Understanding Myeloproliferative Neoplasms (MPN)

Formally called Myeloproliferative Disorders (MPD)

Including
- Polycythaemia vera
- Essential thrombocythaemia
- Idiopathic myelofibrosis

A guide for patients and families
<table>
<thead>
<tr>
<th>CONTENTS</th>
<th>PAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>3</td>
</tr>
<tr>
<td>The Leukaemia Foundation</td>
<td>4</td>
</tr>
<tr>
<td>Bone marrow, stem cells and blood cell formation</td>
<td>8</td>
</tr>
<tr>
<td>What are myeloproliferative neoplasms?</td>
<td>13</td>
</tr>
<tr>
<td>What causes myeloproliferative neoplasms?</td>
<td>14</td>
</tr>
<tr>
<td>Which doctor?</td>
<td>15</td>
</tr>
<tr>
<td>Polycythaemia (rubra) vera</td>
<td>16</td>
</tr>
<tr>
<td>Essential thrombocythaemia (ET)</td>
<td>25</td>
</tr>
<tr>
<td>Primary myelofibrosis</td>
<td>30</td>
</tr>
<tr>
<td>Chronic eosinophilic leukaemia/hypereosinophilic syndrome</td>
<td>34</td>
</tr>
<tr>
<td>Chronic neutrophilic leukaemia</td>
<td>35</td>
</tr>
<tr>
<td>Systemic mastocytosis or mast cell disease</td>
<td>36</td>
</tr>
<tr>
<td>Complementary therapies</td>
<td>37</td>
</tr>
<tr>
<td>Making treatment decisions</td>
<td>38</td>
</tr>
<tr>
<td>Information and support</td>
<td>41</td>
</tr>
<tr>
<td>Useful internet addresses</td>
<td>42</td>
</tr>
<tr>
<td>Glossary of terms</td>
<td>43</td>
</tr>
<tr>
<td>Requesting more information</td>
<td>55</td>
</tr>
</tbody>
</table>
ACKNOWLEDGEMENTS

The Leukaemia Foundation gratefully acknowledges the following groups for their assistance in the development and revision of the information in this publication: people who have experienced a myeloproliferative neoplasm as a patient or carer, Leukaemia Foundation support services staff, nursing staff and clinical haematologists representing the various states and territories of Australia. The cartoon illustrations were drawn by Brett Hansen.

The Leukaemia Foundation values feedback from people who have been affected by an MPN and health care professionals working with them. If you would like to make suggestions, or tell us about your experience of using this booklet, please contact the National Manager, Support Services at info@leukaemia.org.au

The Leukaemia Foundation gratefully acknowledges Novartis Oncology for their support in the production of this booklet through an unrestricted education grant.

February 2013
INTRODUCTION

This booklet has been written to help you and your family to understand more about myeloproliferative neoplasms (also known as MPN, or myeloproliferative disorders or MPD).

Some of you may be feeling anxious or a little overwhelmed if you or someone you care for has been diagnosed with a myeloproliferative neoplasm. This is normal. 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 raise other questions, which you should discuss 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 and/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 and team.

Finally, we hope that you find this booklet 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 people living with leukaemias, lymphomas, myeloma and related blood disorders and their loved ones. Since 1975, the Foundation has been committed to improving survival for these people and providing them with much needed support. The Foundation 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 support services at no charge to people with myelodysplastic neoplasms and their loved ones. This support may be offered over the telephone, face to face at home, hospital or at the Foundation’s office or accommodation centres, depending on the location and individual needs. Support may include providing information, education seminars and programs that provide a forum for peer support and consumer representation, practical assistance, accommodation, transport, and emotional support.

The Leukaemia Foundation funds leading research into better treatments and cures. Through its National Research Program, the Foundation has established the ALLG Leukaemia and Lymphoma Tissue Bank, situated at the Princess Alexandra Hospital, and the Leukaemia Foundation Research Unit at the Queensland Institute for Medical Research. In addition, the Foundation funds research grants, scholarships and fellowships for talented researchers and health professionals.
Support Services

“Foundation staff provide patients and their families with information and support across Australia”

The Leukaemia Foundation has a team of highly trained and caring Support Services staff with qualifications and experience in nursing or allied health that work across the country. They can offer individual support and care to you and your family when it is needed.

Support Services may include:

Information

The Leukaemia Foundation has a range of booklets, fact sheets, DVDs, and website resources that are available free of charge. These can be ordered via the form at the back of this booklet or downloaded from the website.

Education & support programs

The Leukaemia Foundation offers you and your family MPN-specific and general education and support programs throughout Australia. These programs are designed to empower you with information about various aspects of diagnosis and treatment and how to support your general health and well being.
Emotional support

A diagnosis of a myeloproliferative neoplasm can have a dramatic impact on a person’s life. At times it can be difficult to cope with the emotional stress involved. The Leukaemia Foundation’s Support Services staff can provide you and your family with much needed support during this time. They may refer you or a loved one to a specialist health professional eg psychologist if required.

Online discussion forum

The Foundation has established an on-line information and support group for people living with blood cancers or related blood disorders, such as MPN. Registration is free and participants can remain anonymous, see www.talkbloodcancer.com

Accommodation

Some people need to relocate for treatment and may need help with accommodation. The Leukaemia Foundation staff can help you to find suitable accommodation close to your hospital or treatment centre. In many areas, the Foundation’s fully furnished self-contained units and houses can provide a ‘home away from home’ for you and your family.

Transport

The Foundation also assists with transporting people to and from hospital for treatment. Courtesy cars and other services are available in many areas throughout the country.

Practical assistance

The urgency and lengthy duration of medical treatment can affect you and your family’s normal way of life and there may be practical things the Foundation can do to help. In special circumstances, the Leukaemia Foundation provides financial support for patients who are experiencing financial difficulties or hardships as a result of their illness or its treatment. This assistance is assessed on an individual basis.
Contacting us

The Leukaemia Foundation provides services and support in every Australian state and territory. Every person’s experience of living with MPN is different. Living with MPN 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

*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*.

As an infant, haemopoiesis takes place at the centre of all bones. In later life, it is limited to the hips, ribs 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).

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, to reproduce vital numbers of red cells, white cells and platelets. All blood cells need to be replaced because they have limited life spans.

There are two main families of stem cells, which develop into the various types of blood cells.
Blood Stem Cells

(MyPN pathway)

Myeloid Stem Cell Line

- Red Cells
- White Cells
- Platelets
- Neutrophils, Eosinophils, Basophils, Monocytes

Lymphoid Stem Cell Line

- B-cells
- T-cells
- Natural Killer Cells
- Plasma Cells

**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 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.
Blood

Blood consists of blood cells and plasma. Plasma is the straw coloured fluid part of the blood that blood cells use to travel around your body, and contains many important proteins.

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. The body uses this oxygen to create energy.

The normal haemoglobin range for a man is approximately 130 – 170 g/L
The normal haemoglobin range for a woman is approximately 120 – 160 g/L

Plasma
60%

Blood cells
40%

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

The normal range of the haematocrit for a man is between 40% and 52%
The normal range of the haematocrit for a woman is between 36% and 46%
Anaemia

Anaemia is a reduction in the number of red cells or low haemoglobin. Measuring 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, also known as leukocytes, fight infection. There are different types of white cells that fight infection together and in different ways.

<table>
<thead>
<tr>
<th>White cell</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophils</td>
<td>mainly kill bacteria and fungi.</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>mainly kill parasites.</td>
</tr>
<tr>
<td>Basophils</td>
<td>mainly work with neutrophils to fight infection.</td>
</tr>
<tr>
<td>Monocytes</td>
<td>mainly work with neutrophils and lymphocytes to fight infection; they also help with antibody production and act as scavengers to remove dead tissue. These cells are known as monocytes when they are found in the blood and macrophages when they migrate into body tissues to help fight infection.</td>
</tr>
<tr>
<td>T-cells</td>
<td>mainly kill viruses, parasites and cancer cells; produce cytokines.</td>
</tr>
<tr>
<td>B-cells</td>
<td>mainly make antibodies which target microorganisms.</td>
</tr>
</tbody>
</table>

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

The normal adult white cell count varies between 3.7 and 11 x 10⁹/L
Neutropenia

*Neutropenia* is the term used to describe a lower than normal neutrophil count. If you have a neutrophil count of less than 1 (1 x 10⁹/L) you are considered to be neutropenic and at risk of developing frequent and sometimes severe infections.

*The normal adult neutrophil count varies between 2.0 and 7.5 x 10⁹/L*

Platelets

Platelets are irregular-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. They also release chemicals (clotting factors) that assist with the blood clotting process.

*The normal adult platelet count varies between 150 and 400 x 10⁹/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 x 10⁹/L), you are at risk of bleeding and tend to bruise easily.

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

‘Myelo’ is the Greek word for marrow and ‘proliferative’ is another word for growing or reproducing. Myeloproliferative Neoplasms are a group of disorders in which the bone marrow cells grow and reproduce abnormally. In myeloproliferative neoplasms, abnormal bone marrow stem cells produce excess numbers of one or more types of blood cells (red cells, white cells and/or platelets). These abnormal cells cannot function properly and can cause serious health problems unless properly treated and controlled.

It is important to remember, as you read through this booklet, that myeloproliferative neoplasms are chronic diseases that, in most cases, remain stable for many years or progress gradually over time. The symptoms and complications of myeloproliferative neoplasms described in this booklet do not occur in everyone, and may not occur for many years.

Types of myeloproliferative neoplasms

Myeloproliferative neoplasms are usually described according to the type of blood cell which is most affected. There are 4 main types of myeloproliferative neoplasms that together represent around 95 per cent of all cases:

1. Chronic myeloid leukaemia – too many white cells - refer CML booklet
2. Polycythaemia vera (PV) – too many red cells
3. Essential thrombocythaemia (ET) – too many platelets
4. Idiopathic myelofibrosis – bone marrow tissue is replaced by fibrous scar-like tissue. This disrupts normal blood cell production.

Myeloproliferative neoplasms are closely related diseases, so it’s not uncommon for people to have features of more than one myeloproliferative neoplasms when they are first diagnosed, or during the course of their illness. In some cases, one neoplasm may
transform over time to another, or to a type of leukaemia called acute myeloid leukaemia (AML).

Less common types of myeloproliferative neoplasms include:

- Chronic neutrophilic leukaemia (CNL) – too many neutrophils (a type of white cell) in blood and bone marrow
- Chronic eosinophilic leukaemia (CEL) / hypereosinophilic syndrome – too many eosinophils (another type of white cell) in blood and bone marrow
- Chronic myelomonocytic leukaemia (CMML) – too many monocytes (a type of white cell) in blood and bone marrow. CMML also has features of Myelodysplasia, another blood stem cell disorder characterised by abnormal blood maturation*. The World Health Organisation (WHO) classifies this condition as a cross-over MDS/MPN disorder.
- Systemic mastocytosis – too many mast cells (a type of white cell) in blood, bone marrow, skin and other tissues
- Myeloproliferative disease – unclassifiable

**WHAT CAUSES MYELOPROLIFERATIVE NEOPLASMS?**

The exact cause of myeloproliferative neoplasms remains unknown but there are likely to be a number of factors involved. Myeloproliferative neoplasms are sometimes described as being clonal (clones of a single cell type) blood stem cell disorders. This means that they result from a change, or mutation, in the DNA (genetic code) of a single blood stem cell. This change (or changes) results in abnormal blood cell development and in this case the overproduction of blood cells. In myeloproliferative neoplasms the original mutation is preserved when the affected stem cell divides (proliferates) and produces a ‘clone’; a group of identical stem cells all with the same defect.

*There is a separate Leukaemia Foundation booklet called ‘Understanding Myelodysplastic Syndrome’.*
Mutations in dividing cells occur all the time and healthy cells have sophisticated mechanisms within them to stop these abnormalities persisting. But the longer we live, the more chance we have of acquiring mutations that manage to escape these safe-guards. That’s why myeloproliferative neoplasms, like most leukaemias and other cancers, become more common as we get older.

A mutation of a particular gene (a segment of DNA that makes proteins) known as Janus kinase 2 (JAK 2) is found in a large proportion of people with myeloproliferative neoplasms. The exact effect of this mutation remains unclear but it appears to play a role in the overproduction of blood cells seen in these disorders. The discovery of a mutation in the JAK2 gene is important because it may have a significant impact on the way myeloproliferative neoplasms are treated in the future.

Finally, myeloproliferative neoplasms are not contagious; you cannot ‘catch’ the disorders by being in contact with someone who has one. Most people with a myeloproliferative neoplasm have no family history of the disease.

**WHICH DOCTOR?**

If your GP suspects that you might have an MPN, 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.
POLYCYTHAEMIA (RUBRA) VERA

Polycythaemia (rubra) vera, also known as primary polycythaemia vera, is a disorder in which too many red cells are produced in the bone marrow, without any identifiable cause. These cells accumulate in the bone marrow and in the bloodstream where they increase the blood volume and cause the blood to become thicker, or more ‘viscous’ than normal. In many people with polycythaemia vera, too many platelets and white cells are also produced.

Polycythaemia vera is a rare chronic disease diagnosed in an estimated 2 to 3 per 100,000 population. Although it can occur at any age, polycythaemia vera usually affects older people, with most patients diagnosed over the age of 55 years. Polycythaemia vera is rare in children and young adults. It occurs more commonly in males than in females.

What is secondary or reactive polycythaemia?

In secondary or reactive polycythaemia, red cell production is increased in response to excess amounts of erythropoietin (a red cell growth factor mainly produced in the kidneys) circulating in the bloodstream. High levels of erythropoietin can be a response to lower than normal levels of oxygen in the blood (for example at high altitudes, in heavy smokers and in people with heart or lung disease). This is a useful compensatory mechanism that helps the body to produce more red cells and haemoglobin to transport more oxygen around the body. Erythropoietin levels, and therefore red cell production may also be increased abnormally in some types of kidney disease and in some types of cancer.

In a condition known as relative, apparent or spurious polycythaemia, the volume of plasma (the liquid portion of the blood) is reduced, usually as a result of dehydration, vomiting or diuretic (fluid loss) therapy. This increases the concentration of red cells in the blood but the actual red cell mass (the total number of red cells) remains normal.
SYMPTOMS AND COMPLICATIONS OF POLYCYTHAEMIA VERA

Many people have no symptoms when they are first diagnosed with polycythaemia vera and the disease is picked up incidentally during a routine blood test or physical examination.

When symptoms do occur, they usually develop gradually over time. They are mainly due to the increased thickness (hyperviscosity) and abnormally high numbers of blood cells in the circulating blood. Common symptoms include:

- headaches
- blurred vision
- fatigue
- weakness
- dizziness
- itchiness (pruritus), especially after a hot bath
- night sweats.

Enlargement of the spleen (splenomegaly) is also common and occurs in around 75 per cent of cases. Symptoms include feelings of discomfort, pain or fullness in the upper left-side of the abdomen. An enlarged spleen may also cause pressure on the stomach causing a feeling of fullness, indigestion and a loss of appetite. In some cases the liver may also be enlarged. This is called hepatomegaly.

Some people experience gout, which usually presents as a painful inflammation of the big toe or foot. This can result from a build up of uric acid, a byproduct of the increased production and breakdown of blood cells. Some individuals may develop erythromelalgia, a rare condition that primarily affects the feet and, less commonly, the hands. It is characterised by intense, burning pain of affected extremities, and increased skin temperature that may be episodic or almost continuous in nature.

In many cases, people with polycythaemia vera have a ruddy (red) complexion, and a reddening of the palms of the hand and soles of the feet, ear lobes, mucous membranes and the eyes. This is due to the high numbers of red cell in the circulation. A raised blood pressure (hypertension) is also common.
Blood clots (thrombosis) and bleeding

As the blood is thicker than normal it cannot flow as easily, especially through the smaller blood vessels. If left untreated, this increases the risk of thrombosis, the formation of a blood clot within a blood vessel. Blood clots can form in various parts of the body including the deep and superficial veins of the legs, in the heart (causing a myocardial infarction or heart attack) and in the brain (a stroke). Blood clots are a common complication of polycythemia vera and occur in around 30 per cent of people, even before they are diagnosed. Older people and those with a history of a previous blood clot are at increased risk. A major aim of treatment in polycythemia vera is to maintain a normal blood count and reduce your risk of thrombosis.

Bleeding and easy bruising can also occur. This is usually minor and occurs in around one quarter of all patients. Occasionally bleeding into the gut can be prolonged or severe.

HOW IS POLYCYTHAEMIA VERA DIAGNOSED?

Polycythemia vera is diagnosed using a combination of laboratory tests and a physical examination.

Full blood count

People with polycythemia vera have a high red cell count, haemoglobin level and haematocrit (>52 % in men or >48% in females) due to the excessive production of red cells. The haematocrit is the proportion of the whole blood that is made up of red cells. A raised white cell count (especially a raised neutrophil count) and a raised platelet count are also common findings.

The red cell mass is the total number of red cells circulating in your blood. Polycythemia vera may be diagnosed when the red cell mass is 25% greater than the average normal expected value. Other findings that help confirm the diagnosis of polycythemia vera include an enlarged spleen (splenomegaly) and the presence of the JAK2 mutation or other cytogenetic abnormalities in your blood or bone marrow cells.
Measuring your red cell mass

The blood test that measures your red cell mass may take a couple of hours to complete. It involves taking a sample of your blood from a vein in your hand or arm, mixing it with a special substance called an isotope, and reinjecting it back into your bloodstream. After this more blood tests are taken over the next hour to measure your red cell mass and compare it to expected normal values.

JAK2 Mutation testing

JAK2 mutations (particularly the V617F mutation) can be found in >95% of people with Polycythaemia vera. This test can be performed on a blood sample and will help to confirm the diagnosis of a myeloproliferative neoplasm. It doesn’t help distinguish polycythaemia vera from essential thrombocythaemia or primary myelofibrosis.

Bone marrow examination

In polycythaemia vera the bone marrow is often very active with abnormally high numbers of cells. Iron stores may be depleted since iron is being used to make more and more red cells.

Bone marrow aspirate and biopsy

A procedure that involves removing a sample of the liquid bone marrow and a small core of bone marrow for examination in the laboratory. The biopsy (or trephine) is taken under local or general anaesthetic, from the back of the pelvis (hip girdle).

Other possible blood tests

- serum vitamin B-12 levels
- uric acid levels
- erythropoietin levels
- coagulation studies (to see if your blood is clotting normally)
- blood oxygen levels
Other possible tests

- Chest X-ray – to rule out lung disease
- Abdominal ultrasound and / or CT scan – to rule out kidney disease and measure spleen / liver size

**HOW IS POLYCYTHAEMIA VERA TREATED?**

The goal of treatment for polycythaemia vera is to reduce the number of cells in your blood and help you to maintain a normal blood count. This helps control any symptoms of your disease and reduces the risk of complications due to blood clotting, or bleeding. The treatment, or combination of treatments chosen for you will depend on several factors including the duration and severity of your disorder, whether or not you have a history of blood clots, your age and your general health.

**Venesection**

Venesection (or phlebotomy) is a procedure in which a controlled amount of blood is removed from your bloodstream. This procedure is commonly used when people are first diagnosed with polycythaemia vera because it can help to rapidly reduce a high red cell count. In a process similar to a blood donation, 450mls to 500mls of your blood is removed, usually from a large vein in the arm, inside the elbow bend. This is usually done in the outpatient’s department of the hospital. It takes about 30 minutes to complete. You will need to have a blood test before to check your blood count, and you must make sure you drink plenty of water before and after the procedure.

This procedure may need to be repeated frequently at first, usually every few days, until your haematocrit is reduced to the desired level. After this, you may need to have the procedure repeated periodically, for example at monthly intervals, to help maintain a normal blood count.

For many people, particularly younger patients and those with mild disease, regular venesection (every few months) may be all that is needed to control their disease for many years.

Many people with polycythaemia vera also need other treatments in addition to, or instead of venesection, to help control their blood count.
Myelosuppressive Drugs

Myelosuppressive (bone marrow suppressing) drugs or chemotherapy are commonly used to reduce blood cell production in the bone marrow. These drugs are commonly used for people with an extremely high platelet count, complications due to blood clotting or bleeding, or symptoms of an enlarged spleen. They are also used for some people who are unable to tolerate venesection or whose disease is no longer responding to venesection.

The most commonly used myelosuppressive agent is a chemotherapy drug called hydroxyurea. It is particularly useful in controlling a high platelet count (thrombocytosis) and therefore reducing the risk of blood clots. Hydroxyurea is taken in the form of a capsule at home every day. As hydroxyurea is a chemotherapy drug, it is known to affect fertility and should be avoided during pregnancy for it can cause harm or death to the foetus. If this could be an issue for you, you should ask your haematologist about your options.

Another less commonly used chemotherapy drug is busulphan. This drug is also given in tablet form.

Chemotherapy taken in capsule form is tolerated well by most people and side effects tend to be few and mild. As these drugs work by suppressing blood formation. Periodic blood tests should be performed when taking these drugs to monitor the blood count and to guard against severe reductions in the white cell or platelet counts.

There is a very small risk of developing leukaemia later on, in people who receive some chemotherapy for prolonged periods of time. It is still unclear whether there is a very small increase in the risk of leukaemia in people receiving hydroxyurea and this must be weighed against the potentially serious complications of uncontrolled disease (thrombosis). Discuss with your doctor if this is a concern to you.

Interferon

Interferon is a substance produced naturally by the body’s immune system. It plays an important role in fighting disease. In polycythaemia vera, interferon is sometimes prescribed for younger patients to help control the production of blood cells. Interferon is usually given three times a week as an injection under the skin.
(subcutaneous injection) using a very small needle. You or a family member (or friend) will be taught how to do this at home. A weekly injection is now available and is becoming more widely used.

Side effects of interferon can be unpleasant but they can be minimised by starting with a small dose, and building up to the full dose over several weeks. The main side-effects are flu-like symptoms such as chills, fevers, aches and pains and weakness. Your doctor or nurse will explain any side effects you might experience while you are having these treatments and how they can be managed.

**Other Treatments**

**Aspirin**

Many people are prescribed small daily doses of aspirin, which have been shown to significantly reduce the risk of thrombosis in people with polycythaemia vera. Aspirin works by preventing your platelets from clumping together to form harmful blood clots in different parts of your body.

Aspirin can irritate the lining of the stomach which can result in pain or discomfort in the stomach, causing nausea, heartburn or loss of appetite. Taking your aspirin with food or milk may help prevent this. In addition, many people are prescribed specially coated aspirin that allows the drug to pass through the stomach and into the intestine before being dissolved. This helps to reduce the risk of stomach upset. You should see your doctor if you are experiencing stomach upset while on aspirin.

Aspirin is taken at home in tablet form. Drug interactions can occur, so it is important to avoid taking other medications while you are on aspirin, unless you are advised to do so by your doctor.

**Anagrelide hydrochloride**

Anagrelide hydrochloride (Agrylin®) is a drug used to reduce high platelet counts in people with polycythaemia vera and essential thrombocythaemia. Anagrelide affects platelet-producing cells in the bone marrow called megakaryocytes, slowing down platelet production and therefore reducing the number of platelets in the circulating blood. This can help to reduce symptoms and the risk of clotting complications in the future. Although anagrelide lowers platelet counts to more normal levels, it does not affect the body’s
natural process to form a clot when needed. Anagrelide is taken in capsule form by mouth. It can be taken with or without food. The capsule strength and the number of times a day you need to take anagrelide will depend on your platelet count, your response to treatment and how well you tolerate the drug.

Your doctor will keep track of your response to anagrelide and adjust your dose as needed to maintain your platelet count at the desired level. Side effects are generally mild to moderate and may decrease with continued therapy. The most commonly reported side effects include headaches, fast or forceful heart beat (palpitations), diarrhoea, weakness, fluid retention, nausea, dizziness, abdominal pain and shortness of breath. You should report any side effects you are experiencing to your doctor as many of them can be treated to reduce any discomfort to you. You need to contact your doctor immediately if you experience the following symptoms: shortness of breath or difficulty breathing, swollen ankles, fast or irregular heart beat, and / or chest pain.

You should not stop taking this or any other medication for polycythaemia vera unless instructed by your doctor. Stopping these medications suddenly can be harmful.

**Radioactive phosphorus (\( ^{32}\text{P} \))**

Radioactive phosphorus (\( ^{32}\text{P} \)) is a radioisotope which may be used for long-lasting control of blood counts in older people. One or two doses of \( ^{32}\text{P} \) are usually given, by injection into a vein in the hand or arm, in the nuclear medicine department of the hospital. This substance is taken up and concentrated in bone marrow where it suppresses the overactive bone marrow and helps to control blood counts.

In addition to the treatments described above, your doctor will advise you on ways to stay healthy and reduce any ‘life-style’ factors that might increase your risk of thrombosis. For example you may be advised to stop smoking, and / or take a series of steps to maintain a healthy weight range and blood pressure.
PROGNOSIS

A prognosis is an estimate of the likely course of a disease. It provides some guide regarding the chances of curing the disease or controlling it for a given time.

The natural course of polycythaemia vera can vary considerably between individuals. In many patients, with treatment, the disease remains stable for long periods of time, often many years. In around 10% of all cases, polycythaemia vera transforms over time into another type of myeloproliferative neoplasm called myelofibrosis, and less commonly, in up to 3 per cent of cases into acute myeloid leukaemia.

In some people, polycythaemia progresses over time despite treatment. The spleen may become increasingly enlarged. Anaemia and thrombocytopenia (low numbers of circulating platelets) is common as the bone marrow is no longer able to produce adequate numbers of red cells or platelets. In addition, abnormal immature blood cells, known as blast cells may start to appear in the blood.

Treatment during this time is supportive and involves making every effort to improve the patient’s quality of life, by relieving any symptoms they might have and by preventing and treating any complications that arise from their disease or its treatment. This may involve blood transfusions if required, pain relief and careful myelosuppression.

In selected cases, surgical removal of the spleen, or low dose radiation to the spleen may be required to relieve symptoms.

Your doctor is the best person to give you an accurate prognosis regarding your disease as he or she has all the necessary information to make this assessment.
ESSENTIAL THROMBOCYTHAEMIA (ET)

Essential thrombocythaemia (ET) is a disorder in which too many platelets are produced in the bone marrow. Platelets are normally needed in the body to control bleeding. However, excess numbers of platelets can lead to abnormal blood clotting which can block the flow of blood in the blood vessels.

There are a number of conditions that can cause a rise in the number of platelets in the circulating blood (thrombocytosis). These include bleeding, infection and some types of cancer. In essential thrombocythaemia however, the blood platelet count is persistently elevated as a result of increased bone marrow production of platelets, in the absence of any identifiable cause.

Like polycythaemia vera, essential thrombocythaemia is a rare chronic disease diagnosed in an estimated 3 per 100,000 population. Although it can occur at any age, even (rarely) in children, essential thrombocythaemia usually affects older people, with most patients diagnosed between the ages of 50 and 70 years. It occurs equally in both males and females.

SYMPTOMS AND COMPLICATIONS OF ESSENTIAL THROMBOCYTHAEMIA

Many people have no symptoms when they are first diagnosed with essential thrombocythaemia and their disease is picked up accidentally during a routine blood test. However if symptoms do occur they generally include tingling or burning in the hands and feet, headache, visual problems, weakness and dizziness. These symptoms and others result from excessive numbers of platelets causing blockages in small or large blood vessels in different parts of the body.

An enlarged spleen is common and occurs in around 30 per cent of cases. Symptoms include feelings of discomfort, pain or fullness in the upper left-side of the abdomen. An enlarged spleen may also cause pressure on the stomach causing a feeling of fullness, indigestion and a loss of appetite. In some cases the liver may also be enlarged (hepatomegaly). Other symptoms include weight loss and generalised itching.
Blood clots (thrombosis) and bleeding

Thrombosis is a major complication of essential thrombocythaemia. Older patients and those with a high platelet count, or a prior history of thrombosis, may be at increased risk. A major aim of treatment in essential thrombocythaemia is to reduce your platelet count, and therefore your risk of thrombosis.

Blood clots can occur in large or small arteries interfering with the blood and therefore oxygen supply to various organs or tissues. Blockages in the smaller blood vessels in the toes and fingers can cause redness of the skin and burning and throbbing pains. These pains are often made worse by heat or exercise and relieved by cooling and elevating the affected area. These symptoms are often dramatically improved using small daily doses of aspirin, and / or reducing the patient’s platelet count.

Blockages in the arteries supplying the heart (causing a myocardial infarction or heart attack), kidneys or brain (causing a stroke) can be serious and can lead to significant tissue damage or ischaemia (tissue death). Blood clots can also develop in the veins of the legs (causing deep vein thrombosis), and less commonly, the spleen and liver occluding the blood flow and causing pain in these areas. A blood clot that breaks off the wall of the vein and travels in the blood stream is known as an embolism. When a blood clot travels to the lungs it is known as a pulmonary embolism and can cause breathing problems.

Less commonly, people experience symptoms of abnormal bleeding including bruising for no apparent reason, or exaggerated or prolonged bleeding following minor cuts or injury. Some people notice frequent or severe nose bleeds or bleeding gums and some women may have unusually heavy menstrual periods.

In pregnancy, uncontrolled essential thrombocythaemia can reduce the blood supply to the placenta or foetus. This can cause problems with foetal growth and may in some cases lead to miscarriage.

HOW IS ESSENTIAL THROMBOCYTHAEMIA DIAGNOSED?

The diagnosis of essential thrombocythaemia is only made when other causes of a raised platelet count have been excluded.
Full blood count

A persistently raised platelet count is the most common sign of essential thrombocythaemia. The platelet count can range from slightly higher than normal to many times higher than normal. Under the microscope the platelets may be abnormally large and pale blue-stained. Fragments of megakaryocytes, the cells from which platelets are released, may also be seen in the blood film. Around a third of people with essential thrombocythaemia will also have a mildly raised red cell and/or white cell count.

If the results of your blood test suggest that you may have essential thrombocythaemia, further investigation and tests including a bone marrow examination may be required to help confirm the diagnosis and rule out other secondary or ‘reactive’ causes of a raised platelet count.

Bone marrow examination

In essential thrombocythaemia the bone marrow is usually found to be overactive, similar to polycythaemia vera. An excess number of abnormal megakaryocytes is a common finding. Cytogenetic and molecular analysis of blood and bone marrow cells may be carried out to help confirm the diagnosis. A mutation in the JAK2 gene is found in a significant proportion (50-60%) of people with ET. Mutations in the c-MPL gene (which produces a protein that responds to a growth factor that stimulates platelet production) account for approximately 10% of cases.

Other blood tests may be done to check your general health and how well your kidneys, liver and other vital organs are functioning.

HOW IS ESSENTIAL THROMBOCYTHAEMIA TREATED?

The goal of treatment for people with essential thrombocythaemia is to prevent complications like abnormal bleeding and bruising and in some cases reducing the number of platelets in the blood. You may not have any symptoms of essential thrombocythaemia when you are first diagnosed and therefore may not require any treatment for some time. Instead your doctor may recommend a ‘watch and wait’ strategy (also called actively monitoring) which involves regular check-ups and blood counts to carefully
monitor your health. In addition he or she will advise you on the steps you can take to stay healthy and reduce any ‘lifestyle-related’ risk factors you may have that increase your chances of developing a blood clot. You may be advised for example on ways to help you stop smoking, and / or maintain a healthy weight range and blood pressure.

For the majority of people, essential thrombocythaemia will require some form of treatment to reduce their platelet count and therefore their risk of thrombosis. The treatment chosen for you will depend on a number of factors that influence your particular risk of complications due to thrombosis or bleeding. These include your age, platelet count and whether or not you have had any previous episodes of blood clots or bleeding in the past. A history of smoking or high blood pressure can affect your risk of thrombosis. These factors and others are taken into account when planning the most appropriate treatment for your disease.

For people at **high-risk** of thrombosis, a chemotherapy drug called hydroxyurea (see polycythaemia vera for a discussion of this and other treatments which are also frequently used in essential thrombocythaemia) with or without low-dose aspirin is often used as first-line treatment. Hydroxyurea works by suppressing the function of your bone marrow and thereby controlling platelet production, while aspirin prevents your platelets from aggregating and forming harmful clots in your body.

Anagrelide hydrochloride (Agrylin®) and interferon (see polycythaemia vera) may also be used. Anagrelide slows down platelet production in your bone marrow, thereby helping to reduce symptoms and your risk of thrombosis. Interferon works by suppressing the abnormal megakaryocyte clone in your bone marrow thereby reducing the overproduction of platelets.

Those at **low-risk** may be simply treated using low-dose aspirin or an equivalent drug alone. They usually have a very good outlook with no difference to the general population.

Your doctor will be able to discuss with you all of the treatment options suitable for you.

**Plateletpheresis**

If your platelet count is very high and you have symptoms of clotting or bleeding, your platelet count will need to be reduced quickly
to prevent further complications. In these emergency situations, excess platelets can be removed from your bloodstream using a procedure known as plateletpheresis. During this procedure all your blood is gradually passed through a special machine called a cell separator. The blood is drawn from a cannula (plastic needle) placed in a vein in one arm. The machine spins the blood very quickly and removes the excess platelets. This is a continuous process. While platelets are being removed the rest of your blood is being returned to you via another cannula, placed in your other arm. If your veins are not suitable for this procedure, a special catheter device can be inserted into a large vein and might be used instead. This line allows blood to be drawn from one of the bigger veins in your body when your smaller veins are hard to access.

Plateletpheresis is usually carried out in hospital. It usually takes about two hours to complete.

**PROGNOSIS**

Essential thrombocythaemia is regarded as an incurable disease but treatment allows many people’s disease to remain stable for long periods of time, often 10-20 years or more. In the longer term, a small number of people with essential thrombocythaemia may develop myelofibrosis. The risk of transforming to acute myeloid leukaemia is relatively low (<1 per cent).

Your doctor is the best person to give you an accurate prognosis regarding your disease as he or she has all the necessary information to make this assessment.
PRIMARY MYELOFIBROSIS

Primary myelofibrosis (also called chronic idiopathic myelofibrosis, agnogenic myeloid metaplasia) is a disorder in which normal bone marrow tissue is gradually replaced with a fibrous scar-like material. Over time, this leads to progressive bone marrow failure.

Under normal conditions, the bone marrow provides a fine network of fibres on which the stem cells can divide and grow. Specialised cells in the bone marrow known as fibroblasts make these fibres.

In primary myelofibrosis, chemicals released by high numbers of platelets and abnormal megakaryocytes (platelet forming cells) over-stimulate the fibroblasts. This results in the overgrowth of thick coarse fibres in the bone marrow, which gradually replace normal bone marrow tissue. Over time this destroys the normal bone marrow environment, preventing the production of adequate numbers of red cells, white cells and platelets. This results in anaemia, low platelet counts and the production of blood cells in areas outside the bone marrow for example in the spleen and liver, which become enlarged as a result.

Primary myelofibrosis is a rare chronic disorder diagnosed in an estimated 1 per 100,000 population. It can occur at any age but is usually diagnosed later in life, between the ages of 60 and 70 years. The cause of primary myelofibrosis remains largely unknown. It can be classified as either JAK2 mutation positive (having the JAK2 mutation) or negative (not having the JAK2 mutation).

Long-term exposure to high levels of benzene or very high doses of ionising radiation may increase the risk of primary myelofibrosis in a small number of cases. Around one third of people with myelofibrosis have been previously diagnosed with polycythaemia (post-polycythaemic myelofibrosis) or essential thrombocythaemia (post-ET myelofibrosis).

SYMPTOMS AND COMPLICATIONS OF PRIMARY MYELOFIBROSIS

Around 20 per cent of people have no symptoms of primary myelofibrosis when they are first diagnosed and the disorder is picked up incidentally as a result of a routine blood test. For others, symptoms develop gradually over time. Symptoms of anaemia are
common and include unexplained tiredness, weakness, shortness of breath and palpitations. Other nonspecific symptoms include fever, unintended weight loss, pruritus (generalised itching) and excess sweating, especially at night.

Virtually all patients with primary myelofibrosis have an enlarged spleen (splenomegaly) when they are first diagnosed. In around a third of cases the spleen is very enlarged. Common symptoms include feelings of discomfort, pain or fullness in the upper left-side of the abdomen. An enlarged spleen may also cause pressure on your stomach causing a feeling of fullness, indigestion and a loss of appetite. Abdominal discomfort can also result from an enlarged liver (hepatomegaly), which occurs in around two-thirds of cases.

Other less common symptoms include bone and joint pain, and bleeding problems.

**HOW IS MYELOFIBROSIS DIAGNOSED?**

Primary myelofibrosis is diagnosed using a combination of a physical examination showing the presence of an enlarged spleen, blood tests and a bone marrow examination. Primary myelofibrosis is only diagnosed when other causes of marrow fibrosis (including leukaemia, lymphoma, other types of cancer that have spread to the bone marrow) have been ruled out.

**Full blood count**

People with primary myelofibrosis commonly present with varying degrees of anaemia. When examined under the microscope the red cells are often described as being ‘teardrop-shaped’. Higher than normal numbers of white cells and platelets may be found in the early stages of this disorder, but low white cell and platelet counts are common in more advanced disease.

**Bone marrow examination**

It is frequently impossible to obtain any samples of bone marrow fluid using a needle and syringe (bone marrow aspiration) due to marrow fibrosis. This is known as a ‘dry tap’. The bone marrow trephine biopsy typically shows abnormal fibrosis of the marrow cavity.

Cytogenetic and molecular analysis of blood and bone marrow cells is also carried out to help confirm the diagnosis and may
help with prognosis. A mutation in JAK2 is found in about 50% of people with primary myelofibrosis. It is unclear at present why some patients with mutations in JAK2 develop myelofibrosis and others don’t.

**HOW IS MYELOFIBROSIS TREATED?**

Some people have no symptoms when they are first diagnosed with primary myelofibrosis and do not require treatment straight away, apart from regular check-ups with their doctor to carefully monitor their disease.

For others treatment is largely supportive and is aimed at preventing complications due to low blood counts and an enlarged spleen (splenomegaly). This involves making every effort to improve your quality of life, by relieving any symptoms of anaemia or an enlarged spleen, and preventing and treating any complications that might arise from your disease or its treatment. This may include periodic blood transfusions and taking antibiotics to prevent and treat any infections.

A chemotherapy drug such as hydroxyurea (see polycythaemia vera), or low-doses of a drug called thalidomide may be used to reduce an enlarged spleen. In some cases, the surgical removal of the spleen (splenectomy) may be considered, especially when your spleen has enlarged so much that it is causing severe symptoms. A splenectomy may also be considered if you have an increased need for blood transfusions. This sometimes happens because the spleen is destroying blood cells, particularly platelets, at a very fast rate. Small doses of radiation to the spleen can also be given to reduce its size. This usually provides temporary relief for about 3 to 6 months.

Some younger patients who have a suitably matched donor may be offered an *allogeneic* (donor) *stem cell transplant*. This is a medical procedure that offers the only chance of cure for patients with myelofibrosis. It involves the use of very high doses of chemotherapy, with or without radiotherapy, followed by infusion of blood stem cells, which have been donated by a suitably matched donor. Stem cell transplants carry significant risks and are only suitable for a small minority of younger patients (usually under 60 years of age).
Jak2 Inhibitors
While no Jak2 inhibitors are currently licenced for use in Australia, a number may be available in clinical trials or may become available soon. These agents are tablets which work by blocking Jak2 which may lead to a reduction in splenomegaly and decreased symptoms. They also appear to work in some patients with myelofibrosis without the Jak2 mutation. Side effects may include worsening anaemia or a low platelet count.

Blood and Platelet 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) when the platelet count is below a critical level.

You do not need to be admitted to hospital for a red blood cell or platelet transfusion. They are usually given in the outpatient department. 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 and shivery or in any way unwell during the transfusion, as this might indicate that you are having a reaction. Steps can be taken to minimise these symptoms and ensure that they don’t happen again.

PROGNOSIS
Primary myelofibrosis is generally regarded as an incurable disease but with treatment many people can remain comfortable and symptom-free for some time.

The natural course of the disease can vary considerably between individuals. In some people their disease remains stable for long periods and they are free to live a normal life with minimal interruptions from their disease or its treatment. For others, myelofibrosis progresses more quickly and people require treatment to help relieve symptoms of their disease. Transformation to a type
of leukaemia called acute myeloid leukaemia occurs in between 10 and 20 per cent of cases.

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

**CHRONIC EOSINOPHILIC LEUKAEMIA/HYPEREOSINOPHILIC SYNDROME**

Chronic eosinophilic leukaemia is a rare myeloproliferative neoplasm in which too many eosinophils (a type of white blood cell) are made in the bone marrow. These cells spill out of the bone marrow and accumulate in the blood and other tissues around the body. This disorder is diagnosed by a full blood count showing persistently elevated numbers of eosinophils. Many patients carry the FIP1L1-PDGFR alpha mutation.

Some people with chronic eosinophilic leukaemia don’t have any symptoms and the disease is picked up incidentally during a routine blood test. Others may go to their doctor because they have one or more of a range of symptoms including fever, fatigue, cough, muscle pains, pruritis (generalised itching) and diarrhoea.

Chronic eosinophilic leukaemia is a rare disease and its natural course can vary considerably between individuals. The disease may remain stable for many years, even decades, or it may quickly progress and transform to acute leukaemia. For this reason, the most appropriate treatment for each patient is decided on an individual basis. Treatment may include corticosteroids, chemotherapy drugs such as hydroxyurea, and interferon therapy. Some patients may respond to a newer drug called imatinib mesylate (GLIVEC®), most often used in the treatment of another type of MPN called chronic myeloid leukaemia. A stem cell transplant may be considered in selected cases.
CHRONIC NEUTROPHILIC LEUKAEMIA

Chronic neutrophilic leukaemia is another rare myeloproliferative neoplasm in which too many neutrophils are made in the bone marrow. These cells spill out into the circulating blood and tend to accumulate in the liver and spleen, which become enlarged as a result.

Chronic neutrophilic leukaemia is usually a slowly progressing disease, closely related to another type of leukaemia called chronic myeloid leukaemia. Its natural course can vary considerably between individuals with survival times ranging from 6 months to over 20 years. Treatment options may include the use of chemotherapy drugs such as busulphan or hydroxyurea, which are given in tablet or capsule form. These drugs are used to control the high white cell count.
SYSTEMIC MASTOCYTOSIS OR MAST CELL DISEASE

Systemic mastocytosis or mast cell disease is a disorder that results from the overproduction of mast cells (a type of white blood cell), in the bone marrow. These cells accumulate in the blood, lymph nodes (glands), skin and other body tissues. Excess numbers of mast cells release large amounts of histamine and other substances which can cause allergic type reactions in affected tissues. For example, when these substances collect in the skin they tend to cause an itchy rash. Other allergic type symptoms may include abdominal pain and difficulty breathing. Over 90% of patients with systemic mastocytosis carry a mutation in the c-KIT gene.

Medications known as antihistamines are used to prevent and reduce allergic reactions. Treatment decisions tend to be made on an individual basis and may include chemotherapy in tablet form and / or interferon to help control the overproduction of mast cells in the bone marrow. Research indicates new tyrosine kinase inhibitors may also be useful as a treatment therapy in some people.
COMPLEMENTARY THERAPIES

Complementary therapies are therapies which are not considered standard medical therapies. Many people however 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 and relaxation.

Complementary therapies should ‘complement’ or assist with recommended medical treatment for myeloproliferative neoplasms. They should not be used as an alternative to medical treatment for MPN. It is important to realise that no complementary or alternative treatment alone has proven to be effective against MPN.

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 balanced and nutritious diet*.

If you are thinking about using herbs or vitamins it is very important to talk this over with your doctor first. Some of these substances can interfere with the effectiveness of chemotherapy or other treatments you are having.

*There is a separate Leukaemia Foundation booklet called ‘Eating Well: a practical guide for people living with leukaemias, lymphomas and myeloma’, that provides more detail.
MAKING TREATMENT DECISIONS

Many people feel overwhelmed when they are diagnosed with a myeloproliferative neoplasm. 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 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.

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.

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.

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 wellbeing. 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 that this is necessary.
Clinical Trials

Clinical trials (also called research studies) test new treatments or ‘existing’ 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. In addition, 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 informed consent. Talk to your doctor as they can guide you in making the best decision for you.

Informed consent

Giving an informed consent means that you can 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 ask for more information from your doctor.

“How can I help with blood cancer research?”

The Australasian Leukaemia and Lymphoma Group (ALLG - clinical trials research group) has established a national Leukaemia and Lymphoma Tissue Bank at the Princess Alexandra Hospital in Brisbane. The Tissue Bank is a temperature controlled facility for storing clinical tissue samples to be used in approved research into leukaemia, lymphoma, myeloma and related blood disorders. Current research focuses on understanding the development of cancers, why different patients respond differently to current treatments and more effective therapies, especially those being

*You can also refer to the information sheets about clinical trials on our website. There are also questions that you can ask your doctor. See www.leukaemia.org.au
assessed in clinical trials. The clinical tissue samples used for this research come from blood and bone marrow samples from patients’ routine testing and from samples taken for monitoring during clinical trials.

In order to donate your blood and/or bone marrow samples to the Tissue Bank you will need to sign a consent form at the time of your diagnosis. This can be obtained from your clinician. Be assured, donating does not involve any additional procedures, it simply involves saving and storing in the Tissue Bank any excess blood or bone marrow extracted during your routine tests. Samples are also welcomed from relapsed patients at re-diagnosis.

The donation of your tissue sample is an invaluable way to support blood cancer research and could bring us closer to finding a cure. Tissues from blood cancer patients are precious materials for researchers because these cancers are relatively rare and are vital for finding cures. For further information on the ALLG Leukaemia and Lymphoma Tissue Bank, contact the Leukaemia Foundation: 1800 620 420.
INFORMATION AND SUPPORT*

People cope with a diagnosis of a myeloproliferative neoplasm in different ways, and there is no right or wrong or standard reaction. For some people the diagnosis can trigger any number of emotional responses ranging from denial to devastation. It is not uncommon to feel angry, helpless and confused. Naturally people fear for their own lives or that of loved ones.

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 including social workers or nurses who have been specially educated to take care of people with blood and bone marrow diseases. Some people find it useful to talk with other patients and family members who understand the complexity of feelings and the kinds of 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 don’t hesitate to request additional support from a mental health professional.

Many people are concerned about the social and financial impact of the diagnosis and treatment on their families. Normal family routines are often 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.

There are a variety of programs designed to help ease the emotional and financial strain created by blood cancers and related disorders. The Leukaemia Foundation is there to provide you and your family with information and support to help you cope during this time. Contact details for the Leukaemia Foundation are provided on the back of this booklet.

*There is a separate Leukaemia Foundation booklet called ‘Living with Leukaemias, Lymphomas, Myeloma & Related Disorders’. This booklet addresses the impact of the diagnosis, family matters, support, survivorship, and other general issues around treatment.
USEFUL INTERNET ADDRESSES

- Leukaemia Foundation
  www.leukaemia.org.au
- American Cancer Society
  www.cancer.org
- Australian Bone Marrow Donor Registry
  www.abmdr.org.au
- Cancer Council of Australia
  www.cancer.org.au
- Leukaemia Foundation’s On-line Support group
  www.talkbloodcancer.com
- Leukemia & Lymphoma Society of America
  www.leukemia.org
- Leukaemia & Lymphoma Research Fund (UK)
  www.beatbloodcancers.org
- Look Good … Feel Better program
  www.lgfb.org.au
- MacMillan Cancer Support
  www.macmillan.org.uk
- MPN Research Foundation (USA)
  www.mpnresearchfoundation.org
- National Cancer Institute (USA)
  www.cancer.gov/cancerinfo
- The Myeloproliferative Disorders Research Consortium (USA)
  http://www.mpd-rc.org/home.php
- MPN Education Foundation
  http://www.mpninfo.org/
GLOSSARY OF TERMS

Acute leukaemias
Rapidly progressing cancers of the blood and bone marrow, usually of sudden onset and characterised by uncontrolled growth of immature blood cells which crowd the bone marrow and spill out into the bloodstream.

Acute myeloid leukaemia (AML)
A rapidly progressing cancer of the blood and bone marrow. AML affects developing blood cells on the myeloid cell line, usually white blood cells. It is more common in adults than in children.

Allogeneic stem cell transplant
The transplant of blood stem cells from one person to another. The donor is usually a sister or brother or an unrelated volunteer donor.

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

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

Antibiotic
A drug used to prevent or treat bacterial infections.

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
A drug which prevents or reduces feelings of sickness (nausea) and vomiting.

Anti-fungal
A drug used to prevent or treat fungal infections.
**Antigen**
A substance, usually on the surface of a foreign body such as a virus or bacteria that stimulates the cells of the body’s immune system to react against it by producing antibodies.

**Antihistamine**
A drug used to prevent or reduce allergic reactions.

**Anti-viral**
A drug used to prevent or treat viral infections.

**Blast cells**
Immature blood cells normally found in the bone marrow. Blast cells normally constitute up to 5 per cent of all bone marrow cells. These cells divide and replenish all the normal blood cells in the marrow and circulating blood. Acute leukaemia is characterised by an accumulation of abnormal blast cells that take over the marrow and spill out into the blood stream.

**Blood cells**
There are three main types of cells. Red blood cells carry oxygen, white blood cells fight infection, and platelets help prevent bleeding. Normal numbers of each cell type must be maintained for the body to remain healthy.

**Blood count**
Also called a full blood count (FBC). A routine blood test that measures the number and type of cells circulating in the blood.

**Blood stem cells**
Primitive blood-forming cells that normally live in the bone marrow. They divide and mature into all the different types of blood cells (red cells, white cells and platelets), including the cells of our immune system.

**B-cell**
A type of white cell normally involved in the production of antibodies to combat infection.
Bone marrow
The tissue found at the centre of many flat or big bones of the body. 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.

Bone marrow aspirate
A procedure that involves removing a small sample of bone marrow fluid for examination in the laboratory. The fluid is drawn, under local or general anaesthetic, usually from the back of the hip, or occasionally from the breastbone.

Bone marrow biopsy
A procedure that involves removing a small core of bone marrow for examination in the laboratory. The biopsy (or trephine) is taken under local or general anaesthetic, from the back of the hip. It is usually done at the same time as the bone marrow aspirate.

Bone marrow transplant
See stem cell transplant.

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)
Also known as a central venous access device (CVAD). A line 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. Nausea and vomiting are also common, but nowadays largely preventable with modern anti-nausea medication. Most side-effects of 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.

Chronic leukaemias
A group of cancers that affect the blood and bone marrow. Chronic leukaemias usually develop gradually and slowly progress, particularly in the early stages of disease. The leukaemia is called chronic because it the leukaemic cells are more mature than those found in acute leukaemia. Chronic leukaemias are sometimes diagnosed by chance, during a routine blood test.

Chronic myeloid leukaemia (CML)
A type of leukaemia which is an initially slow growing (indolent) disease where the bone marrow produces too many white cells. Over time, CML rarely transforms into acute leukaemia, a more aggressive type of disease where the bone marrow produces large numbers of abnormal immature granulocytes, known as blast cells or leukaemic blasts. CML is also called chronic myelogenous or chronic granulocytic leukaemia (CGL).

Clone
A population of genetically identical cells arising from a single parent cell.

Clotting factors
A group of naturally occurring substances found in the blood (factors I to XIII) which, when activated, interact to help blood clot and prevent bleeding.
**Coagulation**
Clotting of the blood. A complex process involving the interaction a series of biochemical components and blood cells known as platelets.

**Computerised axial tomography (CT scan or CAT scan)**
A specialised x-ray or imaging technique that produces a series of detailed three dimensional (3D) images of cross sections of the body.

**Corticosteroids (steroids)**
A group of man-made hormones including prednisone, prednisolone, methylprednisolone and dexamethasone used in the treatment of certain blood and bone marrow cancers. As well as having anti-cancer effects, corticosteroids also have anti-inflammatory and immunosuppressive (anti-rejection) effects.

**Cytogenetic tests**
The study of the genetic make-up of the cells, in other words, the structure and number of chromosomes present. Cytogenetic tests are commonly 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.

**Cytokines**
See growth factors.

**Cytopenia**
A reduction in the number of blood cells circulating in the bloodstream.

**Disease progression**
This means that the disease is getting worse despite treatment.

**Echocardiogram**
A special ultrasound scan of the heart.

**Electrocardiogram (ECG)**
Electrical trace of the heart.
**Essential thrombocytemia**
A condition caused by abnormal bone marrow growth (myeloproliferative disease). It is characterised by the production of large numbers of platelets. Symptoms include bleeding, blood clots and enlargement of the spleen.

**Growth factors**
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 or bone marrow or peripheral blood cell transplantation. For example G-CSF (granulocyte colony stimulating factor).

**Haemoglobin**
The iron containing pigment in red blood cells, which carries oxygen to all the body’s tissues.

**Haemopoiesis**
The formation of blood cells.

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

**Idiopathic myelofibrosis (see Primary myelofibrosis)**
A type of myeloproliferative neoplasm in which bone marrow tissue is replaced with abnormal fibrous tissue and is unable to produce adequate numbers of blood cells.

**Immune system**
The body’s defense system against infection and disease.

**Immunocompromised**
When the function of the immune system is reduced

**Immunophenotyping**
Specialised laboratory tests used to detect markers on the surface of cells. These markers identify the origin of the cell.

**Immunosuppression**
The use of drugs to reduce the function of the immune system.
Leukaemia
A cancer of the blood and bone marrow characterised by the widespread, uncontrolled production of large numbers of abnormal and/or immature 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.

Leukaemic blasts
Abnormal immature blood cells that multiply in an uncontrolled manner, crowding out the bone marrow and preventing it from producing normal blood cells. These abnormal cells also spill out into the blood stream and can accumulate in other organs.

Lymph nodes or glands
Structures found throughout the body, for example in the neck, groin, armpit, chest and abdomen, which contain both mature and immature lymphocytes. There are millions of very small lymph glands in all organs of the body.

Lymphocytes
Specialised white cells that help defend 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.

Lymphoid
Term used to describe a pathway of maturation of blood cells in the bone marrow. White blood cells (B-lymphocytes and T-lymphocytes) are derived from the lymphoid stem cell line.

Matched (Volunteer) unrelated donor (MUD) transplant
An allogeneic stem cell transplant where the donor is unrelated to the patient, but with a similarly matched tissue type. Also called voluntary unrelated donor (VUD) transplant.

Malignancy
A term applied to tumours characterised by uncontrolled growth and division of cells (see cancer).

Mucositis
An inflammation of the lining of the mouth, throat or gut.
**Mutation**

A change in the DNA code of a cell, caused for example by exposure to hazardous chemicals or copying errors during cell division. If mutations affect normal cell function this can lead to the development of disease due to the loss of normal function or the development of abnormal functions of that cell.

**Myeloid**

Term used to describe a pathway of maturation of blood cells in the bone marrow. Red cells, white cells (neutrophils, eosinophils, basophils and monocytes) and platelets are derived from the myeloid stem cell line.

**Myelodysplastic disorders**

Also known as myelodysplastic syndromes (MDS). These are a group of blood diseases that affect normal blood cell production in the bone marrow. In MDS, the bone marrow produces too few red cells, white cells and platelets, and an excess of immature blood cells known as blast cells.

**Myelofibrosis**

A disorder in which the bone marrow becomes replaced by fibrous tissue and is unable to produce adequate numbers of blood cells.

**Myeloproliferative neoplasms**

A group of disorders characterised by the over-production of blood cells by the bone marrow. One or more of the cell families - red, white, platelets or support tissue, may be involved and treatment varies depending on the type and severity of the disease. Includes chronic myeloid leukaemia, polycythemia rubra vera, essential thrombocythemia and idiopathic myelofibrosis.

**Neoplasm (or Clonal disorder).**

A disease where there is an abnormal growth of cells arising from a single mutant cell.

**Neutropenia**

A reduction in the number of circulating neutrophils, an important type of white cell. Neutropenia is associated with an increased risk of infection.
Neutrophils
Neutrophils are the most common type of white cell. They are needed to mount an effective fight against infection, especially bacteria and fungi.

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

Petechiae
Red or purple flat pinhead sized spots on the skin, especially on the legs. They are caused by tiny bleeds under the skin, usually as a result of a severe shortage of platelets.

PICC line
Peripherally inserted central venous catheter (see central venous catheter). It is inserted in the middle of the forearm. PICCs are sometimes used for people having chemotherapy.

Platelets
Tiny disc-like fragments that circulate in the blood and play an important role in clot formation.

Prognosis
An estimate of the likely course of a disease.

Purpura
Purple spots on the skin, often accompanied by bleeding from the gums. It is caused by a shortage of platelets as well as fragile skin.

Radiotherapy (radiation therapy)
The use of high energy x-rays to kill cancer cells and shrink tumours.

Relapse
The return of the original disease.

Resistant or refractory disease
This means that the disease is not responding to treatment.

Remission
When there is no evidence of disease detectable in the body. This is not the same as a cure as relapse may still occur.
**Spleen**
An organ that accumulates lymphocytes, acts as a reservoir for red cells for emergencies, and destroys blood cells at the end of their lifespan. The spleen is found high in the abdomen on the left-hand side. It cannot normally be felt on examination unless it is enlarged. It is often enlarged in diseases of the blood or bone marrow – this is known as hypersplenism or splenomegaly.

**Splenomegaly**
Another term used to describe an enlarged spleen.

**Stable disease**
When the disease is stable it is not getting any worse or any better with treatment.

**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 cells in the body. Bone marrow (blood) stem cells have the ability to grow and produce all the different blood cells including red cells, white cells and platelets.

**Stem cell transplant**
General name given to bone marrow and peripheral blood stem cell transplants. These treatments are used to support the use of high-dose chemotherapy and/or radiotherapy in the treatment of a wide range of cancers including leukaemia, lymphoma, myeloma and other serious diseases.

**Thrombocytopenia**
A reduction in the number of circulating platelets. Thrombocytopenia is associated with an increased risk of bleeding and bruising.

**T-cell**
A type of white cell involved in controlling immune reactions.

**Ultrasound**
Pictures of the body’s internal organs built up from the interpretation of reflected sound waves.

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

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:

- Bankcard - Visa - Mastercard - Amex - Diners

__ __ __ __ / __ __ __ __ / __ __ __ __ / __ __ __ __ / __ __ __

Cardholder’s name: ...........................................................................
Cardholder’s signature: ........................................................................
Expiry date: ......../........
Contact Telephone number: .............................................................

Please send to:
The Leukaemia Foundation
GPO Box 9954
in your Capital City.
Please send me a copy of the following information booklets:

- Eating well: a practical guide for people living with leukaemias, lymphomas & myeloma
- Living with Leukaemias, Lymphomas, Myeloma & Related Disorders, Information and Support
- Understanding Allogeneic Transplants
- Understanding Autologous Transplants

Please send me the following:

- Regular copies of MPN News
- Information on the Foundation’s activities

Or information about:

- The Leukaemia Foundation’s Support Services
- MPN Telephone Forums
- Workplace giving
- Regular deduction scheme
- National Fundraising Campaigns
- Leaving the Leukaemia Foundation in my will
- Volunteering
- How I or my family/friends can help the work of the Foundation

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.au

Further information is available on the Leukaemia Foundation’s website
www.leukaemia.org.au
Understanding Myeloproliferative Neoplasms (MPN)

Formally called Myeloproliferative Disorders (MPD)

Including
- Polycythaemia vera
- Essential thrombocythaemia
- Idiopathic myelofibrosis

A guide for patients and families

Printed by:

February 2013

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.

Please support our work by calling 1800 620 420 or by mailing your donation to:
The Leukaemia Foundation
GPO Box 9954
in your capital city

WP #11