Your guide to

Essential Thrombocythaemia & Polycythaemia Vera

Information and advice about causes, symptoms and management







Supporting patients and families affected by MPN

Established by a group of MPN patients over 17 years ago, MPN Voice, registered under the auspices of Guy's & St Thomas' Foundation, has a website with a lively online community and up to date information on essential thrombocythaemia (ET), polycythaemia vera (PV), and myelofibrosis (MF).

Backed by leading healthcare professionals, MPN Voice also publishes a newsletter, MPN disease leaflets and drug leaflets, runs regular regional patient forums, funds MPN research and offers a buddy scheme.

For more information visit the website **www.mpnvoice.org.uk**Email **info@mpnvoice.org.uk**

MPN Voice previously known as MPD Voice Join our buddy programme **MPDlife MPDlife** Exciting and rapid change in MPN **MPN** Interferon Anagrelide Aspirin

Being diagnosed with essential thrombocythaemia (ET) or polycythaemia vera (PV) can be a shock, particularly when it's a condition that you've probably never heard of.

If you have questions about ET or PV – what causes it, who gets it, how it affects your body, what symptoms to expect and likely treatments – this leaflet covers the basics for you.

You'll also find useful advice about how to get the best from your haematologist, plus practical tips on how to help important people in your life understand such a rare condition.



Confused by all the terminology linked to your condition?

Or perhaps you've come across some medical terms you don't recognise? If so, our glossary – an A-Z list of words often associated with ET and PV – at the back of this brochure – might come in handy.

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With special thanks to Professor Claire Harrison (DM, FRCP, FRCPath); Consultant Haematologist and Dr Rachel Davis (PhD, MSc, BSc (Hons), CPsychol); Chartered Health Specialist



What are essential thrombocythaemia and polycythaemia vera?

Essential thrombocythaemia (ET) and polycythaemia vera (PV) are closely related chronic diseases that develop when your bone marrow – the soft, fatty tissue inside your bones – produces too many mature blood cells too quickly. This can trigger serious health problems unless properly treated and controlled.

Both ET and PV belong to a group of conditions called MPNs, or myeloproliferative neoplasms. ET occurs when too many platelets (tiny blood cells that help blood clot) are made. PV occurs when too many red blood cells (which transport oxygen around the body) are made. The white blood cells (that fight infection) and platelets can also be increased in PV.

Another MPN that's closely related to ET and PV is myelofibrosis (MF). This disorder occurs when the bone marrow is replaced by fibrous (or scar) tissue. Scarring of the bone marrow leads to not enough blood cells being produced. MF can occur on its own as primary myelofibrosis, or as a progression of ET or PV.



As time goes on we are learning more about ET and PV and their causes. Whilst we do not know the exact cause, we do know that many MPNs are related to a genetic mutation in a protein in our bodies called JAK2 – a protein which regulates blood cell production. Approximately 50% of people with ET and 97% of people that have PV will have this mutation. A smaller number of people with ET will have other mutations such as MPL or CALR. The common factor to all these mutations is that they make JAK2 overactive.

It is also important to note that ET and PV are not inherited and are not passed on from parents to child, although some families do seem to develop the disease more readily than others.

Some researchers believe that viral infections, exposure to toxins, exposure to radiation or something else may cause myeloproliferative neoplasms by causing a change in the genetic code of the bone

ET and PV in numbers...

ET is most common among those over the age of 60, though it does sometimes affect younger people, most often women under the age of 40.

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ET is more common among women, with two women diagnosed for every man.

PV is more likely to affect people over 60 and is very rare in children.

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Q

PV affects more men than women.

marrow cells. Unfortunately current research still does not offer any proof as to what causes these conditions and MPN Voice has funded a preliminary epidemiology study to look at whether there are ways to research potential causes of MPNs. This study is called MOSAICC.

How common are ET and PV?

ET and PV are considered to be rare diseases. The number of people diagnosed each year with ET and PV is:

ET between 1.5 and 3 cases per 100,000.

PV 2 cases per 100,000.

That might explain why you probably haven't heard of ET or PV, or met anyone with the conditions before.



How do ET and PV affect your body?

In someone without ET or PV...

...bone marrow (the soft, fatty tissue inside your bones) contains blood stem cells that in time develop into mature blood cells – red blood cells (to carry oxygen to the tissues of your body); white blood cells (to fight infection and disease); or platelets (to help prevent bleeding by causing blood clots to form).



In someone with ET...

...the bone marrow makes more platelets than the body needs. Platelets are needed to help blood clot, but in people with ET, overproduction means they don't work properly.

This excess of platelets may cause blood clots (thrombosis) – which block a vein or an artery and stop blood flowing – or it may cause excess bleeding. The most common complications are blood clots in the:

- Arteries (arterial thrombosis which may lead to heart attacks, strokes or damage of intestinal tissue, such as gangrene)
- Veins (venous thrombosis)
- Lungs (pulmonary embolism a blood clot which travels through the bloodstream and causes a blockage in one of the arteries of the lungs)

PV

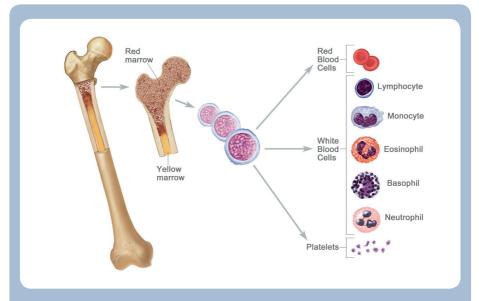
In someone with PV...

...the bone marrow makes too many red blood cells (although white blood cell and platelet counts can also be increased), making your blood thicker than normal.

In 30% of patients with PV, this excess of red blood cells may cause blood clots to form more easily. Clots can block blood flow through your arteries and veins, potentially leading to heart attacks or strokes. Also, thicker blood doesn't flow as quickly as normal blood, preventing your organs from getting enough oxygen, which may lead to other serious problems such as angina (chest pain) and heart failure.

An enlarged spleen (splenomegaly) is another problem that affects up to 75% of PV patients. When the bone marrow does not function correctly, the spleen compensates by producing red blood cells, causing it to enlarge. More rarely, the liver may also be affected and become enlarged (hepatomegaly).

"There is unprecedented dialogue in the MPN community in trying to better understand these diseases."



What are stem cells?

Stem cells are 'master cells' found in many organs and tissues of the body, which can divide and develop into many other types of cell – such as blood cells, muscle cells and brain cells – to replenish those lost or damaged. Blood stem cells (called haematopoietic stem cells) circulate in our blood and bone marrow, as well as in the umbilical cords of newborn babies. In the bone marrow, they have the potential to develop into mature blood cells.

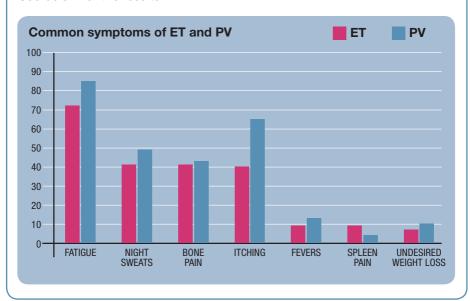
Are ET and PV types of cancer?

In the early part of this decade there was some debate about whether MPNs such as ET and PV were types of cancer. This is because the word 'neoplasm' (new growth) is a term that has been used both for cancers (malignant neoplasms) and non-cancerous tumours (benign neoplasms). Now, because both ET and PV are characterised by uncontrolled cell growth, haematologists and cancer organisations do classify them as a blood cancer. For new patients this can be alarming terminology but it is important to remember that the symptoms and prognosis can vary widely. Your specialist will advise you depending on your individual circumstances.



What are the symptoms of ET and PV?

Some people with ET and PV don't experience any symptoms in the early stages. And, remember, everyone is different, so not every person has the same combination of symptoms to the same degree of severity. One study asked 709 patients with ET or PV about their most significant symptoms. See below for the results...



It's sensible to monitor how you're feeling and what symptoms you're experiencing. If you notice them changing or getting worse, you can tell your haematologist and explain how they are affecting you on a day-to-day basis.

"The symptom that probably impacts most on daily life is fatigue."

Clinical trials

You may be invited to participate in a clinical trial. All new treatments must be tested thoroughly in different phases of a trial. Through trials, researchers find out if new drugs are effective and safe in patients. Your haematologist will discuss this with you and your decision will not affect any current treatment options that you already receive.

What happens next?

Your individual situation and health history, as well as the ways you respond to treatment, can all affect your prognosis (the predicted outcome of the disease). Your haematologist will be able to provide you with a more accurate picture.

In general, patients with ET without severe clotting or bleeding complications have an excellent chance of living out a near-normal life span if properly monitored and treated as necessary.

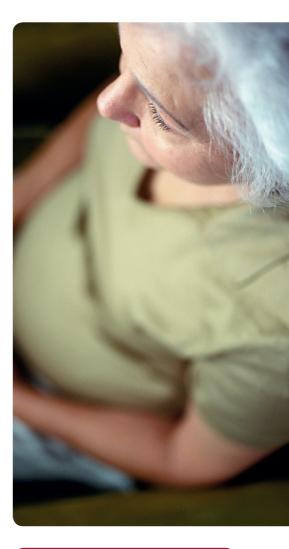


In general, patients with PV who do not progress to MF or leukaemia can expect to have a normal to slightly

reduced life expectancy if properly monitored and treated as necessary.

Bear in mind when you're reading up about the condition, though, that in some patients the disease may remain stable or gradually progress over time. This means that you may never experience many of the symptoms and outcomes that you read about – or if you do, it may not be for many years. Many people with ET or PV live normal lives for years at a time without experiencing complications.

You will read that ET and PV can develop into MF or acute myeloid leukaemia – life-threatening types of blood and bone marrow cancer. Don't panic, as this is rare. If you have any concerns, talk to your haematologist.



"It is not always true that an increase in symptoms heralds an advancing or changing disease."



Treating ET and PV

The majority of treatments for ET and PV are aimed at managing symptoms and reducing complications, so that your quality of life is better. For both conditions, if you have no symptoms or risk factors when you are first diagnosed, a 'watch and wait' approach is often recommended. This usually involves regular check-ups and blood counts, as well as your haematologist advising you on ways to live a healthy lifestyle.

Other than aspirin many people with ET don't need treatment for many years, but eventually most do need some kind of further treatment. Your treatment plan will depend on your own unique situation and take into account the symptoms you are experiencing as well as any lifestyle risk factors like high blood pressure and whether or not you smoke. There are a number of medications available as well as a rarely-used procedure called plateletpheresis – a method of collecting platelets from your blood.







Treatments for PV aim to slow the production of blood cells to help to maintain a normal blood volume and thickness, or blood flow.

There are a number of medications available as well as a procedure called venesection or phlebotomy.

Venesection/phlebotomy

Commonly carried out in people with mild PV or people who have been newly diagnosed, this procedure can control PV for many years.

An intravenous (IV) needle connected to a tube with a bag at the end is inserted into one of your blood vessels. Your blood flows through a tube and is collected in the bag in the process similar to blood donation. The effect is temporary and the procedure may need to be repeated regularly – perhaps every few weeks or months until you reach an acceptable blood thickness level.



Drug treatment

Your haematologist will discuss the options tailored to your needs.

Antiplatelet drugs

Such as low dose aspirin may be suitable. Aspirin can cause bleeding and ulcers in the stomach and gut. Sometimes alternative drugs may be used similar to aspirin such as dipyridamole and clopidogrel.

Anticoagulant

Warfarin or other anticoagulant drugs such as the injections of heparin or low molecular weight heparin are used to treat blood clots and often used to prevent them in high risk situations e.g. after surgery.

To control blood counts

We have provided summary information here. For full details refer to either product insert sheet provided with the medicine or the drug information leaflet we provide.

Hydroxycarbamide (Hydroxyurea)

This drug interferes with cell metabolism and is taken daily. Blood counts need regular monitoring. Hydroxycarbamide is generally well tolerated. However this drug can damage cells and may affect fertility therefore women who are pregnant or those trying to conceive, should not use it. There is a small chance that Hydroxycarbamide can increase the risk of acute leukaemia.

Anagrelide

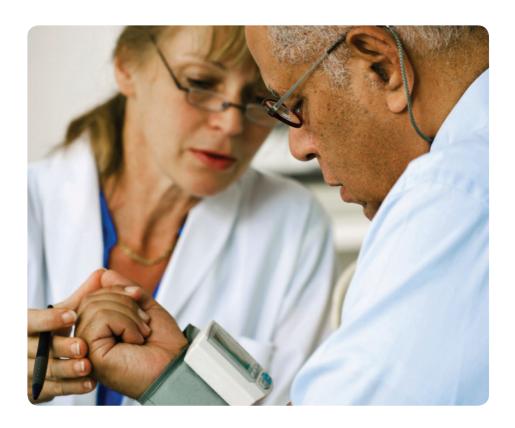
This medication lowers the platelet count and has some effect on the red blood cells. It does not generally affect fertility or increase the risk of developing acute leukaemia. It is not suitable for pregnant women and is used with caution for people with heart disease.

Busulfan

This is used when there are side effects with hydroxycarbamide, or when it is difficult to take the hvdroxvcarbamide tablets. Like hydroxycarbamide, busulfan also affects the bone marrow directly and can lead to a fall in the blood count. This tablet is generally well tolerated and prescribed in short courses. It can be taken in one large dose or split over a prescribed number of days and blood counts are monitored regularly. Busulfan can cause lung problems, damage to fertility and the bone marrow, and is known to increase the risk of the disease changing into acute leukaemia.

Interferon

This is a natural agent that reduces the production of bone marrow cells. Interferon is given by injection and is available as Pegulated interferon, a slow releasing formula which only needs to be taken once a week or less. It does not increase the risk of leukaemia and can be used in pregnancy. Interferon has been shown in some studies to reduce the amount of abnormal JAK2 in a proportion of patients.



JAK inhibitors

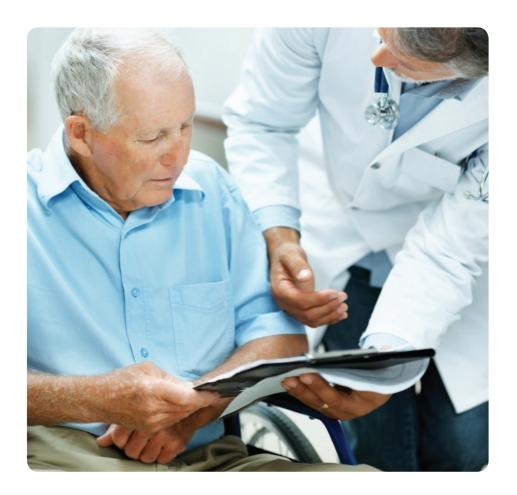
Ruxolitinib or Jakavi®

Ruxolitinib blocks the function of JAK2 and its relation JAK1. This slows down blood cell production, reduces spleen size and symptoms. Whilst the European Medicines Agency has approved the use of Ruxolitinib in PV patients who are intolerant or resistant to other lines or treatment, in the U.K it is currently only available via special application.

Medical exemptions for treatment

MPN patients in England (there are no prescription fees in Scotland, Wales and N Ireland), are entitled to an exemption certificate and should obtain a FP92A form from their GP or haematologist. Further details can be found on our website at www.mpnvoice.org.uk in the living with MPNs, everyday challenges/cost of medication section.





Talking to your haematologist

ET and PV are very rare conditions. "For this reason, it's important to form a good working partnership with your haematologist to ensure you're getting the best treatment possible," says Prof Claire Harrison. Her advice?

- If it's an initial consultation, take along a list of your medications and doses, and a list of any allergies
- If you have a complicated medical history, take a list of diagnoses, previous procedures and/or complications
- It can be useful to repeat back what you have heard so that you can be sure that you have understood fully

- Make a list of questions to take to your appointment. This will help the discussion with your haematologist
- Bring someone along to your appointment. They can provide support, ask questions and take notes
- Note information down to help you to remember later what was said
- Be open when you discuss your symptoms and how you are coping. Good patient-doctor communication tends to improve outcomes for patients
- Don't be afraid to ask for a second opinion. Most doctors are happy for you to ask and, as your condition is rare, it is usually seen as the standard practice

You need to tell your haematologist if...

You're having any medical treatments or procedures such as dental work or operations.

Experiencing any symptoms or taking any products, such as prescribed medicines, over-the-counter treatments or vitamins

You're pregnant or planning to become pregnant, as many treatments can affect your baby's development in the womb

Your partner is planning to become pregnant, as some therapies can affect male fertility and sperm quality





Talking to other people

If you tell someone you've got diabetes or breast cancer, they'll probably have heard of it. Having a rare condition like ET or PV can be harder to explain. This simple summary may help:

"I have a condition where my bone marrow is not working properly and this affects the number of blood cells it produces. This can affect my body in several ways and sometimes makes me [list your symptoms here - e.g. I feel tired, I experience a lot of pain etc]. I have good days and bad days and sometimes I may need [explain what you need here e.g. a bit more support with my day-to-day activities; someone to talk to; someone to come to appointments etcl."

There are also other things you can do to make it easier to explain what you're experiencing, how the condition affects you and the support that you need:

Find out moreTry to find out more about your condition - if you know more about ET or PV then you will have a better chance of sharing it in simple terms with other people.

Change perspectives Think about what your family and

friends might like to know about your condition. Perhaps have a read of the section for carers and loved ones at www.mpnvoice.org.uk to find out the kinds of questions they may be wanting to ask.

Have a print-out to hand It might help to print out basic information about your condition, and share this with family and friends. Not only can they take the print-out away with them to read in their own time. but it also takes the pressure off you having to explain the details yourself.

Explain your needsFamily and friends will be keen to help - think about what people can help you with and make some suggestions, whether it's doing your weekly shop, coming round to cook dinner or driving you to an appointment.

Be open about how you feel "If you find you're feeling like you don't want to burden your loved ones and friends with your problems, remember people who care about you will want to help, so don't be afraid to be open about how you're feeling," says Dr Rachel Davis. "Saying that, you don't need to be open about your feelings at all times - it may help to explain to family and friends in advance that you are likely to have days when you feel like talking and other days when you don't. People can then take their cue from you."

YOUR GUIDE TO ET & P

Coping with a rare condition

"Discovering you have a rare and potentially life-threatening condition can be difficult. It is common to feel lost, confused and isolated because you are unlikely to know anyone else who's going through the same experience, and there's so much new and complex information – and jargon – to take in", says Dr Rachel Davis. "But help and support does exist – and seeking it out can help you to get your head around the facts and help you feel you are part of a community of people all coping with ET or PV, too."

"An MPN patient may need support in coming to terms with their diagnosis and any changes they experience in their condition"

There are a number of helpful sources including:

- Your haematologist and healthcare team
- Your family and friends
- A psychologist (you can ask your haematologist for a referral)
- Specialist clinics in your area or nearby city that study ET and PV where you can find out further information
- The online community at HealthUnlocked www.healthunlocked.com/mpnvoice

See www.mpnvoice.org.uk for more ideas on how you can talk to your haematologist about ET or PV, questions you may want to ask and how you can prepare yourself for each appointment.

Complementary therapies

Although there's no scientific evidence to support the use of complementary therapies alone in MPNs, many people do find that they may be helpful in coping with their disease alongside standard medical treatments. Options include acupuncture, exercise, yoga, meditation and relaxation. Always discuss any complementary therapies with your haematologist.



Glossary

In this glossary some words and medical terms often associated with ET and PV are accompanied by a brief explanation.

A

Abdomen The abdomen is an anatomical area that is bounded by the lower margin of the ribs and diaphragm above, the pelvic bone (pubic ramus) below, and the flanks on each side. Organs within the abdominal cavity include the stomach, small intestine, colon, liver, gallbladder, spleen, and pancreas.

Abdominal pain Pain that is felt in the abdomen [above].

Acute myeloid leukaemia (AML, acute myelogenous leukaemia or acute non-lymphocytic leukaemia). A quickly progressive malignant disease in which there are too many immature bloodforming cells in the blood and bone marrow, the cells being specifically those destined to give rise to types of white blood cells that fight infections.

Anaemia A medical condition in which the red blood cell count or haemaglobin is less than normal.

B

Blood cells See red blood cells, white blood cells, platelet.

Blood clot (or thrombus, or thrombosis) Blood that has been converted from a liquid to a solid state; also called a thrombus. A blood clot is stationary within a vessel or the heart. If it moves from that location through the bloodstream, it is referred to as an embolus.

Blood transfusion The transfer of blood or blood components donated and collected from one person (the donor) into the bloodstream of another person (the recipient). Often a life saving technique to replace blood cells or blood products lost through bleeding, or when your body can't make blood properly because of an illness such as some MPNs.

Bone marrow The soft blood-forming tissue that fills the cavities of bones and contains fat and immature and mature blood cells, including white blood cells, red blood cells, and platelets.

Bone marrow transplant (BMT)

A procedure in which bone marrow that is diseased or damaged is replaced with healthy bone marrow. The bone marrow to be replaced may be deliberately destroyed by high doses of chemotherapy and/or radiation therapy. The replacement marrow may be the patient's own marrow, treated, or it may come from another person (donor).

C

CALR Calreticulin is a protein involved in calcium flow within the cell which is also important in growth signals.

Chemotherapy Therapy for cancer using chemicals that stop the growth of cells.

Chronic A chronic condition is one that is long term in nature. It comes from the Greek 'chronos' and means lasting a long time. MPNs are considered chronic conditions, and many symptoms of MPNs are also chronic.

Complementary therapy

Complementary therapies such as meditation, yoga, acupuncture and aromatherapy are therapeutic disciplines that can be used alongside conventional medicine.

Complete Blood Cell count (CBC)

A set values of the cellular (formed elements) of blood. These measurements are determined by machines that analyse the different components of blood. It is possible to take blood counts for each individual element of the blood, e.g. white blood cells, red blood cells, platelets, etc.

D

Deep vein thrombosis (DVT)

A blood clot in a deep vein in the thigh or leg. The clot can break off as an embolus and make its way to the lung, where it can cause respiratory distress or respiratory failure.

Ε

Essential thrombocythaemia (ET)

A rare acquired myeloproliferative neoplasm (MPN) characterised by a sustained elevation of platelet number with a tendency for thrombosis and haemorrhage.

F

Fatigue A condition characterised by exhaustion and a lessened capacity for work, domestic and social activities, and reduced efficiency of accomplishment, usually accompanied by a feeling of weariness and tiredness. Fatigue can be acute and come on suddenly or be chronic and persist.

Fever Technically any body temperature above 98.6 degrees F / 37 degrees C. In practice a person is usually not considered to have a fever until the temperature is above 100.4 degrees F / 38 degrees C.

Full Blood Cell count (FBC) A set of values of the cellular (formed elements) of blood. These measurements are determined by machines that analyse the different components of blood. It is possible to take blood counts for each individual element of the blood, e.g. white blood cells, red blood cells, platelets, etc.



Н

Heart attack The death of heart muscle due to the loss of blood supply. The loss of blood supply is usually caused by a complete blockage of a coronary artery, one of the arteries that supplies blood to the heart muscle. A heart attack can cause chest pain and electrical instability of the heart muscle tissue.

Haematocrit HCT or Packed Cell Volume. The proportion (or percentage) of red blood cells in relation to the rest of the blood cells.

Haematologist A doctor who is specially trained in haematology [below].

Haematology The diagnosis, treatment, and prevention of diseases of the blood and bone marrow as well as of the immunologic, haemostatic (blood clotting) and vascular systems.

Haemorrhage Bleeding or the abnormal flow of blood. Bleeding into the spleen or liver is an internal haemorrhage. Bleeding from a cut on the face is an external haemorrhage.

Hepatomegaly An enlarged liver.

J

JAK2 JAK2 is a molecule (called an enzyme) that exists in all people. It forms a communications pathway for messages travelling inside the cell.

JAK2 V617F Researchers in 2005 found a mutation (known as JAK2 V617F) in the JAK2 molecule in people with MPNs. The mutation affects the signalling performance of the JAK2 molecule.

L

Liver An organ in the upper abdomen that aids in digestion and removes waste products and worn-out cells from the blood.

M

Myelofibrosis (MF) Fibrosis or spontaneous scarring of the bone marrow. It is characterised by significant anaemia and an enlarged spleen.

Myeloproliferative neoplasms

(MPNs) Myeloproliferative neoplasms are diseases of the blood and bone marrow, and sometimes referred to as blood cancers. Four main types of MPNs make up around 95% of cases: myelofibrosis, essential thrombocythaemia, polycythaemia vera and chronic myeloid leukaemia (CML).

Neutropenia A condition in which the number of neutrophils (a type of white blood cell) in the bloodstream is decreased

Next generation sequencing (NGS) DNA sequencing technology which has revolutionised genomic research.

Night sweats Severe hot flushes that occur at night and result in a drenching sweat.

P

Packed cell volume (PCV) See haematocrit.

Phlebotomy (or venesection) The removal of a volume of blood (usually 450mls) for medical reasons.

Plateletpheresis Procedure in which thrombocytes (blood platelets) are removed.

Platelet An irregular, disc-shaped cell fragment in the blood that assists in blood clotting. During normal blood clotting, the platelets clump together (aggregate). Although platelets are often classed as blood cells, they are actually fragments of large bone marrow cells.

Platelet count The calculated number of platelets [see above] in a volume of blood, usually expressed as platelets per cubic millimetre of whole blood. Normal platelet counts are in the range of 150,000 to 450,000 per microlitre (or 150 - 450 x 109 per litre).

Polycythaemia vera (PV).

PV is a myeloproliferative neoplasm that results from an over production of mainly red blood cells but also platelets and white blood cells.

Pruritus Another word for itching. Pruritus can result from drug reaction, food allergy, kidney or liver disease, cancers, parasites, aging or dry skin, contact skin reaction, such as poison ivy, and for unknown reasons.

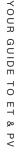
Pulmonary embolism The obstruction of the pulmonary artery or a branch of it leading to the lungs by a blood clot, usually from the leg, or foreign material causing sudden blockage of the vessel.

R

Radiotherapy (or radiation)

The treatment of disease with ionising radiation. High-energy rays are used to damage cancer cells and stop them from growing and dividing.

Red blood cell (or erythrocyte) The blood cell that carries oxygen. Red cells contain haemoglobin, which permits them to transport oxygen (and carbon dioxide).



S

Spleen An organ located in the upper left part of the abdomen near the stomach. The spleen produces lymphocytes (a type of white blood cell), filters blood, serves as a reservoir for blood, and destroys old blood cells. The spleen can also supplement the bone marrow in the production of red blood cells in certain situations (as with MPNs). This can sometimes lead to an enlarged spleen (splenomegaly). An operation to remove the spleen is called a splenectomy.

Stem cells Stem cells are cells that have the potential to develop into many different or specialised cell types.

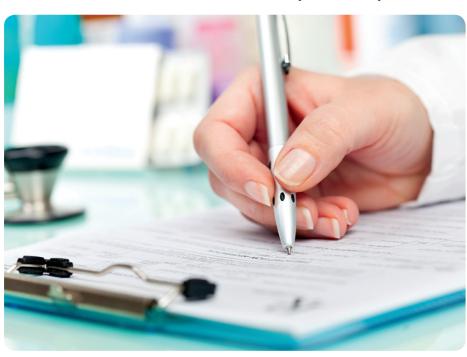
Stroke (Cerebrovascular Accident or CVA) The sudden death of some brain cells due to a lack of oxygen when the blood flow to the brain is impaired by blockage or rupture of an artery to the brain.

Т

Thrombocythaemia An abnormally high number of platelets in the blood, typically above 450,000 per microlitre.

Thrombocytopenia A lower than normal number of platelets in the blood, typically below 150,000 per microlitre.

Thrombosis The formation or presence of a blood clot in a blood vessel. The vessel may be any vein or artery. The clot itself is termed a thrombus [see blood clot].







Venesection See phlebotomy.

W

White blood cell (or leukocyte)
One of the cells the body makes to help
fight infections. There are several types
of white blood cells. The two most
common types are the lymphocytes
and neutrophils.



Yoga A way of life that includes dietary prescriptions and physical exercise. Yogic meditation can help control such things as blood pressure, heart rate, respiratory function, and many other bodily functions.



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Supporting people with MPN