leukaemia & blood cancer NEW ZEALAND

Vision to Cure. Mission to Care.

ACUTE PROMYELOCYTIC LEUKAEMIA (APL)

A fact sheet for patients, families and whānau

WHAT IS ACUTE PROMYELOCYTIC LEUKAEMIA (APL)?

Acute promyelocytic leukaemia (APL, also called APML) is a form of blood cancer that affects your white blood cells. It is a rare subtype of acute myeloid leukaemia (AML).

APL occurs when there is an abnormal build-up of immature white blood cells, called promyelocytes (pro-my-el-oh-sites), in the bone marrow. These immature cells are unable to function properly and grow out of control, often quickly. They crowd out other healthy blood cells (red blood cells, white blood cells and platelets) in the bone marrow and in the bloodstream.

Your blood

Your 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 – red blood cells, white blood cells and platelets. These blood cells are created in your bone marrow and are then released into your bloodstream so they can function around the body

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 (he-ma-glow-bin) in each red blood cell that carries the oxygen throughout the body and gives blood its 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 many different types of white blood cells that all 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 number of neutrophils in your body is called neutropenia (new-tra-pee-nee-a).

Platelets help your blood to clot and prevent or stop bleeding. Clotting factors help this process. For example, if you cut yourself, 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

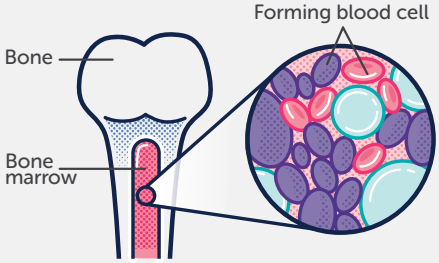
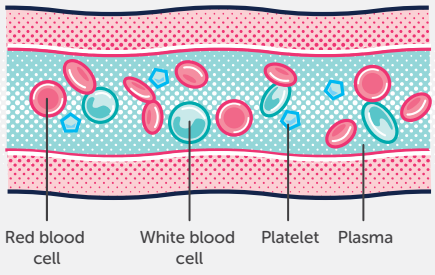


Figure 02



What causes APL?

APL is more common in adults than in children. In New Zealand, around 15 people a year are diagnosed with APL.

The exact cause of APL is not always known, but for 95% of patients it is thought to result when there is damage to the genes, causing translocation (or swapping) of parts of chromosomes 15 and 17 during cell division (see Figure 03).

The new faulty gene (or mutation) formed is called PML-RARα, which stops the promyelocytes from maturing properly and results in them becoming cancerous.

This is an acquired mutation, meaning it has happened randomly over your lifetime. You were not born with it and did not inherit it. It is not your fault, and you cannot pass it on to someone else.

Knowing this gene fault has occurred helps to not only diagnose APL but also target the abnormality with treatment. Most people with APL will respond well to treatment and it is one of the most curable types of acute leukaemia.

What are the symptoms of APL?

Serious bleeding abnormalities are more frequent in people with APL than in other types of leukaemia. APL affects both platelets and clotting factors, resulting in bleeding that can be life threatening if it is not treated quickly. It can also result in blood clots forming in the wrong places. Blood clots in the leg can cause pain and swelling, blood clots in the lungs can cause difficulty breathing, and blood clots in the brain can cause vomiting, headaches and visual disturbances.

Other common symptoms from a low platelet count include:

- Bruising easily
- Frequent or severe nose bleeds or bleeding gums
- Minor cuts or wounds that take a long time to stop bleeding
- Red or purple pinhead-sized spots on your skin called petechiae (pe-tee-kee-i)
- Unusually heavy periods in women.

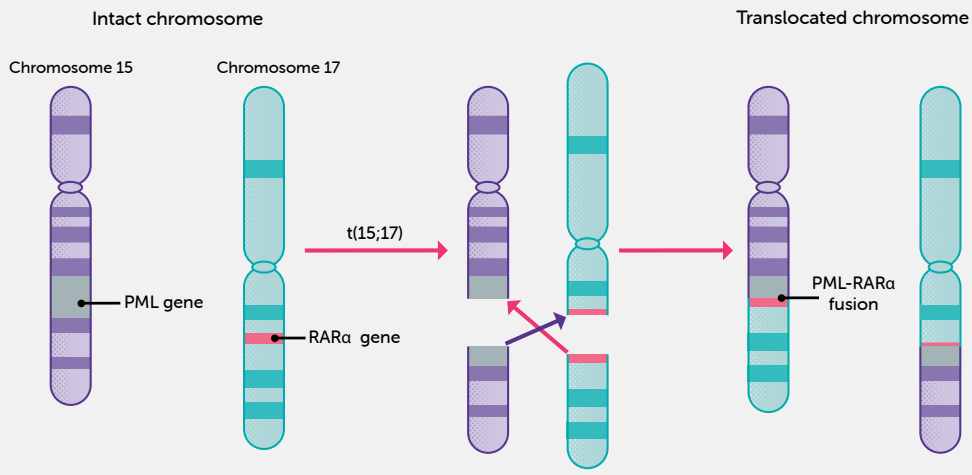
Common symptoms from a low red blood cell count include:

- Chest pain
- Dizziness
- Fatigue (extreme tiredness)
- Headaches
- Irregular heartbeat
- Lack of energy (lethargy)
- Weight loss
- Pale skin
- Shortness of breath while exercising.

Common signs of infection due to a low white blood cell count include:

- Coughing up yellow or green phlegm
- Fatigue (extreme tiredness)
- Fever (high temperature of 38°C or above)
- Shivering or rigors (shaking).

Figure 03
Translocated chromosome



Acute promyelocytic leukaemia is associated with a chromosomal translocation of chromosomes 15 and 17, which results in the fusion of the PML and RARα genes.

How is APL diagnosed?

Your doctor will ask you to do some tests and examinations to confirm a diagnosis of APL.

These may include:

- A full medical history
- A physical examination
- Blood tests – including a full blood count (FBC), clotting and genetic tests to look at mutations in genes
- Bone marrow biopsy and examination.

Detailed information

A bone marrow biopsy is a test where your doctor takes a sample of your bone marrow and sends it to a laboratory (lab) to be looked at under a microscope. The sample is usually taken from the back of your hip bone (iliac crest). To do a bone marrow biopsy, your doctor inserts a long needle through the numbed skin into the bone, where they draw out some of the bone marrow. Your doctor will numb the area where the biopsy is taken and might give you medication to make you relaxed and sleepy. You may also have some pain relief.

You may begin treatment for APL before you have had all your tests and results back, to prevent any serious complications from bleeding.

How is APL treated?

APL is a highly curable form of acute leukaemia and usually responds well to treatment. Due to the rapid onset of APL, treatment will usually start straight away.

You may hear the terms 'active treatment' or 'supportive care'. Active treatment involves taking medications with the purpose of killing leukaemia cells. Supportive care focuses on resolving some of the problems caused by APL (such as bleeding) and managing symptoms or side effects such as nausea and infections. Supportive care can be provided on its own or alongside other treatments.

Medications used in active treatment may include:

- **All-trans-retinoic acid (ATRA)** – 95% of people with APL have the PML-RARα gene mutation, which will respond to ATRA, a derivative of vitamin A. It is a tablet that works by encouraging the immature promyelocytes to mature into healthy white blood cells. ATRA is not a chemotherapy drug.
- **Arsenic trioxide (ATO)** – ATO is a chemotherapy drug often used together with ATRA. ATO is given via IV/drip into your vein and works by speeding up the death of the leukaemia cells. You may have heard of arsenic being a poison, but small doses can be safely used as a medicine. It is a very effective treatment for APL.
- **Anthracyclines** – these chemotherapy drugs damage the DNA in cancer cells, causing them to die.

Treatments used in supportive care may include:

- **Anti-nausea medications** for nausea (feeling sick) and vomiting (being sick)
- **Corticosteroids** which are used to prevent or treat a complication of APL treatment called differentiation syndrome (see below for more information on differentiation syndrome).
- **Medications to prevent infections** such as antibiotics (for bacterial infections), antivirals (for viral infections) and antifungals (for fungal infections).
- **Blood transfusions** of donated blood or platelets if your levels are low. Blood transfusions are given via IV/drip into your vein and relieve symptoms caused by low red blood cell or low platelet counts.
- **Growth factors** such as granulocyte colony stimulating factor (G-CSF), which are used to increase your white blood cell count. G-CSF is given as an injection just under your skin (a subcutaneous or sub-cut injection).

Important information

Infections can escalate quickly if you have low blood cell counts, so it is important to seek immediate medical advice if you suspect an infection or have a fever.

- Call the hospital if you have a temperature over 38°C.
- Don't wait to see if your temperature goes away.
- Make sure you have a thermometer at home, and you know how to check your temperature correctly.
- Don't take any medications (such as paracetamol) to bring your temperature down before you see a doctor.
- Don't take aspirin or ibuprofen in any form. This can increase your risk of bleeding if your platelets are low. Always check with a doctor or nurse first.
- Ask a member of your health care team for the phone numbers of the hospital and write them here:
  Monday to Friday (during office hours)
  ph:.....
  Evenings/nights/weekends
  ph:.....

You may have a repeat bone marrow biopsy or blood test to measure PML-RARα during and after your treatment, to see how well your APL has responded. You will continue to be monitored by your health care team after your treatment is complete, usually for at least two years.

Complications of treating APL

Differentiation syndrome

Sometimes when ATRA and ATO force leukaemia cells to mature, it can happen too quickly for your body to cope. This is called differentiation syndrome and it affects 20–25% of patients during induction treatment. It is most likely to happen in the first two weeks of treatment, so you will be monitored closely during this time. You may be given corticosteroids alongside your ATRA or ATO to prevent differentiation syndrome. If you do develop it, high-dose corticosteroids are also given as treatment.

Symptoms of differentiation syndrome include:

- Breathlessness, coughing, chest pain
- Fever
- Swelling, weight gain
- Low blood pressure, dizziness
- Dehydration, passing urine more than normal
- Diarrhoea (loose bowel motions)
- Feeling sick, vomiting
- Unusual tiredness, drowsiness, confusion.

It is important to tell your health care team immediately if you experience any of these symptoms.

QT interval prolongation (or long QT syndrome)

Treatment with ATO can cause changes in heart rhythm due to QT interval prolongation (a change in the heart's electrical rhythm that may cause a slower or irregular heartbeat). To monitor for an abnormal heart rhythm, a simple non-invasive test called an electrocardiogram (ECG) will be performed regularly. You will also have regular blood tests to monitor your potassium and magnesium levels, which help protect your heart.

Idiopathic intracranial hypertension (IIH)

IIH, also called pseudotumor cerebri, is when the pressure inside your skull increases for no reason. IIH is associated with ATRA use and is most common

in younger patients. Symptoms of IIH can include severe headaches, vision loss or vision changes, nausea and vomiting, dizziness, and a buzzing or whooshing sound in the ears. It is important that you tell your health care team immediately if you experience any of these symptoms.

Other potential side effects from APL treatment

- Fevers, chills (due to infection)
- Nausea, vomiting
- Changes to taste and smell
- Mucositis (pain and inflammation in the mouth and gut)
- Bowel changes (e.g. diarrhoea or constipation)
- Hair loss
- Fatigue
- Rash, itching
- Headaches
- Bruising, aches and pains
- Reduced fertility (see the Fertility fact sheets on the LBC website for more information)
- Nerve damage to hands and feet
- Birth defects if you are pregnant (a pregnancy test will be performed before any treatment).

Living well with APL

After a diagnosis of APL, it is important to look after your health. Some things you can do to keep your body healthy are:

- Eat a variety of healthy foods
- Drink plenty of water
- Keep active with gentle exercise
- Brush your teeth regularly with a soft toothbrush
- Get a good amount of sleep
- Reduce stress.

If you have low levels of red blood cells, white blood cells or platelets, you may need to take extra care to protect your body. It is a good idea to:

- **Rest when you need to.**
- **Avoid contact sports**. Due to the risk of bleeding associated with a low platelet count, avoid activities that may result in a cut or fall.
- **Protect yourself from germs/infections.** You can reduce your risk of infection with frequent handwashing and by avoiding sick people. Wear protective gloves when doing work around the home or garden, and wear a mask when gardening or out in crowded areas.
- **Ensure food is prepared and stored safely.** If you are neutropenic (a low level of white blood cells called neutrophils) your health care team may recommend you follow a special diet called a neutropenic diet.

Receiving a diagnosis of APL can be stressful and emotional. Some things you can do to help are:

- **Research your disease.** Learning more about APL can help you feel better prepared to make treatment decisions.
- **Ask questions**. You can ask your health care team about anything related to your disease or treatment that you don't understand. It may help to record or write down what they tell you.
- **Talk to others.** Family/whānau and friends can be a good source of emotional support. Consider joining an online or in-person support group to talk to others with similar experiences.
- **Let your health care team know how you are doing,** especially if you are finding it hard to cope. They can help you get the support you need.

There is support available to help you and those around you to cope. Speak to your health care team or LBC Support Services Coordinator to find out more.

More information available

For more information about being treated for APL, please see the LBC booklet on Acute Myeloid Leukaemia (AML) available on the LBC website or from your local LBC Support Services Coordinator.
www.leukaemia.org.nz

QUESTIONS & NOTES

If you would like to get in touch:
Call: 0800 15 10 15
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Mail: PO Box 99182, Newmarket, Auckland 1149
Or visit one of our Support Services offices in Auckland, Hamilton, Wellington, Christchurch or Dunedin.