leukaemia & blood cancer NEW ZEALAND

Vision to Cure. Mission to Care.

MYELOPROLIFERATIVE NEOPLASMS – PRIMARY MYELOFIBROSIS (MF)

A fact sheet for patients, families and whānau

WHAT IS A MYELOPROLIFERATIVE NEOPLASM (MPN)?

MPNs are a group of diseases in which the bone marrow makes too many cells (either red blood cells, white blood cells or platelets). MPNs are a type of blood cancer. There are four main types of chronic myeloproliferative (my-low-pro-lif-er-a-tiv) neoplasms:

- Essential thrombocythaemia (ET)
- Polycythaemia vera (PV)
- Primary myelofibrosis (MF)
- Chronic myeloid leukaemia (CML)

Less common types of MPNs include:

- Chronic eosinophilic leukaemia (CEL)
- Chronic neutrophilic leukaemia (CNL)

Your blood

Blood is made up of blood cells and plasma. Plasma is a light-yellow coloured liquid in which blood cells travel around your body.

You have three main types of blood cells, which are red blood cells, platelets and white blood cells. These blood cells are created in your bone marrow and are then released into your bloodstream so they can be used.

Bone marrow is the spongy material inside your bones (see Figure 01). In your bone marrow there are cells called blood stem cells. Blood stem cells create the new blood cells in your body.

Red blood cells transport oxygen from the lungs to all the cells in the body. There is a protein called haemoglobin (heem-a-glow-bin) in each red blood cell that carries the oxygen throughout the body and gives it the red colour. A low level of haemoglobin in your body is called anaemia (a-nee-me-a).

White blood cells fight infections. If your white blood cell count is low, you are more at risk of getting an infection. There are five different types of white blood cells that work slightly differently to protect the body against infection. Neutrophils (new-tra-fils) are the most common type of white blood cell and are the first-line defence against bacteria entering your body. A low amount of neutrophils in your body is called neutropenia (new-tra-pee-nee-a).

Platelets help your blood to clot and prevent or stop bleeding. For example, if you get a cut, the platelets go to where the injury is, stick together and stop the bleeding (see Figure 02 for the different cells in your blood).

What is primary myelofibrosis (MF)?

Primary myelofibrosis (my-low-fibe-row-sis) is a serious blood disorder where abnormal cells in the bone marrow cause scarring, also known as fibrosis. The scar tissue in the bone marrow prevents normal, healthy blood cells being made.

Figure 01
Bone marrow

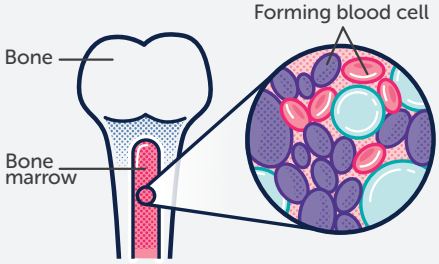
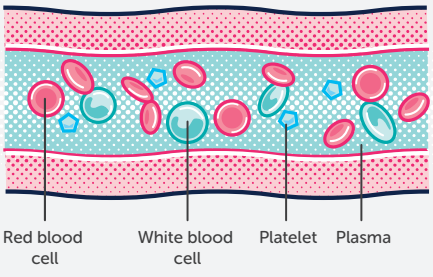


Figure 02



Both adults and children can be diagnosed with MF but it is more commonly seen in people over the age of 60 years old. Approximately 40 people are diagnosed with MF each year in New Zealand.

Primary myelofibrosis may also be called myelosclerosis, myeloid metaplasia or idiopathic myelofibrosis.

What causes MF?

The cause of MF is not fully understood but it is believed that mutations of particular genes lead to the production of scar tissue in the bone marrow. The most common gene that is affected in MF is called JAK2. Other genes (like CALR, MPL and TN) may also be involved, which cause mutations.

Below are the percentages of gene mutations for MF:

JAK2 60%
CALR 25-30%
TN 10%
MPL <5%

MF can arise on its own or as a progression from another MPN like essential thrombocythaemia (ET) or polycythaemia vera (PV).

Risk factors associated with MF include:

- Age: risk increases as you get older
- Environment: exposure to certain chemicals and ionising radiation may increase risk

MF is not contagious. For most people the gene mutations that cause MF are not inherited and occur during a person's lifetime.

What are the symptoms of MF?

Some people have no noticeable symptoms when they are first diagnosed with MF and it might have only been picked up in a routine blood test. More significant symptoms can develop over time.

Common signs of MF include:

- Enlarged spleen, which can cause abdominal pain, bloating and feeling full
- Low blood counts, which can cause bleeding, bruising (low platelets), infections (low white blood cells), fatigue and pale skin (low red blood cells)
- Unexplained weight loss and loss of muscle mass
- Unexplained fever
- Drenching night sweats
- Fatigue or tiredness
- Bone pain

The spleen is an organ that sits at the bottom of your left ribcage. Its main function is to filter the blood. When the bone marrow isn't working properly this can cause the spleen to work harder and faster. The spleen can become enlarged when there are a lot of abnormal blood cells being filtered through it.

Complications of MF

If MF is not well managed with drugs and a balanced lifestyle, the scarring in the bone marrow can continue to get worse.

The only known cure for this condition is allogeneic blood stem cell transplant (bone marrow/stem cells donated from another person) and is only an option for some people. A stem cell transplant might be offered for someone with advanced disease and in healthier and younger people (the risk of treatment can be too high for some individuals).

Medications can reduce some of the symptoms but won't slow down the scarring in the bone marrow. Over time, less and less healthy blood cells are made, which can cause more symptoms and complications. If enough unhealthy cells accumulate then it can transform into acute myeloid leukaemia (20% of people in 10 years). Acute myeloid leukaemia is an aggressive bone marrow cancer.

Increased risk of infection can be another complication of MF if someone has a low number of white blood cells. It is important to have good hand hygiene, check your body temperature if feeling hot or unwell, and be careful when other people have infections. It is important to let your health care team know if you have a high temperature or are showing signs of infection.

How is MF diagnosed?

There are some tests and examinations the doctor will do before confirming a diagnosis of MF. In most cases it is ruling out other blood conditions as well.

The four main things a doctor will do before confirming MF are:

- Take a medical history
- Physical examination, which includes assessing the spleen and skin
- Blood tests including genetic tests to see if there is a mutation
- Bone marrow examination and biopsy

Bone marrow biopsy is a test where the doctor takes a sample of your bone marrow to be examined under a microscope. The sample is usually taken from the back of your hip bone (iliac crest).

The doctor might give you a drug to make you relaxed and sleepy. You might also have some pain relief.

To do a bone marrow biopsy the doctor puts a long needle through the numbed skin into the bone, where they draw out some of the liquid bone marrow.

We recommend you take someone with you for this procedure for support and also to drive you home as you might feel drowsy from the drugs.

How is MF managed?

Your doctor will regularly monitor your blood count so they can determine the stage of MF, and to ascertain if there is a potential cure with an allogeneic stem cell transplant in those who are young, otherwise healthy and have advanced disease.

Unfortunately, the majority of people who are diagnosed with MF are over 60 years of age and often aren't eligible for an allogeneic stem cell transplant. For those who are ineligible, treatment includes the best supportive management with the use of drugs and blood transfusions.

Blood transfusion

If your levels of red blood cells and platelets are dangerously low then a blood transfusion may be given to you at the hospital. This will boost the amount of red blood cells or platelets circulating in your bloodstream.

Some people with MF will need regular blood transfusions to keep their blood levels at a functioning level.

Drugs

The most common drugs used in MF are:

- Hydroxyurea
- Interferon-alpha
- Ruxolitinib

Hydroxyurea (Hydrea)

Hydroxyurea is classed as a chemotherapy drug because it causes cell death. It works by suppressing the function of your bone marrow and controlling blood cell production. It interferes with the DNA of blood cells so instead of growing and maturing normally, they die.

Common side effects of hydroxyurea include symptoms of low blood counts like increased risk of infection, anaemia and bruising/bleeding.

Other common side effects include:

- Fatigue and extreme tiredness
- Diarrhoea or constipation
- Gout (pain and inflammation in joints)

Less common side effects that affect less than 1% of people include:

- Nausea, vomiting, loss of appetite
- Itchy skin, ulcers, skin rashes
- Changes in kidney function
- Headache, dizziness or hallucinations
- Fever or chills

Interferon-alpha

Interferon-alpha is a drug that slows down the production of platelets, more specifically the megakaryocyte clone in the bone marrow. Interferons are substances that are part of our immune system to help fight viruses and bacteria.

Interferon-alpha may be used if people can't have hydroxyurea. It has been shown to normalise high blood counts and reduce clotting.

Common side effects include:

- Flu-like symptoms (reduced appetite, fever, fatigue)
- Reduced white blood cells
- Headache
- Diarrhoea
- Hair loss or thinning

Interferon is given as an injection and most people learn to do this themselves at home.

Ruxolitinib (Jakavi)

Ruxolitinib is now funded in New Zealand for people with MF with more advanced disease. It is a protein kinase inhibitor drug that helps control the number of blood cells. It works by interfering with the function of JAK2, which is often abnormal in people with MF. Interestingly, ruxolitinib works for all MF regardless of the mutation. The main effect is to reduce the spleen size and the major symptoms. Unfortunately, despite blocking the JAK2 mutation, it doesn't appear to slow down the progression of the disease.

Side effects include:

- Low blood counts
- Bleeding
- Bruising
- Fever
- Tiredness
- Shortness of breath
- Infection
- Headache
- Increased cholesterol
- Increased risk of non-melanoma skin cancer

Infection can escalate very quickly if you have low blood counts so it is important to contact your health care team if you suspect you have an infection.

Signs of infection may be different for each person. Most likely you will have a high temperature (above 37.5°C) so it is important to check this with a thermometer.

Other common signs of infection are:

- Skin feels hot to touch
- Feeling cold or shivery
- Aching muscles
- Feeling tired
- Headache
- Feeling confused or dizzy
- New pain in your body
- Cold-like symptoms (sore throat, coughing)
- Nausea, vomiting and/or diarrhoea

Clinical trials

Clinical trials are research studies that help determine whether a new treatment is safe, effective and works better than the current treatment. Ask your haematologist if there are any clinical trials that you are eligible to be on. The benefits of participating in a clinical trial are that you have access to the latest treatments or developments to current treatments. There may also be some risks involved, which depend on the type of clinical trial and your own health.

MF and pregnancy

In general, pregnancy increases a woman's risk of blood clots so if you have MF as well then there is a greater risk. Many drugs used to treat MF should be avoided if pregnant due to the risk on the developing foetus. You should discuss the options with your haematologist if you are planning on getting pregnant in the future, and what the safest and most effective treatments are.

Future treatments

There is ongoing research into developing a cure for MF and more effective ways to manage different MPNs. For the latest information on specific drugs it is best to ask your haematologist. Drugs that are publicly funded in New Zealand may be different to other countries.

Looking after your health

It is important to try and have a balanced lifestyle with a focus on quality sleep, good nutrition, adequate hydration and regular exercise. Drinking plenty of water each day is very important. It is also good to reduce stress in your life as much as possible.

A history of smoking or high blood pressure can increase your risk of thrombosis even more. Your doctor may advise you on ways to stop smoking and/or maintain a healthy weight and blood pressure.

It can be hard to know how to make these changes so please ask your health care team or LBC Support Services Coordinator for more information. They may be able to refer you to other helpful organisations that can also support you.

Important information available online

For more information and to download other fact sheets, see our website **www.leukaemia.org.nz**