recommend regular checkups to carefully monitor your health.

There are several treatment options available for you if you develop symptoms from your disease.

Supportive care

Supportive care is the mainstay of treatment for the majority of people with MDS. This involves making every effort to improve your quality of life by relieving any symptoms you might have and by preventing and treating any complications that arise from your disease or treatment.

Blood transfusions, antibiotics and, in some cases, the use of *growth* factors, which promote the production of blood cells in your bone marrow, are all important elements of supportive care.

Blood transfusions

If symptoms of anaemia are interfering with your normal daily activities, your doctor may recommend that you have a red blood cell transfusion. Platelet transfusions are sometimes given to prevent or treat bleeding (for example a persistent nose bleed).

You do not need to be admitted to hospital for a red blood cell or platelet transfusion and they are usually given in the clinic or outpatient department of the hospital. Transfusions these days are relatively safe and they don't usually cause any serious complications. Nevertheless you will be carefully monitored throughout the transfusion. In the meantime, remember to call the nurse if you are feeling hot, cold, shivery or in any way unwell, as

this might indicate that you are having a reaction to the transfusion. Steps can be taken to minimise these effects and ensure that they don't happen again.

Side-effects of repeated transfusions

Risk of infection

All blood donors and each unit of blood are screened separately to ensure that harmful viruses are not passed on in a transfusion.

Transfusion reactions

Careful checks are made both in blood bank and at the chair-side to ensure that the transfusion you are receiving is compatible with your blood type. However, people can become sensitised to red cell (and platelet) transfusions over time and this can cause, in some cases, a minor transfusion reaction such as a fever or rash. These reactions are usually caused by a small number of white cells present in bags of donated blood and platelets. More recently, these reactions have been dramatically reduced by the use of special white cell filters during a transfusion, or the use of filtered blood.

Fluid overload

Each bag of blood adds nearly 400 mls of fluid to your circulation which puts an extra load on the heart. The body usually adjusts to this by producing more urine. Elderly people's heart and kidneys may have difficulty in coping with this relatively sudden increase which can make you feel a bit breathless. To prevent or to treat this, a drug is often given to help you pass urine. The nurse will ensure that you are told when this is given and that you have easy access to toilet facilities as the drug can be very effective and may start working within 15 minutes.

Iron overload

Over time, repeated red blood cell transfusions can lead to a build-up of high levels of iron in the body. Your doctor will be able to tell if this is happening from a simple blood test. If needed, a special drug can be given which binds the iron and helps to safely remove it from the body.

Antibiotics

When your white cell count is low you are at risk of developing an infection. If you develop an infection it is important that you are

treated promptly, with antibiotics. Don't hesitate to contact your doctor or hospital if you develop any of the following:

- a temperature of 38° C and/or an episode of shivering, called a rigor (where you shake uncontrollably)
- coughing or shortness of breath
- a sore throat and/or a head cold
- passing urine frequently or pain when passing urine
- if you are feeling generally unwell
- if you cut, or otherwise injure yourself
- if you are bleeding (for example blood in your urine, stools, sputum, bleeding gums or a persistent nose bleed) or bruising easily

Please also advise your doctor if any surgery is planned by another medical practitioner as advice may be required from your haematologist as to the best supportive treatment with red cells, platelets and antibiotics to ensure that your surgery is completed successfully without problems due to your MDS.

Growth factors

As mentioned earlier, growth factors are natural chemicals in your blood that stimulate the bone marrow to produce different types of blood cells. Some of them can be made in the laboratory and used to help manage your MDS.

Erythropoietin (EPO) is an example of a growth factor which is used to stimulate the production of more red blood cells and can in some cases reduce the need for frequent blood transfusions. *Granulocyte-colony* stimulating factor (G-CSF) may be given to stimulate the bone marrow to produce more white cells, particularly neutrophils. These white cells help fight bacterial and fungal infections in particular.

Growth factors are given as an injection under the skin (subcutaneous). They don't usually cause any major side effects but some people experience fevers, chills, headaches and some bone pain while using G-CSF. You doctor may recommend that you take paracetamol to relieve any discomfort you may be feeling. stimulating factor (G-CSF) may be given to stimulate the bone marrow to produce more white cells, particularly neutrophils. These white cells help fight bacterial and fungal infections in particular.

Standard drug therapies

Chemotherapy

Chemotherapy literally means therapy with chemicals. Many chemotherapy drugs are also called cytotoxics (cell toxic) because they kill cells; especially ones that multiply quickly like cancer cells.

In general, chemotherapy is only used in MDS in situations when there is a need to control a rising white cell count or if the MDS is transforming or has transformed into leukaemia. Chemotherapy is also given to treat a subtype of MDS called Chronic myelomonocytic leukaemia (CMML), which is characterised by a higher than normal white cell count in the blood.

The aim of chemotherapy is to reduce the number of blast cells in your bone marrow and by doing so, allowing the remaining normal stem cells to make normal red blood cells, white blood cells and platelets.

Chemotherapy may be administered in three different situations in MDS.

1. Low-dose oral chemotherapy for CMML

Low doses of oral chemotherapy (chemotherapy that is taken by mouth) can be very effective at controlling a high white cell count. *Hydroxyurea*, is an example of an oral chemotherapy drug used in the treatment of a CMML. *Hydroxyurea* can be taken in capsule form. It is usually very well tolerated and does not usually cause nausea (feeling sick) or significant hair loss, although it can cause a dry skin.

The dose of the chemotherapy drug can be adjusted to the response of the white cells and also the response of other blood cells such as red cells and platelets. For example, sometimes a balance has to be made between the effect on lowering the white count and the increase in anaemia and thrombocytopenia caused by the drug. Blood counts are monitored frequently while you are receiving chemotherapy.

2. Low-dose Cytotoxic therapy for high-risk MDS/AML

Low-doses of oral and/or intravenous chemotherapy can be used to control a rising blast count in the peripheral blood. This is often seen when MDS is transforming to acute leukaemia. In this case chemotherapy is often given in combination with regular blood and platelet transfusions.

The aim of this treatment is to control the leukaemia while avoiding any severe side-effects from chemotherapy. It is hoped that this will enable you to have a reasonable quality of life, continuing living at home, although visits to the chemotherapy day centre or clinic may be necessary two or three times a week.

Some patients who receive low dose chemotherapy do as well as others who receive more aggressive therapy. Unfortunately neither approach will produce a cure of the underlying disease. The choice of which course to take will depend on many factors, including your wishes, the nature of your individual disease and your haematologist's advice.

3. Standard-dose chemotherapy for high-risk MDS/AML

People who have MDS that is transforming, or has transformed, into acute myeloid leukaemia*, may benefit from standard anti-leukaemia therapy if they are fit enough. Not everyone is suitable for this form of treatment, especially if they are elderly or frail. However, older people do respond similarly to younger patients if they are well enough to tolerate the treatment. Unfortunately, even if a complete remission is achieved, most patients will relapse and the leukaemia will reappear, usually within a year. The decision to have this type of treatment needs to be discussed by you and your family in detail with your doctor.

This treatment is given in hospital and the side-effects can be more severe. If you are having chemotherapy your doctor and nurse will tell you about the side-effects you might experience and how they can be best managed.

**There is a separate Leukaemia Foundation booklet called 'Understanding Acute Myeloid Leukaemia' which provides more details of this type of chemotherapy.*

Potential side effects of chemotherapy

- *feeling sick - nausea and vomiting*
 - *feeling tired and weak*
 - *hair loss and thinning*
 - *mouth problems*
- *diarrhoea or constipation*
 - *skin problems*
- *drop in blood counts*
 - *fertility problems*

Stem cell transplantation*

Stem cell transplantation (also called a bone marrow transplant) using a suitably matched donor, is the only potential cure for MDS. This treatment carries significant risks however and is only suitable for a very small minority (<5%) of younger patients with MDS (usually under 50 years of age).

A stem cell transplant involves giving very high doses of chemotherapy, sometimes in combination with radiotherapy, in an attempt to completely destroy the abnormal stem cells in your bone marrow. These cells are then replaced with healthy stem cells which have been donated, usually from a brother or sister who has the same tissue type as yours. This is called an *allogeneic* (donor) *stem cell transplant*. In some cases the donor is not a family member, but has a similarly matched tissue type. This type of transplant is called a *matched unrelated donor transplant* (MUD) or *volunteer unrelated donor transplant* (VUD).

**There is a separate Leukaemia Foundation booklet called 'Understanding Autologous Transplants - A guide for patients and families' and 'Understanding Allogeneic Transplants - A guide for patients and families' that provide more detail on these types of treatments.*

A newer approach in stem cell transplantation involves using less intensive doses of chemotherapy. This approach may be suitable for selected patients older than 50 years of age. The theory is that moderate doses of chemotherapy will destroy enough abnormal stem cells in the bone marrow and suppress the patient's immune system sufficiently for it to accept the new, donated stem cells. This is called a *mini* transplant, or a *mini-allogeneic* (miniallo) stem cell transplant.

New and experimental drug therapies

There are several new approaches being developed for the treatment of MDS. These include new chemotherapy drugs, *biological modifiers* and *immunomodulatory* drugs which harness the power of the immune system to help fight disease. Side effects vary according to the type of drug used.

Some examples of newer treatments being developed for MDS are listed below. Many of these drugs are not freely available, but are currently being used in **clinical trials** in Australia and other parts of the world. Your doctor will be able to discuss with you all of the treatment options suitable for you.

New and experimental drugs for MDS

Angiogenesis Inhibitors

(inhibit growth factors and new blood vessels)

Thalidomide

Lenalidomide

Arsenic Trioxide

DNA Methyl Transferase Inhibitors

(inhibit abnormal gene activity)

5-Azacytidine (5-Aza)

5-Aza-2'-Deoxycytidine

Histone Deacetylase Inhibitors

(inhibit abnormal gene activity)

Phenylbutyrate

Valproic acid

Farnesyl Transferase Inhibitors

(inhibit abnormal cell growth signals)

Tipifarnib

Lonafarnib

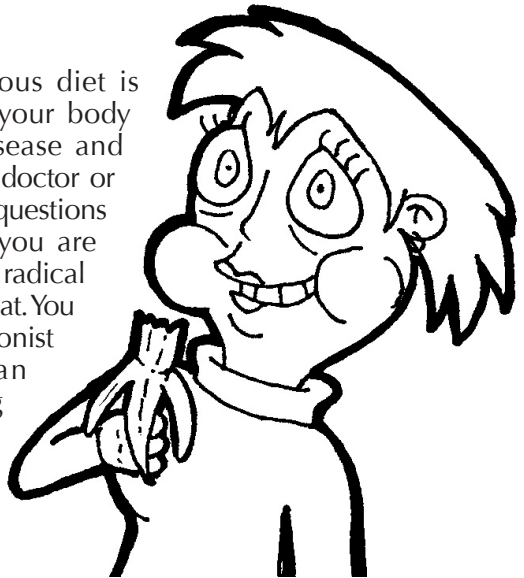
Complementary therapies

Complementary therapies are therapies which are not considered standard medical therapies. Many people find that they are helpful in coping with their treatment and recovery from disease. There are many different types of complementary therapies. These include yoga, exercise, meditation, prayer, acupuncture, relaxation and herbal and vitamin supplements.

Complementary therapies should 'complement' or assist with recommended medical treatment. **They should not be used as an alternative to medical treatment for MDS.** It is important to realise that no complementary or alternative treatment alone has proven to be effective against MDS. It is also important to let your doctor or nurse know if you are using any complementary or alternative treatments, in case they interfere with effectiveness of chemotherapy or other treatments you may be having.

Nutrition*

A healthy and nutritious diet is important in helping your body to cope with your disease and treatment. Talk to your doctor or nurse if you have any questions about your diet or if you are considering making any radical changes to the way you eat. You may wish to see a nutritionist or dietician who can advise you on planning a well-balanced and nutritious diet.



**The Leukaemia Foundation has a booklet called 'Eating Well: a practical guide for people living with leukaemias, lymphomas and myeloma' which provides information about eating well before, during and after treatment.*

MAKING TREATMENT DECISIONS

Many people feel overwhelmed when they are diagnosed with MDS. In addition to this, waiting for test results and then having to make decisions about proceeding with the recommended treatment can be very stressful. Some people do not feel that they have enough information to make such decisions while others feel overwhelmed by the amount of information they are given, or that they are being rushed into making a decision.

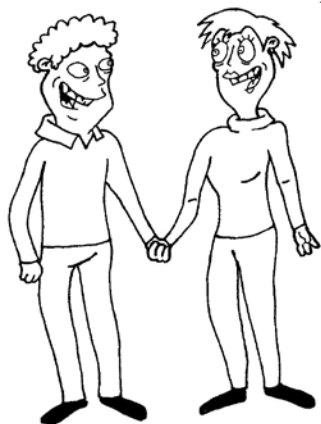


It is important that you feel you have enough information about your illness and all of the treatment options available, so that you can make your own decisions about which treatment to have.

Before going to see your doctor make a list of the questions you want to ask. It is handy to keep a notebook or some paper and a pen handy as many questions are thought of in the early hours of the morning.

Sometimes it is hard to remember everything the doctor has said. It helps to bring a family member or a friend along who can write down the answers to your questions, prompt you to ask others, be an extra set of ears or simply be there to support you.

Your treating doctor (haematologist) will spend time discussing with you and your family what he or she feels is the best option for you. Feel free to ask as many questions as you need to, at any stage. You are involved in making important decisions regarding your well-being. You should feel that you have enough information to do this and that the decisions made are in your best interests. Remember, you can always request a second opinion if you feel this is necessary.



INFORMATION AND SUPPORT



People cope with a diagnosis of MDS in different ways and there is no right or wrong or standard reaction. It is not uncommon to feel concerned, afraid, angry or confused.

It is worth remembering that information can often help to take away the fear of the unknown. It is best for patients and families to speak directly to their doctor regarding any questions they might have about their disease or treatment. It can also be helpful to talk to other health professionals like social workers or nurses who have been specially educated to take care of people with diseases like MDS. Some people find it useful to talk with other patients and family members who understand the different feelings and issues that come up for people living with an illness of this nature.

If you have a psychological or psychiatric condition please inform your doctor and request additional support from a mental health professional.

Many people are concerned about the social and financial impact of the diagnosis and treatment on themselves and their loved ones. Medical appointments and traveling to and from the hospital can be inconvenient, costly and they can interfere with your everyday life. In some cases normal family routines are disrupted and other

members of the family may suddenly have to fulfill roles they are not familiar with, for example cooking, cleaning, doing the banking and taking care of children.

Many hospitals have psychologists, social workers and pastoral care workers who can assist you and your loved ones in coping better with any psychological, emotional or financial difficulties you may be experiencing. There are a variety of programs designed to help ease the emotional and financial strain created by cancer.

The Leukaemia Foundation is there to provide you and your family with information and support to help you cope during this time. The Leukaemia Foundation's support service coordinators are at hand to help and are just a phone call away. Contact details for your state office of the Leukaemia Foundation are provided on the back of this booklet.

USEFUL INTERNET ADDRESSES

- American Cancer Society
www.cancer.org
- Aplastic Anaemia & MDS International Foundation, Inc.
www.myelodysplasticsyndromes.org or www.aamds.org
- CancerBACUP (A UK cancer information site)
www.cancerbacup.org.uk
- Cancer Council of Australia
www.cancer.org.au
- Centre for Grief and Loss
www.grief.org.au
- Leukaemia Foundation of Australia
www.leukaemia.org.au
- Leukaemia Foundation of Australia - Online Support Group
www.talkbloodcancer.com
- Leukemia & Lymphoma Society of America
www.leukemia-lymphoma.org
- Leukaemia Research Fund (UK)
www.lrf.org.uk
- Look Good ... Feel Better program
www.lgfb.org.au
- Myelodysplastic Syndromes Foundation
www.mds-foundation.org
- National Cancer Institute
www.cancer.gov/cancerinfo/

GLOSSARY OF TERMS

Alopecia

Hair loss. This is a side effect of some kinds of chemotherapy and radiotherapy. It is usually temporary.

Anaemia

A reduction in the haemoglobin level in the blood. Haemoglobin normally carries oxygen to all the body's tissues. Anaemia causes tiredness, paleness and sometimes shortness of breath.

Antibodies

Naturally produced substances in the blood, made by white blood cells called B-lymphocytes or B-cells. Antibodies target antigens on other substances such as bacteria, viruses and some cancer cells and cause their destruction.

Antiemetic

Drug which prevents or reduces feelings of sickness.

Bone marrow

The tissue found at the centre of many flat or big bones of the body. The bone marrow contains stem cells from which all blood cells are made. The tissue found at the centre of our bones. Active or red bone marrow contains stem cells from which all blood cells are made and in the adult this is found mainly in the bones making up the axial skeleton – hips, ribs, spine, skull and breastbone (sternum) The other bones contain inactive or (yellow) fatty marrow, which, as its name suggests, consists mostly of fat cells.

Blast cells

Immature blood cells normally found in the bone marrow.

Blood count

A routine blood test that measures the number and type of cells circulating in the blood.

Cancer

A malignant disease characterised by uncontrolled growth, division, accumulation and invasion into other tissues of abnormal cells from the original site where the cancer started. Cancer cells can grow and multiply to the extent that they eventually form a lump or swelling. This is a mass of cancer cells known as a tumour. Not all tumours are due to cancer; in which case they are referred to as non-malignant or benign tumours.

Cannula

A plastic tube which can be inserted into a vein to allow fluid to enter the blood stream.

Central Venous Catheter (CVC)

A line or tube passed through the large veins of the neck, chest or groin and into the central blood circulation. It can be used for taking samples of blood, giving intravenous fluids, blood, chemotherapy and other drugs without the need for repeated needles.

Chemotherapy

Single drugs or combinations of drugs which may be used to kill and prevent the growth and division of cancer cells. Although aimed at cancer cells, chemotherapy can also affect rapidly dividing normal cells and this is responsible for some common side-effects including hair loss and a sore mouth (mucositis). Nausea and vomiting are also common, but nowadays largely preventable with modern anti-nausea medication. Most side-effects are temporary and reversible.

Chromosomes

Chromosomes are made up of coils of DNA (deoxyribonucleic acid). DNA carries all the genetic information for the body in sequences known as genes. There are approximately 40,000 genes on 23 different chromosomes. The chromosomes are contained within the nucleus of a cell.

Cure

This means that there is no evidence of disease and no sign of the disease re-appearing, even many years later.

Cytogenetic tests (studies)

The study of the structure of chromosomes. Cytogenetic tests are carried out on samples of blood and bone marrow to detect chromosomal abnormalities associated with disease. This information helps in the diagnosis and selection of the most appropriate treatment.

Growth factors and cytokines

A complex family of proteins produced by the body to control the growth, division and maturation of blood cells by the bone marrow. Some are now available as drugs as a result of genetic engineering and may be used to stimulate normal blood cell production following chemotherapy, bone marrow or peripheral blood stem cell transplantation.

Haemopoiesis

The processes involved in blood cell formation.

Haematologist

A doctor who specialises in the diagnosis and treatment of diseases of the blood, bone marrow and immune system.

High dose therapy

The use of higher than normal doses of chemotherapy to kill off resistant and / or residual (left over) cancer cells that have survived standard-dose therapy.

Immune system

The body's defense system against infection and disease.

Leukaemia

A cancer of the blood and bone marrow characterised by the widespread, uncontrolled production of large numbers of abnormal blood cells. These cells take over the bone marrow often causing a fall in blood counts. If they spill out into the bloodstream however they can cause very high abnormal white cell counts.

Lymphocyte

Specialised white blood cell which are involved in defending the body against disease and infection. There are two types of lymphocytes - B lymphocytes and T-lymphocytes. They are also called B-cells and T-cells.

Mucositis

Inflammation of the lining of the mouth and throat, which also can extend to the lining of the whole of the gastro-intestinal tract (stomach and intestines).

Neutropenia

A reduction in the number of circulating neutrophils, an important type of white blood cell. Neutropenia is associated with an increased risk of infection.

Neutrophils

Neutrophils are the most common type of white blood cell. They are needed to effectively fight infection, especially bacterial and fungal infections.

Pathologist

A doctor who specialises in the laboratory diagnosis of disease, and how disease is affecting the organs of the body.

Prognosis

An estimate of the likely course of a disease.

Radiotherapy (radiation therapy)

The use high energy X-rays to kill cancer cells and shrink tumours.

Relapse

The return of the original disease.

Remission (or Complete Remission)

When there is no evidence of disease detectable in the body; note this is not always equivalent to a cure as relapse may still occur.

Resistant or Refractory Disease:

This means that the disease is not responding to treatment.

Spleen

The spleen is found high in the abdomen on the left-hand side and cannot normally be felt on examination unless it is enlarged. It is an organ that is part of the blood system and is a specialized collection of lymphoid and haematopoietic tissue. It plays a minor role in the immune system and contributes to the destruction of red blood cells, white blood cells and platelets at the end of their life-span. It is often enlarged in diseases of the blood - this is known as hypersplenism.

Splenectomy

Surgical removal of the spleen. This can be done by an open operation, or, in selected cases, using small incisions and operating through a laparoscope.

Splenomegaly

Enlargement of the spleen.

Standard therapy

The most effective and safest therapy currently being used.

Stem cells

Stem cells are primitive blood cells that can give rise to more than one cell type. There are many different types of stem cell in the body. Bone marrow stem cells have the ability to grow and produce all the different blood cells including red cells, white cells and platelets.

Syndrome

A characteristic collection of medical symptoms and signs; for example, the syndrome in myelodysplastic syndromes, refers to the fatigue due to anaemia, increased tendency to infections and increased bruising which are all features of myelodysplasia.

Tumour

An abnormal mass of cells which may be non-malignant (benign) or malignant (cancerous).

White blood cells

Specialised cells of the immune system that protect the body against infection. There are five main types of white blood cells: neutrophils, eosinophils, basophils, monocytes and lymphocytes.



Leukaemia
Foundation
VISION TO CURE
MISSION TO CARE

The Leukaemia Foundation is the only national not-for-profit organisation dedicated to the care and cure of patients and families living with leukaemias, lymphomas, myeloma and related blood disorders.

You can help by making a donation. Please fill out the form below or visit www.leukaemia.org.au to make your gift online.

Dr/Mr/Mrs/Ms/Miss:

Address:

..... Postcode.....

Telephone: (h).....

(w)

Email:

Please accept my tax deductible donation for \$

My cheque, made payable to the Leukaemia Foundation, is enclosed, or please charge \$..... to my credit card:

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Cardholder's name:

Cardholder's signature:

Expiry date:/.....

Please send to:

The Leukaemia Foundation
GPO Box 9954
in your capital city.



Please send me a copy of the following information booklets:

- Living with Leukaemias, Lymphomas, Myeloma & Related Disorders: Information and Support
- Understanding Leukaemias, Lymphomas, Myeloma & Related Disorders
- Understanding Acute Myeloid Leukaemia
- Understanding Acute Lymphoblastic Leukaemia
- Understanding Chronic Lymphocytic Leukaemia
- Understanding Chronic Myeloid Leukaemia
- Coping with Childhood Leukaemia
- Understanding Lymphomas (Non-Hodgkin's Lymphomas or B-Cell and T-Cell Lymphomas)
- Understanding Allogeneic Transplants
- Understanding Autologous Transplants
- Understanding MDS
- Understanding Multiple Myeloma
- Eating Well: A Practical Guide for People Living with Leukaemias, Lymphomas and Myeloma

Or information about:

- The Leukaemia Foundation's support services
- Workplace giving
- Regular deduction scheme
- Making a bequest to the Leukaemia Foundation
- Volunteering
- Receiving the Foundation's newsletters

Name:

Street or Postal Address:.....

Suburb.....

State/Postcode

Email: Tel: (.....).....

Please send to:

Leukaemia Foundation, GPO Box 9954, In Your Capital City

or freecall 1800 620 420

or email: info@leukaemia.org.auFurther information is available on the Leukaemia Foundation's website
www.leukaemia.org.au



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This information booklet is produced by the Leukaemia Foundation and is one in a series on blood cancers and related disorders.

Some booklets are also available in other languages. Copies of this booklet and the other booklets can be obtained from the Leukaemia Foundation in your state by contacting us on

Freecall: 1800 620 420
Email: info@leukaemia.org.au
Website: www.leukaemia.org.au

The Leukaemia Foundation is a non-profit organisation that depends on donations and support from the community.

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May 06

