leukaemia & blood cancer NEW ZEALAND

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MYELOPROLIFERATIVE NEOPLASMS – ESSENTIAL THROMBOCYTHAEMIA (ET)

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).

Figure 01
Bone marrow

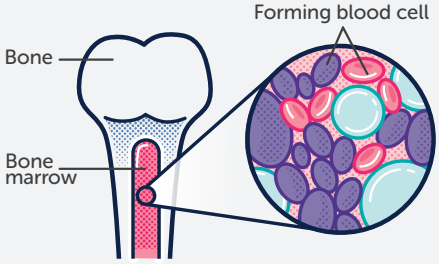
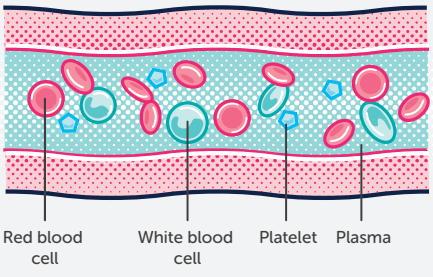


Figure 02



What is essential thrombocythaemia (ET)?

Essential thrombocythaemia (throm-bow-si-theem-eea) is a disease where too many platelets are made in the bone marrow. Platelets are normally needed in the body to control bleeding, however when there are too many platelets they may clump together and make it hard for the blood to flow. This can lead to abnormal blood clotting.

ET is a rare chronic disease with approximately 40 people diagnosed in New Zealand each year. It may also be called idiopathic thrombocythaemia or essential thrombocytosis. Although it can be diagnosed at any age, most people are diagnosed around 60 years of age. It is also more common in females than males. On average, individuals with ET have a normal life expectancy if they are monitored and treated well. In a small number of people with ET, the disease may transform to polycythaemia vera (PV), myelofibrosis (MF), acute myeloid leukaemia (AML) or, less frequently, myelodysplastic syndrome (MDS).

What causes ET?

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

Below are the percentages of gene mutations for ET:

JAK2 50-60%

CALR 20-25%

TN 10-15%

MPL <5%

ET is not contagious. For most people the gene mutations that cause ET are not inherited and occur during a person's lifetime. There is a rare type of ET called familial essential thrombocythaemia, which is inherited. There are also about 10% of people with ET who don't have a JAK2, MPL or CALR gene mutation and their ET might be referred to as 'triple-negative'.

What are the symptoms of ET?

Many people have no symptoms when they are first diagnosed with ET and it might have only been picked up in a routine blood test that their platelet count is high.

One of the first symptoms of ET may be the development of a blood clot (thrombus) or you may notice increased bleeding in the soft tissues that form bruises.

Below is a list of common symptoms of having too many platelets that cause blockages around the body:

- Weakness
- Dizziness or fainting
- Enlarged spleen
- Tingling in the hands and feet
- Chest pain

If there is a clot in the blood vessels that supply blood to the brain, there can be serious symptoms that cause a mini-stroke or transient ischemic attack (TIA).

Symptoms might include:

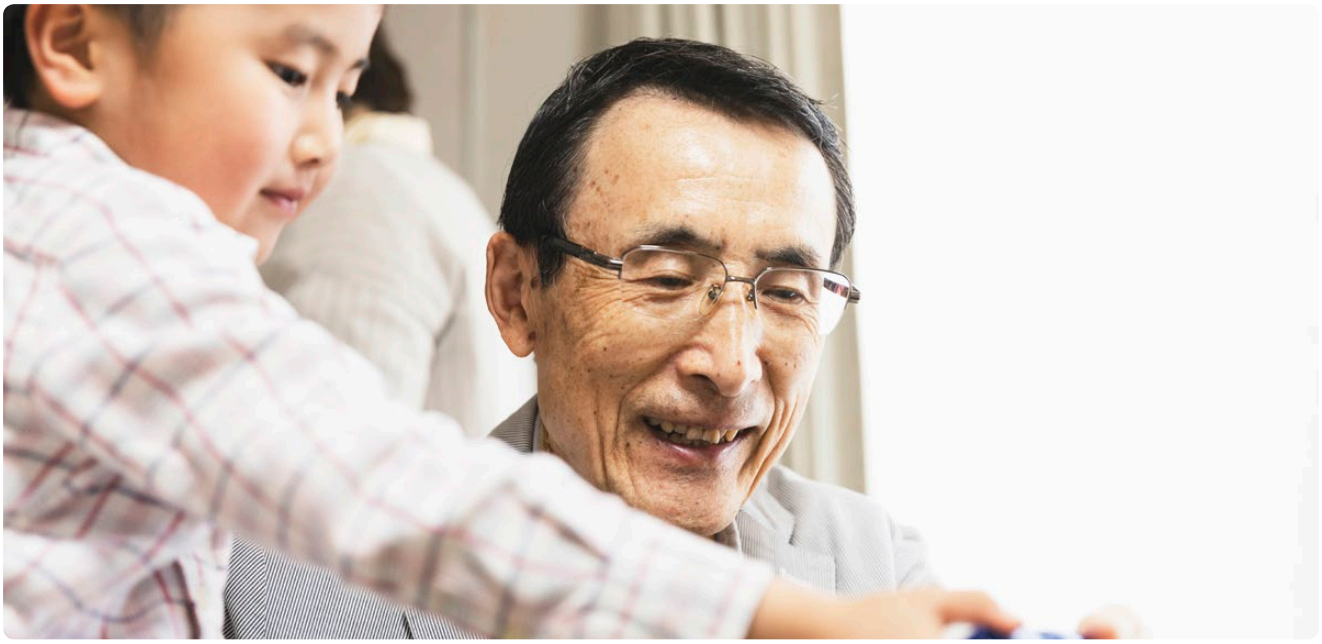
- Headaches
- Visual problems
- Weakness or numbness on one side of the body
- Dizziness
- Trouble speaking or slurred speech

In a small group of people with ET, it might actually cause bleeding even though their platelets are extremely high. This occurs because the excessive platelets lead to the absorption of other important clotting factors in the bloodstream, which can result in bleeding.

Symptoms of bleeding may include:

- Bruising easily
- Nosebleeds
- Bloody bowel motions
- Gastrointestinal bleeding (in stomach and/or bowels)

If there is a clot in your leg, this is called a deep-vein thrombosis (DVT). It may cause leg pain and/or swelling.



Complications of ET

Thrombosis is a major complication of ET and occurs when a blood clot (thrombus) blocks your blood vessel. Older people with a high platelet count or people with a prior history of thrombosis may be at greater risk of getting a thrombus. A major aim of treating ET is to reduce the risk of thrombosis.

An enlarged spleen might also be a complication of ET and can cause various symptoms from the spleen putting pressure on the stomach and liver.

Having an enlarged spleen might cause symptoms like:

- Weight loss
- Indigestion or bloating
- Loss of appetite
- Generalised itching

How is ET diagnosed?

There is a criteria used to diagnose ET. In most cases it is ruling out other blood conditions as well as determining why there are high levels of platelets.

The criteria includes:

- **Major**
  - Platelet count greater than 450 x 109/L
  - Typical bone marrow changes for ET
  - Bone marrow fibrosis (scar tissue) is minimal
  - Can exclude other forms of myeloproliferative neoplasm
  - Identify the three known driver mutations (JAK2, CALR and MPL)
- **Minor**
  - No other cause for the elevated platelets
  - Other less common mutations present or not

The main tests used for identifying ET are blood tests. The different blood tests that may be done are:

- Full blood count (FBC) or complete blood count (CBC) to check the amount of red blood cells, white blood cells and platelets
- Blood chemistry tests to check sodium, potassium and uric acid for liver and kidney function
- Genetic tests that look at mutations in genes

A recent change in the diagnostic criteria has also increased the requirement for a bone marrow 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 ET managed?

To date there is no cure for ET but there is treatment to try and manage symptoms and reduce thrombosis and/or bleeding.

Some people may not need any treatment straight away and may just be monitored by their doctor. This is called active monitoring or 'watch and wait'. You will usually have blood tests and regular appointments with your doctor.

Drugs

The most common drugs used in ET are:

- Hydroxyurea
- Anagrelide
- Interferon-alpha
- Aspirin

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 platelet production. It interferes with the DNA of blood cells so instead of growing and maturing normally, they die.

A small number of people who have ET may go on to develop primary myelofibrosis, which is another type of MPN. Hydroxyurea is also used to treat other MPNs so may reduce the chances of any development.

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

Anagrelide (Agrylin)

Anagrelide is a medication used to treat ET. Its brand name in New Zealand is Agrylin.

Anagrelide works by reducing the number of platelets in the blood. It stops the production of new platelet cells developing, thereby reducing the risk of blood clots.

Common side effects are headaches and palpitations.

Less common side effects include:

- Gut changes
- Skin rash
- Anaemia
- Fatigue
- Swollen hands and feet
- Nausea and dizziness

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.

Aspirin

Aspirin is used to reduce the risk of blood clots and manage any clots that have already formed by making them less 'sticky'. It is part of a group of drugs called non-steroidal anti-inflammatory drugs (NSAID). This means that it reduces inflammation but isn't a steroid.

Common side effects include stomach discomfort or indigestion, bruising and bleeding.

Regular monitoring by your doctor is important to watch out for any new symptoms.

Plateletpheresis

If you are very unwell with high levels of platelets, the platelets might be removed from your bloodstream through plateletpheresis. This procedure involves being connected up to a special machine with two IV (intravenous) cannulas. Your blood exits your blood vessel through an IV cannula then passes through the special machine where the platelets are removed. The rest of the blood goes straight back into the body through the second cannula. This would only be done in an emergency.

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.

ET and pregnancy

In general, pregnancy increases a woman's risk of blood clots so if you have ET as well then there is a greater risk. Many drugs used to treat ET 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 ET 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, balanced 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**

QUESTIONS & NOTES

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If you would like to get in touch:
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