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#Reference From NCCN Guidelines

Contents

NCCN Foundation seeks to support the millions of patients and their families affected by a cancer diagnosis by funding and distributing NCCN Guidelines for Patients. NCCN Foundation is also committed to advancing cancer treatment by funding the nation's promising doctors at the center of innovation in cancer research. For more details and the full library of patient and caregiver resources, visit NCCN.org/patients.

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1
MPN basics

Myeloproliferative neoplasms are a type of blood cancer. Also called MPNs, these cancers grow slowly, so many people with MPNs have long lives. The impact of MPNs on quality of life greatly varies between people. For some, MPNs cause life-changing symptoms.

What are MPNs?

Myeloproliferative neoplasms (MPNs) are a group of rare blood cancers with an unusual name. What exactly does the name mean?

- The first part of the first word—**myelo**—refers to bone marrow. Almost all bones have a soft center, called marrow, where most blood cells are formed.
- The second part of the first word—**proliferative**—refers to the rapid growth of cells.
- A **neoplasm** is an abnormal growth of cells.

Put together, the name myeloproliferative neoplasms means cancers of blood cells in the bone marrow. There are many types of blood cells, so there are many types of blood cancers. Let's review in the next section how blood cells are made to further understand what MPNs are.

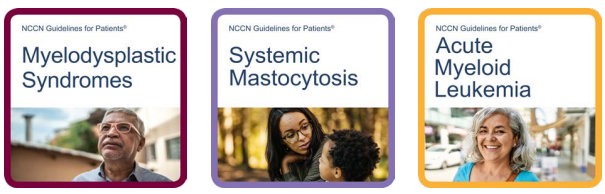
MPNs are not...

Myelodysplastic syndromes (MDS)
Like MPNs, MDS are cancers of blood stem cells within the myeloid cell line. MDS cause low numbers of blood cells.

Myelodysplastic syndromes/ myeloproliferative neoplasms (MDS/ MPN)
MDS/MPN is a group of cancers distinct from MPN and MDS. The mature blood cells are abnormal, and there are high numbers of blood cells.

Systemic mastocytosis
Systemic mastocytosis is a buildup of a type of white blood cells, called mast cells, in the body, excluding the skin. A subtype called systemic mastocytosis with an associated hematologic neoplasm (SM-AHN) can occur with MPN.

Acute myeloid leukemia (AML)
AML is a cancer of myeloid cells in bone marrow. It causes many abnormal myeloid blasts, which cannot become mature blood cells. An MPN may transform into AML although it rarely does.



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MPNs affect very young blood cells

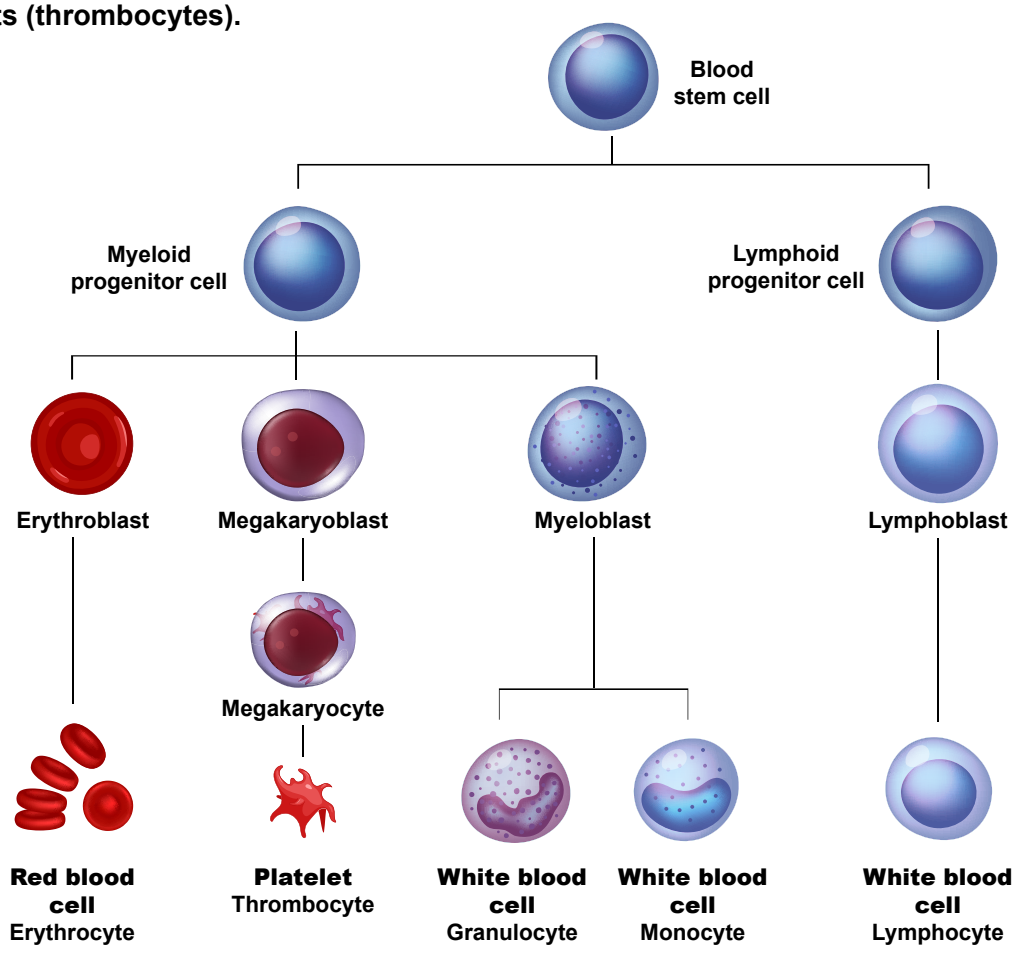
Blood cells do not live long, so they need to be replaced often. They arise from changes in a series of cells. The process can be simplified into 3 steps:

1. Hematopoietic stem cells develop into every type of blood cell, including red blood cells, white bloods cells, and platelets. They make exact copies of themselves and make different cells that are a step closer to being blood cells. These different cells are called progenitor cells.

2. Progenitor cells belong to one of two families of blood cells—myeloid or lymphoid cell lines. Progenitor cells change into blast cells. Blasts, for short, are young (or immature) blood cells.

Blood cells

Blood stem cells are the cells from which all blood cells are formed. They go through a series of changes to become mature blood cells. The three main types of blood cells are red blood cells (erythrocytes), white blood cells (granulocytes, monocytes, and lymphocytes), and platelets (thrombocytes).



3. Each type of blast is set to become a certain type of mature blood cell. Mature blood cells are fully developed cells that perform specific functions. The main types of blood cells are red blood cells, white blood cells, and platelets.

MPNs affect cells in the first step of blood cell formation. They are cancers of blood stem cells but only affect the myeloid family of cells. Myeloid blasts mature into blood cells, but too many blood cells are made. The type of mature blood cell that is in excess depends on the type of MPN.

MPNs are classified as a blood cancer, but it is a cancer with a very small c! It is easy to become fearful and obsessed when first diagnosed (I know I was!), but MPNs are for most people highly treatable. Find a doctor that is an MPN specialist and join reputable online MPN patient forums, it makes all the difference."

What are the classic MPNs?

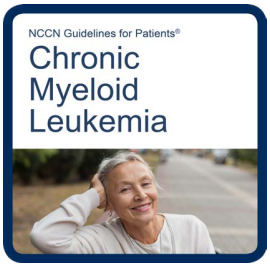
There are several types of MPNs, but this book is about the most common (or classic) types:

- **Polycythemia vera (PV)** causes an excess of red blood cells.
- **Essential thrombocythemia (ET)** causes an excess of platelets.
- **Primary myelofibrosis** causes an excess of megakaryocytes that trigger a buildup of scarring (fibrosis) in bone marrow.

More information on the classic types of MPN is in *Chapter 2: Tests for MPN.*

Chronic myeloid leukemia (CML) is an MPN with too many granulocytes, a type of white blood cell. Some people call it a classic MPN, but it is often discussed by itself. Its treatment is based on a cancer marker that the other classic MPNs do not have.

More information on CML is available NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



What's the best treatment?

There's no treatment for MPNs that's best for everyone. The best treatment is the treatment that's right for you. Your treatment plan should follow best practices—cancer care based on science and expert consensus. The following chapters explain the best practices of testing for and treating classic MPNs.

Treatment may not be needed

MPNs are chronic cancers. Chronic cancers can be stable for several years and typically progress slowly. Treatment may not be needed right away or ever, but these blood cancers are not typically cured.

People with MPN often live many years with proper treatment. Many people have near-normal lifespans. But for some, the cancer worsens more quickly. The course of the cancer depends on the MPN type, features of the cancer, and your age and health.

Relief of symptoms

MPNs cause a wide range of symptoms—fatigue, headaches, and abdominal pain, just to name a few. In recent years, valid surveys to assess symptoms have been developed. To learn more, read *Chapter 3: Symptoms and surveys.*

The burden of MPN symptoms varies greatly between people. For many people, though, the burden is intense and reduces their quality of life. Symptoms may restrict everyday activities and work hours. Relief of symptoms is discussed in *Chapter 6: Supportive care.*

Preventing complications

Your care team will watch for 3 major complications of MPNs:

- Abnormal bleeding
- Blood clots
- Disease progression

Abnormal bleeding (hemorrhage) and blood clots (thrombi) are most common in PV and ET. But both also occur with myelofibrosis. Abnormal bleeding is often minor but can be severe. Blood clots can block blood vessels. They can be fatal, though this is rare.

MPNs can progress into more severe diseases but most do not. ET and PV can progress into myelofibrosis. Though rare, MPNs can progress into acute myeloid leukemia (AML). When MPNs progress to AML, the term MPN blast-phase (MPN-BP) is commonly used.

Preventing complications is discussed in *Chapter 4: Clotting in PV and ET* and in *Chapter 5: Myelofibrosis.*

Advocate for yourself

You are a member of your cancer care team. Discuss the recommendations in this book with your team. Together, you can make a care plan that's best for you.

There is a list of suggested questions in Chapter 7 to ask your team. You're more likely to get the care you want by asking questions and making decisions with your team.

Key points

- Myeloproliferative neoplasms, also called MPNs, are a type of blood cancer. MPNs cause high numbers of blood cells.
- The three classic MPNs are polycythemia vera (PV), essential thrombocythemia (ET), and primary myelofibrosis (PMF).
- MPNs are chronic cancers, which means they worsen slowly.
- With treatment, most people live a long life, though many struggle with intense symptoms. For others, the cancer may worsen quickly or cause a fatal complication.

"You need to be your own advocate, particularly since this is a rare cancer and the significant majority of healthcare experts are not aware of MPNs. If I didn't observe my own blood work, push for appointments with hematologists, and not stop asking 'why,' I still would not know about my diagnosis and may not have learned until it was potentially too late."

2
Tests for MPN

Several tests are needed if your health care provider suspects a myeloproliferative neoplasm (MPN). These tests are described in this chapter.

Tests to take

Testing does not differ much between the myeloproliferative neoplasm (MPN) types. Each type—polycythemia vera (PV), essential thrombocythemia (ET), and primary myelofibrosis (PMF)—requires blood work. Tests of bone marrow are also very common. **See Guide 1** for a list of tests used to diagnose and plan treatment of MPNs.

Ask for copies of your test results and take notes as your health care provider explains the reports. Don't let your nerves stop you from asking questions. MPNs can be hard to understand.

Bringing someone with you to your appointments can be helpful. Keep your reports and other paperwork handy and organized in a file (such as a binder) for when you need them again.

Guide 1
Tests for myeloproliferative neoplasms

Health history and exam	• Medical history including transfusions and medicines • Physical exam • Symptom scale
Blood tests	• Complete blood count (CBC) with differential • Blood smear • Comprehensive metabolic panel, liver function tests, lactate dehydrogenase (LDH), uric acid • Erythropoietin (EPO) and iron • Human leukocyte antigen and coagulation tests are sometimes needed
Bone marrow tests	• Bone marrow biopsy and aspirate • Study of bone marrow using special stains and a microscope
Biomarker tests	• Fluorescence in situ hybridization (FISH) or multiplex RT-PCR for *BCR-ABL1* • Molecular tests or multigene next-generation sequencing (NGS) for *JAK2*, *CALR*, and *MPL* mutations • Cytogenetics using karyotype with or without FISH

Health history

Expect your health care provider to review your health in detail. This is known as taking a medical history. Your health care provider will want to know a lot about your past and current health. You will likely be asked about:

- Illnesses and diseases
- Prescribed and over-the-counter medicines and supplements, surgeries, and blood transfusions
- Lifestyle choices including your diet, how active you are, and whether you smoke or drink alcohol
- Symptoms and complications of MPNs, such as headache, bone pain, abdominal pain, itching or tingling, extreme fatigue

MPNs rarely run in families. It is very rare to be born with an abnormal gene that causes an MPN. Most people acquire changes in genes after birth that may lead to an MPN.

Some other types of cancers and health conditions do run in families. Be prepared to discuss the health problems of your close blood relatives. These include your siblings, parents, and grandparents.

Physical exam

Your health care provider will also perform a thorough physical exam of your body. This exam may include:

- Checking your vital signs—blood pressure, heart rate, breathing rate, and body temperature—and assessing your overall appearance
- Feeling and listening to organs, including your spleen and liver
- Assessing your level of pain, if any, when you are touched

“Much diagnosis and treatment is blood work number based and can be done virtually. Get a second opinion or third. Had I not sought out an amazing MPN expert and instead trusted my first oncologist–I am sure I would not be where I am now–healthy, good numbers, and confident in my MPN treatment journey and medical team."

Blood tests

Blood tests can measure blood cells, proteins, and chemicals in the bloodstream. They are commonly used to screen for disease and to plan treatment of blood cancers.

Some blood tests are done with a machine while others need a pathologist to complete. A pathologist is a doctor who's an expert in tissues and cells.

For MPN, a doctor called a hematopathologist may be part of your care team. A hematopathologist is an expert at diagnosing cancers of blood and immune cells.

Complete blood count with differential

A complete blood count (CBC) with differential is a very common lab test. Test results include:

- Counts of white blood cells, red blood cells, and platelets
- The percentage of red blood cells in blood (called hematocrit)
- The amount of a protein called hemoglobin within red blood cells
- Counts of the most common types of white blood cells in the blood—basophils, neutrophils, eosinophils, monocytes, and lymphocytes

Blood smear

A pathologist will inspect your blood using a microscope. This is known as a blood smear. With a microscope, a pathologist can see the size and shape of blood cells. Abnormal features of blood cells can be a clue as to what disease you have.

A blood smear can also show if there are immature blood cells called blasts in the blood. Normally, blasts are only in bone marrow, but sometimes myelofibrosis forces them out.

Metabolic panel and liver tests

A comprehensive metabolic panel measures up to 14 types of chemicals that come from your organs. It is a screening test for many diseases. It can also show if the MPN is affecting your organs, such as your bones and liver.

Likewise, liver function tests are used to assess if the MPN is affecting your liver. These tests measure a yellow-colored fluid called bile and liver proteins and enzymes.

Lactate dehydrogenase and uric acid

Most cells have a protein called lactate dehydrogenase (LDH) and a chemical called uric acid. High levels of LDH and uric acid may be signs of myelofibrosis. During certain phases, myelofibrosis causes many blood cells to die. Dying blood cells release LDH and uric acid.

Erythropoietin and iron

Erythropoietin (EPO) is a hormone made by the kidneys. It helps to make red blood cells, and iron is needed to make hemoglobin in red blood cells. Blood tests of EPO and iron help diagnose PV. In PV, high red blood cell counts suppress EPO levels. Also, iron levels may be low despite having high hemoglobin levels.

Other blood tests

Other blood tests are sometimes needed. People who will have a treatment called an allogeneic hematopoietic cell transplant (HCT) need human leukocyte antigen testing. To learn more about allogeneic HCT, read *Chapter 5: Myelofibrosis*.

Coagulation testing may be done to assess how well your blood clots. Some people are diagnosed with acquired von Willebrand syndrome (aVWS) or another blood clotting disorder based on these tests.

Bone marrow tests

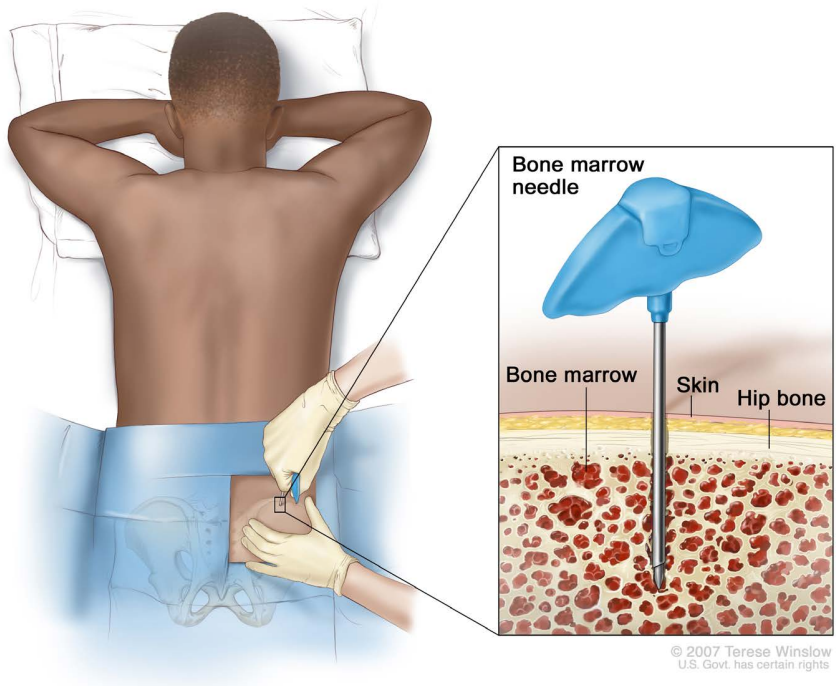
Bone marrow is the soft center in the middle of most bones. It is like a sponge holding liquid and cells.

A bone marrow biopsy removes a core sample of marrow. A bone marrow aspiration removes liquid and cells. These procedures are often done at the same time. They're performed on the back of the hip bone. You may receive an injected pain blocker or light sedative to relax you beforehand.

A pathologist will inspect your bone marrow using a microscope. This is known as bone marrow histology. Histology can detect abnormal numbers of bone marrow cells. It can also show how much bone marrow is scarred (fibrosis).

Removing bone marrow samples

Samples of your bone marrow might be removed and tested for diagnosis or treatment planning. A bone marrow aspiration removes a small amount of liquid bone marrow. A bone marrow biopsy removes a small piece of bone with marrow. These procedures are often done on the back of the hip one after the other.



Biomarker tests

Biomarker tests look for biological clues, or markers, of cancer. Molecular tests are a type of biomarker test that look for abnormal genes called mutations. Some people call them genetic tests. Cytogenetic tests show if there are abnormal chromosomes.

Biomarker test for CML mutation

The hallmark of chronic myeloid leukemia (CML) is the *BCR-ABL1* fusion gene. Fluorescence in situ hybridization (FISH) and multiplex RT-PCR are molecular tests that detect *BCR-ABL1* in either a blood or bone marrow sample. If *BCR-ABL1* is missing, CML is ruled out.

Biomarker tests for MPN mutations

If CML is ruled out, molecular testing is used to look for markers of classic MPNs.

Tests for diagnosis

One of the markers is the *JAK2* V617F mutation. If this marker is not found, the next markers to be tested are:

- *JAK2* exon 12 mutations if PV is suspected
- *CALR* and *MPL* mutations if ET or PMF is suspected

A newer technology called next-generation sequencing (NGS) can test for multiple genetic markers at the same time. It may be used instead of single molecular tests.

Tests for prognosis

If tests confirm that you have an MPN, NGS testing is recommended to assess for prognosis if it wasn't done before. A prognosis predicts how the cancer will behave and respond to treatment.

Biomarker tests for abnormal chromosomes

Cytogenetics are useful for diagnosis and treatment planning. Results can help with identifying MPN subtypes, grading bone marrow fibrosis, and assessing the prognosis of the cancer.

A picture of chromosomes called a karyotype is used for cytogenetics. A FISH test may be done, too. These tests are done on bone marrow aspirate or a blood sample.

> **"I'm happy I found the right hematologist after 2 tries. Make sure your doctor is an MPN researcher, and does the right genetic tests for mutations."**

How to diagnose MPNs

The International Consensus Classification (ICC) and World Health Organization (WHO) have created diagnostic standards for MPN. These standards include major criteria and related minor criteria. A pathologist will use the tests described in this chapter to decide if the criteria for an MPN are met.

Primary myelofibrosis

Myelofibrosis is called primary myelofibrosis or PMF if it is the only MPN that you have had. There are 2 stages of PMF based on the amount of scarring (fibrosis) in bone marrow:

- Prefibrotic PMF (pre-PMF or early PMF)
- Overt PMF

The first criterion of myelofibrosis is a high number of abnormal megakaryocytes in bone marrow. The bone marrow in pre-PMF has either minor or no scarring, whereas there is major scarring in overt PMF. In pre-PMF, the number of bone marrow cells is higher than normal, although at times the production of red blood cells may be low.

Myelofibrosis can only be diagnosed after other blood cancers have been excluded. The second criterion requires other types of MPN, myelodysplastic syndromes (MDS), and other myeloid neoplasms to be ruled out.

The third criterion is having a *JAK2, CALR,* or *MPL* mutation. A *JAK2* mutation is the most common, and a *CALR* mutation is the second most common. About 1 out of 10 people with PMF don't have any of these three mutations. In these cases, the MPN is described as triple negative.

To be considered PMF, the minor criterion—another sign of myelofibrosis—must be detected with blood tests. This sign may be low red blood cell counts or hemoglobin (anemia), high levels of white blood cells or LDH, or an enlarged spleen. Another sign of overt PMF is blasts in a blood smear.

Polycythemia vera

The first major criterion for PV is a high hemoglobin, hematocrit, or red cell mass. Your health care provider may reorder blood work to check that a high level persists.

- Hemoglobin is a protein within red blood cells. Hemoglobin is high when it is greater than 16.5 g/dL if assigned male at birth or 16.0 g/dL for female.
- Hematocrit is the percentage of red blood cells in blood. Hematocrit is high when greater than 49 percent in those born male and 48 percent in those born female.
- Red cell mass is the volume of red blood cells in the blood. It is a nuclear medicine test and is not often used to diagnose MPNs. The red cell mass is high when it is 25 percent greater than the normal value.

The second criterion for PV is a high number of myeloid blood cells compared to fat cells in bone marrow. This is called hypercellularity. Myeloid blood cells include red blood cells, platelets, and granulocytes. For more information on blood cells, read *Chapter 1: MPN basics.*

The third criterion for PV is a *JAK2* mutation, but it is not required for diagnosis. Almost

everyone with PV has a *JAK2* V617F mutation. The few people without this mutation most often have a *JAK2* exon 12 mutation instead.

If no *JAK2* mutation is found, PV is diagnosed if the first two major criteria are met, and you have low EPO levels (the minor criterion).

Essential thrombocythemia

The first major criterion for ET is a high platelet count. A high platelet count is 450 × 10^9/L or above.

The second criterion is a high number of abnormal megakaryocytes in bone marrow. Megakaryocytes in ET are larger than normal. Their nucleus—the brain of the cell—has more divisions (lobes) than normal.

ET can only be diagnosed after other blood cancers have been excluded. The third criterion requires other types of MPN, MDS, and other myeloid neoplasms to be ruled out.

The fourth criterion is having a *JAK2, CALR,* or *MPL* mutation, but it is not required for diagnosis. A JAK2 mutation is the most common, and a *CALR* mutation is the second most common. About 1 out of 10 people with ET don't have any of these three mutations. In these cases, the MPN is described as triple negative.

When the fourth criterion is not met, ET can be diagnosed based on the minor criteria. These criteria include another genetic marker or no underlying cause of the high platelet count. Other causes of high platelet counts include low iron, chronic inflammation, and effects of medicine.

Know your MPN

- ✓ What is the subtype?
- ✓ What are the mutations, if any?
- ✓ What treatment are you on?

It is important to tell any clinician who treats you about the MPN and treatment. Otherwise, you could receive care that is harmful.

"My friend, a nurse, advised that I get a second opinion for my ET diagnosis. He went with me, and at the end he asked, 'What's the prognosis?' Doc says, 'I understand you ride a road bike and stay in shape. More than likely, if you follow your hematologist advice, you'll live 20 years, unless you get hit by a bus.' That was 12 years ago, and I am still pedaling. I am almost 79 years old."

Challenges to diagnosis

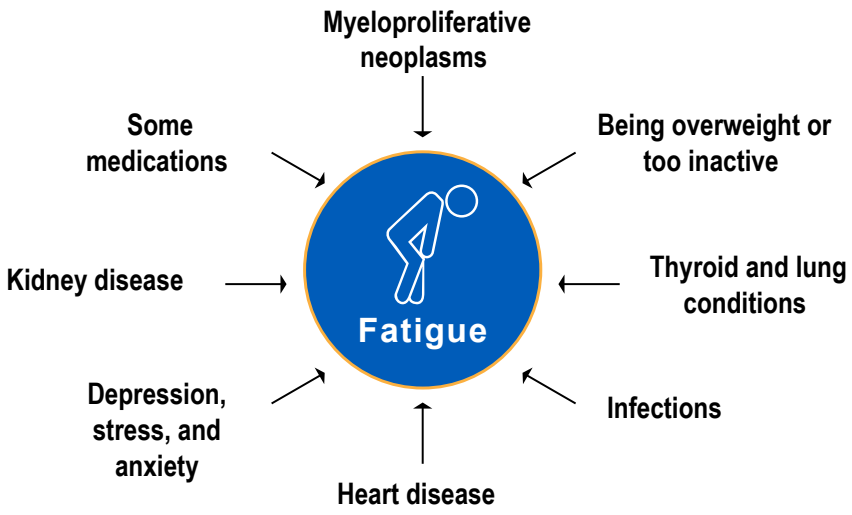
Making a diagnosis of MPN can be tricky. Some of the challenges to diagnosis are as follows:

- Signs and symptoms of MPNs can have other causes, too. Other causes need to be ruled out.
- The classic MPNs can have very similar test results. Early PMF may look like ET because there may be little bone marrow scarring.
- Recent bleeding can change test results and hide the correct diagnosis.
- Symptoms and test results differ between the early, middle, and late phases of an MPN. Health care providers need to know what each MPN looks like as it progresses.

The pathologist will identify the MPN subtype when possible. Although rare, there are times when the MPN subtype is not clear. These cancers are called MPN, not otherwise specified (NOS).

Why am I so tired?

Symptoms caused by MPNs can also be caused by other conditions. The overlap may make a diagnosis of MPN challenging. Take fatigue, for example. Fatigue is the most common symptom of MPNs. Fatigue is also caused by some medications, many diseases, and poor mental health and physical fitness.



Key points

- If an myeloproliferative neoplasm (MPN) is suspected, a group of tests is needed for diagnosis. Testing does not differ much between the MPN types.
- Be ready to tell your care team about any health problems and treatments you've had in your lifetime.
- Your health care provider will examine your body for signs of disease. The exam will include touching parts of your body to see if anything feels abnormal.
- You will also need to provide samples of blood, bone marrow, or both. Your blood and bone marrow will be sent to a lab to be tested for signs of MPNs and other diseases.
- Despite criteria to diagnose MPN types, diagnosis can be challenging. Most MPNs have a genetic marker. These markers include *JAK2*, *CALR*, and *MPL* mutations.

"I am grateful for science, and for ongoing research that has turned some kinds of cancers into chronic diseases, not death sentences. I am grateful to have a good doctor and treatments that are working for me. In some ways, my cancer turned out to be lucky because it has inspired me to live in a healthier, more mindful way."

3
Symptoms and surveys

Symptoms of myeloproliferative neoplasms (MPNs) can have a major impact on life. A short survey is often used to check for symptoms. This chapter explains the symptoms that you might experience with an MPN.

MPN symptoms

A symptom is a physical or mental change that may be related to a disease. Most people with myeloproliferative neoplasms (MPNs) have symptoms related to the cancer. Symptom burden is often severe even in people with polycythemia vera (PV) or essential thrombocythemia (ET).

MPNs cause a wide range of symptoms. Generally, there are 3 types of symptoms that your care team will plan treatment with:

- Microvascular symptoms
- Enlarged spleen symptoms
- Constitutional symptoms

These symptoms are described next. For information on treating symptoms, read *Chapter 6: Supportive care.*

Microvascular symptoms

Microvascular symptoms are caused by slow blood flow in small blood vessels called capillaries.

PV symptoms

PV reduces blood flow due to high numbers of red blood cells. This can lead to headaches and blurred vision. It can also cause a condition called erythromelalgia. Erythromelalgia includes a burning pain in skin, reddened skin, and warm skin.

ET symptoms

In ET, high numbers of platelets can cause headaches, vision problems, dizziness, high-pitched ringing in the ears (tinnitus), and numbness and tingling in the limbs (paresthesia). Other microvascular symptoms include poor concentration, sleep problems, and sexual problems.

Enlarged spleen symptoms

Among people with MPNs, bone marrow may become unable to make enough healthy blood cells. When the bone marrow makes too few blood cells, other parts of the body may start producing the cells instead.

The spleen is a very common backup to bone marrow for blood cell production. It is a small organ to the left of the stomach.

When the spleen supplies the body with blood cells, it gets bigger. An enlarged spleen is called splenomegaly. Your health care provider

will be able to feel an enlarged spleen during an exam.

An enlarged spleen causes symptoms because it presses against other body parts. It may partly fill the space where the stomach is. In turn, you will feel full quicker when eating (early satiety).

The spleen may press against the diaphragm, which prevents the lung from fully expanding. In turn, you may have shortness of breath or a cough.

An enlarged spleen can also cause discomfort or pain if it presses on a nerve. Many people become less active due to these symptoms.

Constitutional symptoms

Constitutional symptoms are the result of a condition that affects the whole body. They are very general and can be caused by more than one factor.

In MPNs, experts believe that constitutional symptoms are related to high levels of small proteins called cytokines. Cytokines trigger inflammation—a defensive reaction—in the body.

One of the most common constitutional symptoms of MPNs is fatigue. Cancer-related fatigue is a distressing, ongoing tiredness that limits one's ability to do day-to-day tasks. It is a major contributor to poor quality of life among people living with an MPN.

You may lose weight and have fevers because an MPN can cause a rapid breakdown of fat and muscle. The rise in body temperature may trigger excessive sweating called night sweats.

Bone pain in the limbs may be due to the rapid making of blood cells, which causes inflammation in the covering of the bone. Another common cytokine-related symptom is itchy skin (pruritus). Itchy skin is triggered by water, so it can interfere with body hygiene.

> **"The impact of MPNs can be quite wide-ranging. There is more to these conditions than the risk of thrombosis. The secondary or constitutional symptoms can be more problematic and deserve equal attention."**

Assessing symptoms with surveys

Surveys are commonly used in research to assess symptoms. Surveys used for research may also be used in clinical practice. For MPNs, there are several reasons to assess symptoms:

- Symptoms often reduce quality of life
- Symptoms may relate to the outcomes of an MPN
- Tracking symptoms will show if a treatment provides relief

The MPN-10

The MPN Symptom Assessment Form Total Symptom Score (MPN-SAF TSS) is a commonly used survey. It's also simply called the MPN-10 because it has 10 questions. **See Guide 2** for a list of the 10 symptoms the survey looks for.

The 10 symptoms in the MPN-10 are the most important and common ones. Each symptom is rated on a scale from 0 to 10. Higher scores point to worse symptoms. An online version of the survey can be found at thehematologist.org/mpn-total-symptom-score.

Guide 2
The top 10 symptoms of myeloproliferative neoplasms

Symptom	Medical term
Ongoing, extreme tiredness	Fatigue
Feeling full quickly when eating	Early satiety
Pain in the belly area	Abdominal pain
Inactivity	Sedentary
Unable to focus for an extended time	Poor concentration
Night sweats	Sleep hyperhidrosis
Itchy skin	Pruritus
Bone pain	Osteodynia
Fevers	Pyrexia
Weight loss	Cachexia

Key points

- Most people with myeloproliferative neoplasms (MPNs) have symptoms related to the cancer.
- Microvascular symptoms are caused by slow blood flow in capillaries. Examples of these symptoms are headaches, dizziness, and tingling in the limbs.
- The spleen gets bigger when it starts making blood cells. An enlarged spleen may cause you to feel full quickly when eating. It may also cause belly pain or discomfort, cough, and shortness of breath.
- Constitutional symptoms are related to high levels of cytokines. Examples of these symptoms include fatigue, losing weight, and fevers.
- The MPN-10 is a short survey of MPN symptoms used in clinical practice to identify and track symptoms over time.

"I take each day at a time. Sometimes the fatigue is greater than other days. You must persevere."

4
Clotting in PV and ET

In polycythemia vera (PV) and essential thrombocythemia (ET), it's important to prevent blood clots. Left unchecked, blood clots are the leading cause of death. This chapter explains how blood clots are prevented.

What is a blood clot?

A blood clot is a gel-like clump of blood. Normally, blood clots develop to stop bleeding and then dissolve when the bleeding is over.

Sometimes a blood clot can form inside a blood vessel when there is no bleeding. This type of clot is called a thrombus (or thrombi if there's more than one). A thrombus that breaks free from the vessel wall and travels in the bloodstream is called an embolus.

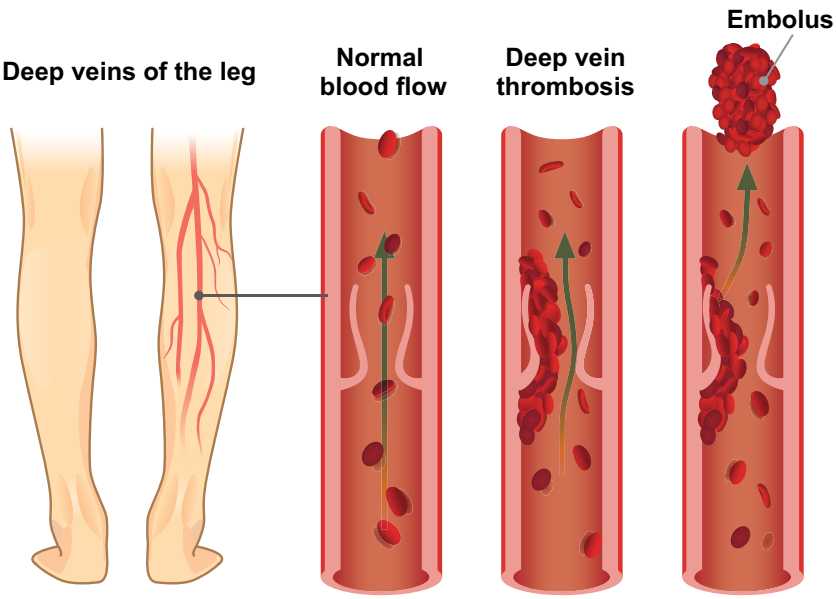
For our purposes, we'll refer to thrombi (or thrombosis) as blood clots for the remainder of this chapter.

People with polycythemia vera (PV) and essential thrombocythemia (ET) are prone to get blood clots. Both slow down blood flow because of the increase in blood cells, and the extra blood cells stick together. Slow-moving, sticky blood cells are likely to form blood clots.

Blood clots are the most frequent, sometimes life-threatening, complication of PV and ET. As blood clots worsen, they can block enough blood flow (thrombosis) to cause symptoms. Blocked blood flow can cause organ damage or failure, including heart attack, or a stroke.

Blood clot in a leg

People with MPNs are at risk for blood clots. This image shows a blood clot forming in a leg vein. Deep vein thrombosis is the most common type of blood clot. If not treated, the clot could break free and get stuck in an artery within a lung. This is called a pulmonary embolism. Pulmonary embolisms can be deadly.



Preventive care reduces the chance of getting blood clots. With prevention, many people with PV or ET live for many years.

Calculating clot risk

The risk of blood clots is not the same for everyone living with an myeloproliferative neoplasm (MPN). Your health care provider will assess your risk and plan treatment based on your risk level. This process is called risk stratification.

People with PV are stratified into one of two groups—low or high risk. Risk is based on age and history of blood clots.

For ET, a tool called the International Prognostic Score of Thrombosis (IPSET-thrombosis) is used for risk stratification. People are assigned to very-low- low-, intermediate-, or high-risk levels based on age, prior blood clots, and a *JAK2* V617F mutation.

Preventing blood clots

The plan to prevent clots differs between people. Your plan will be based on what MPN type you have, your risk of clots, and if you have symptoms of an MPN. Options for initial preventive care based on risk level are listed in **Guide 3** for PV and **Guide 4** for ET and are described next.

Managing cardiovascular risk factors

Your cardiovascular system consists of your heart, blood vessels, and blood. Cardiovascular risk factors are things that will likely damage this system. Having a

Guide 3
Initial preventive care for blood clots related to polycythemia vera

Risk level	Prevention options
Low risk of blood clots You are under 60 years of age and never had a blood clot.	• Manage cardiovascular risk factors • Aspirin • Phlebotomy

High risk of blood clots
You are 60 or more years of age or you have had a blood clot.
	• Manage cardiovascular risk factors
	• Aspirin
	• Phlebotomy
	• Cytoreductive therapy to reduce blood counts:
	  • Hydroxyurea (preferred)
	  • Ropeginterferon alfa-2b-njft (preferred)
	  • Peginterferon alfa-2a
	  • Ruxolitinib is sometimes useful

cardiovascular risk factor may increase your chance of getting a blood clot.

Your health care provider will assess for and help you manage cardiovascular risks that can be changed:

- Smoking
- Overweight and obesity
- Too little exercise
- High blood pressure (hypertension)
- High blood sugar (diabetes)

Aspirin

Taking a baby aspirin every day reduces the risk of blood clots. It prevents clots by making platelets less sticky. It may reduce microvascular symptoms in ET.

NCCN experts recommend taking 80 to 100 milligrams of aspirin each day for most people with PV or ET. If you're still experiencing symptoms, you can take aspirin twice a day.

Aspirin prevents blood clots among people with either low- or high-risk PV. It also works

Guide 4
Initial preventive care for blood clots related to essential thrombocythemia

Risk level	Prevention options
Very low risk of blood clots You are 60 years of age or under, never had a blood clot, and do not have a *JAK2* mutation.	• Manage cardiovascular risk factors • Aspirin if you have microvascular symptoms
Low risk of blood clots You are 60 years of age or under and never had a blood clot. You do have a *JAK2* mutation.	• Manage cardiovascular risk factors • Aspirin
Intermediate risk of blood clots You are at least 61 years of age. You never had a blood clot and do not have a *JAK2* mutation.	• Manage cardiovascular risk factors • Aspirin

High risk of blood clots
You are at least 61 years of age, have had a blood clot, and have a *JAK2* mutation.
	• Manage cardiovascular risk factors
	• Aspirin
	• Cytoreductive therapy to reduce blood counts:
	  • Hydroxyurea (preferred)
	  • Peginterferon alfa-2a
	  • Anagrelide

well among people with ET, but not everyone with ET needs it.

Aspirin can cause more harm than good in people with very-low-risk ET, especially those with acquired von Willebrand syndrome (aVWS).

Bleeding is a side effect of aspirin for some people. People with aVWS are likely to have bleeding because their blood doesn't clot as it should.

Higher doses should be avoided for most people. High doses increase the chance of bleeding in your bowels. Your blood counts may need to be lowered before starting aspirin. High blood counts increase the risk of bleeding.

Smoking blocks the action of aspirin. If you smoke, you'll have to quit for aspirin to work. Ask your health care providers about counseling and medicine to help you quit.

Phlebotomy

Hematocrit is a measure of red blood cells compared to the total amount of blood. Although aspirin works well for PV, the main way to prevent blood clots is to reduce hematocrit.

At diagnosis, hematocrit is often above 55 percent (55%). Hematocrit should be below 45 percent for most people. Some people need a target of below 42 percent.

Phlebotomy is the key strategy to reducing hematocrit. It is a procedure that removes a small amount of blood with a needle, like when donating blood.

Phlebotomy works by removing the iron-carrying red blood cells from the blood. With less iron in the body, bone marrow makes fewer red blood cells. If you are receiving phlebotomy therapy, don't take iron supplements unless they're prescribed by your care team.

Blood clots aren't as likely if the bloodstream is less congested with red blood cells. After phlebotomy, you may also get quick relief from MPN symptoms—headaches, itchiness, and blurred vision.

Your health care provider will assess how often you need phlebotomy. Some people need it every other week. If your hematocrit is high, you may need it once or twice a week. Once the hematocrit and MPN symptoms are under control, the time between phlebotomies can be lengthened.

Cytoreductive therapy

People who are highly likely to get blood clots may take medication that lowers blood counts. These cytoreductive therapies are also sometimes given to relieve symptoms when blood clots aren't likely.

Some cytoreductive therapies are preferred by NCCN experts. Preferred therapies work better, are safer, or cost less than other options or there is better research supporting their use.

Hydroxyurea

Hydroxyurea (Hydrea) has been a standard cytoreductive therapy for a long time. It's a preferred initial treatment in high-risk PV and ET. For many people, it lowers blood counts and prevents blood clots for years.

Hydroxyurea works by stopping new cells from being made. It is made as a capsule, so you can take it at home. It is given in low doses, so many people can tolerate its side effects.

Hydroxyurea can cause below-normal blood counts, fatigue, skin changes, diarrhea, constipation, and skin cancer.

Interferon alpha

Interferon alpha naturally exists in your body and helps fight infections. It can also be created in the lab as a treatment. Interferon curbs the making of blood cells in bone marrow.

The two interferons used to treat MPNs are:

- Pegylated interferon, usually called peginterferon (PEGASYS), is a treatment option for high-risk PV and ET. It is sometimes given to people who are younger, pregnant, or delay taking similar medicines like hydroxyurea.
- Ropeginterferon alfa-2b-njft (BESREMi) is a preferred treatment option for high-risk PV.

You can take interferon at home. It is injected under the skin every 2 weeks. Over time, it may be needed less often.

Interferon can cause flu-like illness, joint pain, fatigue, itching, throat swelling, musculoskeletal pain, and depression.

Anagrelide

Anagrelide (Agrylin) is an antiplatelet medicine for high-risk ET. It lowers the number of platelets that your body makes. Anagrelide is a capsule that is taken twice a day. It may cause headaches, digestive problems, anemia, and heart palpitations.

Ruxolitinib

Ruxolitinib is sometimes useful for high-risk PV. It is a medicine that is called a JAK inhibitor. Read more about ruxolitinib in *Chapter 5: Myelofibrosis*.

"I found out in 2018 at my annual physical that my platelet count was elevated and that led to a diagnosis of ET with JAK 2 genetic mutation. I have no symptoms and my only treatment is two low-dose aspirin per day. I don't believe that this needs to be called blood cancer. I tell people that I have a blood disorder so it isn't so frightening."

Clot prevention during pregnancy

Consider meeting with an obstetrician who's an expert in high-risk pregnancies before getting pregnant. This doctor can assess for and manage health risks during pregnancy.

Pregnancy is at high risk if you have had a blood clot, bleeding due to PV or ET, or related problems during prior pregnancies.

Pregnancy care for standard risk includes:

- Taking a baby aspirin every day until the baby is born.
- After birth, many people take low-molecular-weight heparin (LMWH) for 6 weeks.
- Aspirin can be restarted once LMWH is finished.

Pregnancy care for high risk includes:

- After a positive pregnancy test, take baby aspirin every day.
- Many people also take LMWH throughout pregnancy and for 6 weeks after giving birth.
- If blood counts are high, they can be lowered with interferon.

Pregnancy care for everyone includes:

- Hydroxyurea should not be taken while trying to get pregnant, during pregnancy, or while breastfeeding. Hydroxyurea may harm your baby.
- You may take peginterferon alfa-2a to lower blood counts, but research on its use during pregnancy is needed.

If you need an anticoagulant (commonly referred to as a blood thinner) while breastfeeding, the safe ones to take are unfractionated heparin, LMWH, warfarin, and fondaparinux. Direct oral anticoagulants should be avoided.

If you have PV, the hematocrit target is based on the trimester. Hematocrit should be under 41 percent (41%) for the first trimester, under 38 percent for the second trimester, and under 39 percent during the third trimester.

Getting the news and diagnosis of ET with the JAK2+ mutation, wasn't going to be the end of my story. In fact, it has been the best part of my story. It has been the most challenging, yet praising God in the worst and best times, marrying my husband, preparing for a family via IVF and a surrogate, meeting new people through this diagnosis, and fighting to one day find a cure. I'm so proud of myself!"

Blood clots and surgery

Surgery increases the chance for blood clots and bleeding. Your surgeon may contact your MPN team to get your health history.

Your surgeon needs to know about any blood clots, bleeding, and your medications.

Before surgery, your blood counts should be close to normal to prevent blood clots and bleeding.

- You may be put on anticoagulants and cytoreductive therapy before surgery.
- People with PV may need more phlebotomies to stay below 45 percent for 3 months before surgery.
- If the surgery has a high risk for venous thromboembolism, you may be given low-molecular-weight heparin.

Just before surgery, you will need to stop taking some medicines. Aspirin is stopped 1 week before surgery.

You may stay on cytoreductive therapy until the surgery unless your surgeon tells you to stop. The time to stop an anticoagulant depends on how long it stays in your body.

After surgery, you will be monitored for blood clots and bleeding. You may restart your medicines if the bleeding risk is low. Aspirin is often restarted 24 hours after surgery.

PV and ET checkups

After starting preventive care, you will need to meet with your care team often. Your team will assess if the MPN is causing health problems and if it is progressing. They will also assess the results of treatment.

Visits with your care team

During visits, you will be asked about new or worsening symptoms and new diagnoses. You may be given a symptom survey called the MPN-10 to complete. For information on treating symptoms, read *Chapter 6: Supportive care.*

If you have PV, your health care provider will want to know how many phlebotomies you've had since the last visit.

Your health care provider will perform a physical exam of your body. The size of your spleen and liver will be checked. Your health care provider will look for signs of blood clots and bleeding.

Blood work may be needed. Your health care provider will monitor your blood counts and other blood values. Liver and kidney functioning tests may be ordered as well. Now and then, a peripheral blood smear may be done. A bone marrow aspiration and biopsy may be needed to rule out progression to myelofibrosis.

Changing preventive care

Your care will likely not change if symptoms greatly improve. Little to no relief in symptoms or worsening symptoms may trigger a change. See **Guide 5** for a full list of events that signal when a change in care may be needed.

If a change in preventive care is needed, a clinical trial may be an option. A clinical trial is a type of medical research study. Read more about clinical trials in *Chapter 5: Myelofibrosis*.

If not received before, cytoreductive therapy may be the next step of care. It may be started

Guide 5
Events that signal that it may be time to change preventive care

Event	Polycythemia vera	Essential thrombocythemia
Blood clot	●	●
Acquired von Willebrand syndrome		●
Major bleeding	●	●
Enlarged spleen	●	●
High or increasing blood counts	●	●
New symptoms	●	●
Ongoing microvascular symptoms despite taking aspirin		●
More phlebotomies are needed to keep blood counts low or phlebotomies are causing problems	●	
Cytoreductive therapy isn't lowering blood counts or is causing problems	●	●
Bone marrow fibrosis	●	●
Blast cells in bloodstream	●	●

if you now have high-risk disease, symptoms, or abnormal bleeding.

Sometimes cytoreductive treatment works at first then stops. Sometimes, it doesn't work enough or at all. In these cases, changing to a care option listed in **Guide 6** is needed.

"I am now in my 10th year after a diagnosis of PV and only within the last month or so changed my daily regime of hydroxyurea 500 mg two times a day. I am fortunate in being largely asymptomatic, though the hydroxyurea does cause skin issues! Learn all you can about MPNs, be persistent in your questions, and be comfortable with your oncologist."

Guide 6
Next options after initial preventive care for blood clots

	Polycythemia vera	Essential thrombocythemia
Start cytoreductive therapy if never taken before	• Clinical trial (preferred) • Ropeginterferon alfa-2b-njft (preferred) • Hydroxyurea • Peginterferon alfa-2a	• Hydroxyurea (preferred) • Peginterferon alfa-2a • Anagrelide
Stop current cytoreductive therapy and start a new treatment	• Clinical trial (preferred) • Ruxolitinib (preferred) when hydroxyurea is stopped • Ropeginterferon alfa-2b-njft, hydroxyurea, peginterferon alfa-2a if not taken before	• Clinical trial (preferred) • Hydroxyurea (preferred) if not taken before • Peginterferon alfa-2a or anagrelide if not taken before • Ruxolitinib is sometimes useful • Removing platelets from blood (plateletpheresis) in emergency situations
New treatment plan if MPN changed into myelofibrosis	Read Chapter 5 for options	Read Chapter 5 for options

PV and ET progression

PV and ET can progress into myelofibrosis. Progression happens in about 1 out of 10 people with PV or ET. It is unknown why these MPNs progress. Researchers are studying the role of inflammation and abnormal genes.

The risk of progression increases the longer you have PV or ET. It is rare for these MPNs to progress right into the blast phase of myelofibrosis, which is like acute myeloid leukemia (AML). If PV and ET do progress, they typically progress into chronic-phase myelofibrosis and then into advanced phases.

Once progression starts, it may be slow and take place over many years. An early sign of progression is a steady decline in the need for treatment to reduce blood counts. Your health care provider may reduce or stop treatment to see if your blood counts stop falling. If they don't, you may have myelofibrosis. Treatment of myelofibrosis is discussed in Chapter 5.

Key points

- People with polycythemia vera (PV) and essential thrombocythemia (ET) are prone to getting blood clots. With preventive care, most people live for many years.
- Preventive care is based on your risk for blood clots. Having a healthy heart and blood vessels is a goal for everyone. Aspirin is also commonly used to prevent clots.
- For PV, phlebotomy is performed to reduce hematocrit. For high-risk PV/ET, cytoreductive treatment may be an option to reduce blood counts.
- Your care may change if you become pregnant and change again after giving birth. Your care may also be changed if you need surgery because it increases the risk of clots and bleeding.
- You will need to meet with your care team often. During visits, the status of the cancer and the results of preventive care will be checked.
- If PV or ET is getting worse, your treatment may be changed. The next treatment will depend on the current clot risk level, your prior treatment, and if there is progression to myelofibrosis.

"Knowledge is power. Do not settle if your questions and concerns are not properly addressed. There are many skilled MPN specialists throughout the nation that can provide relief, comfort, and improved quality of life. Advocate for yourself and your needs."

5
Myelofibrosis

Myelofibrosis is almost hidden in some people but rapidly progresses in others. Its treatment is discussed in this chapter including the newest ways to treat myelofibrosis with anemia.

Types of myelofibrosis

Myelofibrosis is a blood cancer that causes scarring of the bone marrow, called fibrosis. It can occur in people with or without a history of a myeloproliferative neoplasm (MPN).

If myelofibrosis is a person's first MPN, it is called **primary myelofibrosis (PMF).** It can also occur when polycythemia vera (PV) or essential thrombocythemia (ET) progresses. In these cases, it is called secondary myelofibrosis or **post-PV** and **post-ET myelofibrosis.**

Myelofibrosis greatly differs between people. It differs in terms of its course, speed of progression, and symptoms.

Treatment is partly based on how aggressive the myelofibrosis is predicted to be. Myelofibrosis slowly progresses in many people. It can be stable for many years.

For others, the MPN is more active. The first step of treatment planning is to assess the prognosis.

Predicting prognosis

The prognosis is the likely course and outcome of the myelofibrosis you have. Experts and care teams use risk stratification scoring systems to assess prognosis.

Scoring systems

For PMF, NCCN experts prefer the MIPPS-70 and MIPSS-70 Plus Version 2.0. These scoring systems are for people who are 70 years of age or under and require broad molecular testing. Other scoring systems for people of any age are the DIPSS and DIPSS-Plus.

The risk stratification system used for post-PV and post-ET myelofibrosis is the MYSEC-PM.

Risk is based on your medical information. Points are given for each response that conveys a risk of poor outcomes. Based on the total number of points, people are assigned a risk level.

Ask your provider what your risk level is and what system was used to calculate it. Risk levels for each system are listed on the next page in **Guide 7.**

NCCN risk groups

NCCN experts divide the total points into 2 risk groups—lower and higher—to plan treatment.

In the next section, treatment for lower- and higher-risk myelofibrosis without anemia is discussed. But most people with myelofibrosis have anemia. If you do, read the section in this chapter called *Treating myelofibrosis with anemia.*

> **Your journey is your own unique journey. Allow it to unfold without trying to predict the outcome."**

Guide 7
Risk systems to assess prognosis of myelofibrosis

System	System risk levels	NCCN risk levels
MIPSS-70	• Low risk is a score of 0 or 1 • Intermediate risk is a score of 2, 3, or 4 • High risk is a score of 5 or above	• Lower risk is a score of 3 or below • Higher risk is a score of 4 or above
MIPSS70-plus version 2.0	• Very low risk is a score of 0 • Low risk is a score of 1 or 2 • Intermediate risk is a score of 3 or 4 • High risk is a score of 5, 6, 7, or 8 • Very high risk is a score of 9 or above	• Lower risk is a score of 3 or below • Higher risk is a score of 4 or above
DIPSS	• Low risk is a score of 0 • Intermediate-1 risk is a score of 1 or 2 • Intermediate-2 risk is a score of 3 or 4 • High risk is a score of 5 or 6	• Lower risk is a score of 2 or below • Higher risk is a score of 3 or above
DIPSS-PLUS	• Low risk is a score of 0 • Intermediate-1 risk is a score of 1 • Intermediate-2 risk is a score of 2 or 3 • High risk is a score of 4 or 5	• Lower risk is a score of 1 or 0 • Higher risk is a score of 2 or above
MYSEC-PM	• Low risk is a score of 11 or below • Intermediate-1 risk is a score of 12 or 13 • Intermediate-2 risk is a score of 14 or 15 • High risk is a score of 16 or above	• Lower risk is a score of 13 or below • Higher risk is a score of 14 or above

Treating myelofibrosis without anemia

Planning treatment of myelofibrosis is based on various information, not just prognosis. Your symptoms will be tracked. Your health care provider will assess the size of your spleen during exams. Blood cell and blast counts will be monitored.

Based on this information, the goals of your treatment may include:

- Relieve symptoms
- Improve blood counts
- Prevent or delay progression to advanced myelofibrosis or leukemia

Treatment options for myelofibrosis are described on the next pages and are listed in **Guide 8.**

Guide 8
Treatment for myelofibrosis without anemia

Risk level	Clinical status	Treatment options
Lower risk	You do not have symptoms	• Watch and wait • Clinical trial

Lower risk	You do have symptoms	• Clinical trial
		• It is sometimes useful to receive:
		  • Ruxolitinib
		  • Peginterferon alfa-2a
		  • Hydroxyurea if lowering blood counts would relieve symptoms
		  • Pacritinib if platelets are less than 50,000
		  • Momelotinib

Higher risk	Your number of platelets falls within the **low to high** range (50,000 or higher)	• Allogeneic hematopoietic cell transplant to try to cure the MPN or • Clinical trial, ruxolitinib, fedratinib, momelotinib, pacritinib
Higher risk	You have a **very low** number of platelets (below 50,000)	• Allogeneic hematopoietic cell transplant to try to cure the MPN or • Clinical trial, pacritinib (preferred regimen), or momelotinib

Clinical trial

If available, a clinical trial is recommended. A clinical trial is a type of medical research study. For more information on clinical trials, read the section in this chapter called *Participating in clinical trials*.

Watch and wait

Lower-risk myelofibrosis is likely to be stable or slowly progress. People with lower-risk myelofibrosis that isn't causing symptoms may start "watch and wait." Also called observation or watchful waiting, watch and wait is a period of testing to assess for changes in myelofibrosis. Treatment may be started if symptoms appear.

Cytoreductive therapy

Cytoreductive therapy is an option for lower-risk myelofibrosis that is causing symptoms. The therapies used for myelofibrosis are peginterferon alfa-2a or hydroxyurea. More information on these therapies is in *Chapter 4: Clotting in PV and ET*.

JAK inhibitors

JAK is a cell protein that helps cells grow. It is key to blood stem cells developing into mature blood cells. JAK is overactive in people with myelofibrosis whether or not there is a *JAK* mutation.

JAK inhibitors stop JAK and reduce the number of new blood cells being made. In turn, they reduce spleen size and core symptoms. Ruxolitinib (Jakafi), fedratinib (INREBIC), pacritinib (Vonjo), and momelotinib (Ojjaara) are JAK inhibitors.

Which JAK inhibitor is recommended?

For **lower-risk myelofibrosis**, ruxolitinib has been often used to treat symptoms when needed. Pacritinib is an option for when platelet levels are very low. Momelotinib may be an option, but more research is needed among people with lower-risk myelofibrosis.

For **higher-risk myelofibrosis**, NCCN experts recommend specific JAK inhibitors based on platelet levels.

Ruxolitinib, momelotinib, and fedratinib are recommended when platelet levels range from low to high. Pacritinib studies in this platelet range are needed.

When platelet levels are very low, NCCN experts prefer pacritinib for treatment. Momelotinib needs to be studied more among people with very low platelets.

What does treatment involve?

JAK inhibitors are a pill you take at home. Your health care provider will determine which medications and dosing is right for you and adjust as needed. Don't stop taking the medicine unless your health care provider directs you to do so.

Allogeneic HCT

A hematopoietic stem cell is a cell that develops into every type of blood cell. In myelofibrosis, hematopoietic stem cells and bone marrow are diseased.

An allogeneic hematopoietic cell transplant (HCT) uses donor cells to form healthy bone marrow and blood cells in you. It extends life and may cure myelofibrosis.

An allogeneic HCT is not safe for everyone. It is an intense treatment, so many people can't get it. A transplant specialist will assess if you can have a transplant. The specialist will also assess donor options

When is an allogeneic HCT an option?

Allogeneic HCT is rarely used to treat lower-risk myelofibrosis but may be an option if platelets are low or the cancer cells have complex cytogenetics. A complex karyotype is when there are 3 or more unrelated defects in chromosomes that occur in 2 or more cells.

Everyone with higher-risk myelofibrosis should receive a transplant evaluation since a transplant is the only chance for a cure. The benefits of a transplant may be worth the risks for PMF that has high-risk mutations, such as *ASXL1*, *EZH2*, and *RAS*.

What does treatment involve?

There are 4 steps to receiving an allogeneic HCT, which can be a grueling process. You may stay on a JAK inhibitor to reduce spleen size and improve symptoms until you get a transplant.

Your care team will give you detailed information about an allogeneic HCT and answer your questions. To give you a general idea of the process, here's a brief description:

1. Your blood will be tested for cell proteins called human leukocyte antigens (HLAs). A donor's HLAs must be a near-perfect match to yours for a transplant to work. Even with a near-perfect match, donor cells may attack your body. This is called graft-versus-host disease (GVHD).
2. You'll receive a treatment called conditioning to kill your bone marrow cells. It also weakens the immune system, so your body does not kill the donor cells.
3. Next, you'll receive the donor cells through a transfusion. A transfusion is a slow injection of blood products into a vein. New, healthy blood cells will form over the next 2 to 4 weeks. This is called engraftment.
4. You'll have to be extra careful to avoid germs for the first few weeks after the transplant. That's because your infection-fighting immune system will be almost gone. You may be given antibiotics to prevent or treat infection. You may receive medicine called immunosuppressants to prevent GVHD.

More information about GVHD is available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.

"Do it for the little things... grandchildren, that is. Had I not undergone the stem cell transplant I wouldn't be here to enjoy them."

Treating myelofibrosis with anemia

Anemia is a term for low levels of hemoglobin. Most people with myelofibrosis develop anemia within 1 year after diagnosis. Anemia may cause you to feel tired and cold or look pale. These symptoms are caused by cells not getting enough oxygen.

If you have anemia, your provider will make a treatment plan based on whether you:

- Have anemia for reasons other than myelofibrosis
- Are taking a JAK inhibitor now
- Have anemia symptoms or myelofibrosis symptoms

Depending on the causes of the anemia, your care team might prescribe supplements to replace low iron, folate, or vitamin B12 levels. Treatment options for anemia related to myelofibrosis are listed in **Guide 9.**

Clinical trials

NCCN experts prefer clinical trials for treatment of anemia. Further research is needed to test current treatments in more people. And despite recent improvements in treatment, better treatment is still needed. For more information on clinical trials, read the section in this chapter called *Participating in clinical trials*.

JAK inhibitors

JAK inhibitors reduce spleen size and core symptoms but may make anemia worse. Because of anemia, the dose of a JAK inhibitor may be reduced, or the treatment may be paused or stopped. There are other options that don't require avoiding or stopping JAK inhibitors.

- One option is to take momelotinib. Momelotinib can improve anemia as well as myelofibrosis symptoms. More information is needed on its use among people who have anemia but no myelofibrosis symptoms.
- A second option is to take pacritinib. Anemia may not be severe during pacritinib because it doesn't suppress the number of new blood cells being made and it may even increase hemoglobin.
- For people taking ruxolitinib, the third option is to keep taking it and start anemia treatment. Luspatercept-aamt, an erythropoiesis-stimulating agent, or danazol can be added to ruxolitinib to treat anemia. But these add-ons don't improve anemia for a prolonged time in many people or may not help at all.

Red blood cell drugs

If a JAK inhibitor isn't needed, you may receive anemia treatment that increases the number of red blood cells. Such anemia drugs include:

- Luspatercept-aamt
- Erythropoiesis-stimulating agents, such as darbepoetin alfa and epoetin alfa, if a hormone called erythropoietin is lower than 500 mU/mL in your blood
- Danazol
- Lenalidomide with prednisone for myelofibrosis with an abnormal gene called 5q deletion

Red blood cell transfusions

The standard treatment of anemia that causes symptoms is a red blood cell transfusion. Red blood cell transfusions are a common procedure for receiving donated blood. Most white blood cells should be removed from donated blood as this will help prevent the donated blood from attacking your body. It will also prevent you from getting a cytomegalovirus (CMV) infection.

Guide 9
Treatment for myelofibrosis with anemia

Treatment for anemia when a JAK inhibitor is controlling myelofibrosis symptoms	The recommended options are: • Clinical trial (preferred) • Add luspatercept-aamt, an erythropoiesis-stimulating agent, or danazol to ruxolitinib • Switching current JAK inhibitor to either momelotinib or pacritinib is sometimes useful • In addition to the options above, you may receive red blood cell transfusions if the anemia is causing symptoms
Treatment for anemia and uncontrolled myelofibrosis symptoms	The recommended options are: • Clinical trial (preferred) • Momelotinib (preferred) • Pacritinib • Add luspatercept-aamt, an erythropoiesis-stimulating agent, or danazol to ruxolitinib • In addition to the options above, you may receive red blood cell transfusions if the anemia is causing symptoms
Treatment for anemia if you don't have myelofibrosis symptoms	The recommended options are: • Clinical trial (preferred) • Luspatercept-aamt • Erythropoiesis-stimulating agents if erythropoietin in your blood is lower than 500 mU/mL • Danazol • Momelotinib • Pacritinib • Lenalidomide with prednisone for 5q deletion • In addition to the options above, you may receive red blood cell transfusions if the anemia is causing symptoms

Treating advanced phases of myelofibrosis

Myelofibrosis can progress to an accelerated or blast phase. Over 20 years, progression occurs in about 1 in 20 people with PV or ET. For PMF, it's about 3 out of 20 people.

The marker of progression is a high percentage of immature blood cells, called myeloblasts, in the bone marrow or the bloodstream. Myeloblasts (simply called blasts) are usually only in bone marrow.

Normally, the blast count in bone marrow is less than 5 percent. In the accelerated phase of myelofibrosis, the blast count is between 10 and 19 percent. The blast phase of myelofibrosis [also called post-MPN acute myeloid leukemia (AML)] has at least a 20 percent blast count. AML may be diagnosed with less than 20 percent blasts if chromosomes have certain abnormal changes.

Lab tests

To confirm progression, lab tests on bone marrow are needed. If bone marrow can't be removed, blood samples may be used. You may know some of the lab tests used for progression as they are used for MPN diagnosis (see Chapter 2):

- Cytogenetics using karyotype with or without fluorescence in situ hybridization (FISH)
- Flow cytometry
- Next-generation sequencing (NGS) of mutations related to AML

Treatment planning

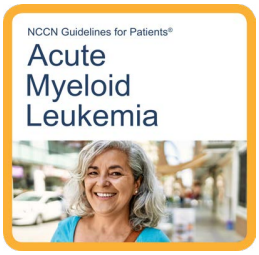
Right after progression is confirmed, you and your care team will discuss treatment. Treatment may include chemotherapy or chemotherapy followed by an allogeneic HCT. If a transplant is an option, you will be referred to a transplant specialist.

Clinical trial

Whether or not you will get a transplant, NCCN experts recommend clinical trials. Ask your treatment team if there is an open clinical trial that's a good fit for you. For more information on clinical trials, read the section in this chapter called *Participating in clinical trials.*

Low-intensity chemotherapy

When a transplant isn't an option, low-intensity chemotherapy is often used for treatment. One type of low-intensity chemotherapy is hypomethylating agents, such as azacitidine and decitabine. Learn about other low-intensity chemotherapy options for AML available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



Sometimes a JAK inhibitor or venetoclax (Venclexta) is included with a hypomethylating agent. A JAK inhibitor may reduce spleen size and myelofibrosis symptoms. Venetoclax is a pill that may help control MPN growth by targeting a protein called BCL2. But it can cause serious health problems and more

information is needed to see if people with MPNs benefit from it.

Induction therapy

Some people who are well enough are treated with induction therapy, which involves a combination of drugs. The goal of induction therapy is to rid the marrow of blasts. Chemotherapy used to treat AML is often used for induction.

Allogeneic HCT

If you're already taking a JAK inhibitor, it may be continued until you get a transplant.

For advanced myelofibrosis, the first step of care is to receive induction therapy before a transplant. Transplants are more successful when induction therapy has good results. Instead of induction, some people take a hypomethylating agent with or without a JAK inhibitor.

There are several steps to receiving an allogeneic transplant. These steps are described earlier in this chapter in the section called *Treating myelofibrosis without anemia*.

"Always be prepared for the worst-case scenario, but maintain a positive outlook and hope for the best. Above all, never give up!"

Participating in clinical trials

NCCN experts recommend a clinical trial for many people with MPNs. A clinical trial is a type of medical research study. It tests potential new ways of fighting cancer and its negative effects in people. After being developed and tested in a laboratory, potential new ways of fighting cancer need to be studied in humans. If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. Food and Drug Administration (FDA).

Everyone with cancer should carefully consider all of the treatment options available for their cancer type, including standard treatments and clinical trials. Talk to your care team about whether a clinical trial may make sense for you.

Phases

Most cancer clinical trials focus on treatment. Treatment trials are done in phases.

- **Phase 1 trials** study the dose, safety, and side effects of an investigational drug or treatment approach. They also look for early signs that the drug or approach is helpful.
- **Phase 2 trials** study how well the drug or approach works against a specific type of cancer.
- **Phase 3 trials** test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.
- **Phase 4 trials** study the long-term safety and benefit of an FDA-approved treatment.

Who can enroll?

Every clinical trial has rules for joining, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. These requirements ensure that participants are alike in specific ways and that the trial is as safe as possible for the participants.

Informed consent

Clinical trials are managed by a group of experts called a research team. The research team will review the study with you in detail, including its purpose and the risks and benefits of joining. All of this information is also provided in an informed consent form. Read the form carefully and ask questions before signing it. Take time to discuss it with family, friends, or others you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.

Start the conversation

Don't wait for your team to bring up clinical trials. Start the conversation and learn about all of your treatment options. If you find a study that you may be eligible for, ask your team if you meet the requirements. If you have already started standard treatment, you may not be eligible for certain clinical trials. Try not to be discouraged if you cannot join. New clinical trials are always becoming available.

Frequently asked questions

There are many myths and misconceptions surrounding clinical trials. The possible benefits and risks are not well understood by many with cancer.

Finding a clinical trial

In the United States

NCCN Cancer Centers
NCCN.org/cancercenters

The National Cancer Institute (NCI)
cancer.gov/about-cancer/treatment/clinical-trials/search

Worldwide

The U.S. National Library of Medicine (NLM)
clinicaltrials.gov/

Need help finding a clinical trial?

NCI's Cancer Information Service (CIS)
1.800.4.CANCER (1.800.422.6237)
cancer.gov/contact

Will I get a placebo?

Placebos (inactive versions of real medicines) are almost never used alone in cancer clinical trials. It is common to receive either a placebo with a standard treatment or a new drug with a standard treatment. You will be informed, verbally and in writing, if a placebo is part of a clinical trial before you enroll.

Are clinical trials free?

There is no fee to enroll in a clinical trial. The study sponsor pays for research-related costs, including the study drug. You may, however, have costs indirectly related to the trial, such as the cost of transportation or child care due to extra appointments. During the trial, you will continue to receive standard cancer care. This care is billed to—and often covered by—insurance. You are responsible for copays and any costs for this care that are not covered by your insurance.

Myelofibrosis checkups

After starting treatment, you will need to meet with your care team often. NCCN experts advise having a visit every 3 to 6 months for lower-risk myelofibrosis under observation. You may need visits more often if receiving active treatment, such as JAK inhibitors.

Visits with your care team

During visits, you will be asked about new or worsening symptoms and new diagnoses. You may be given a symptom survey called the MPN-10 to complete. For information on treating symptoms, read *Chapter 6: Supportive care.*

Your health care provider will perform a physical exam of your body. The size of your spleen and liver will be checked.

Blood work will be ordered. Your health care provider will monitor your blood counts and other blood values. You may undergo a bone marrow biopsy and aspiration if symptoms worsen or there are signs of possible progression.

Treatment response

In research, there are standards for assessing the results of medicines. Know that your treatment may be working but may not match these standards. Your health care provider will assess treatment results mostly based on whether symptoms are improving.

Changing treatment

Your treatment will likely not change if symptoms improve and your blood counts are acceptable. Reasons to change treatment include little to no symptom relief or worsening symptoms. Also, worsening blood counts or signs of progression may trigger a change in treatment.

Treatment decisions may be guided by molecular testing. Testing may find new mutations since the last testing was done. Next-generation sequencing (NGS) tests on biopsy samples can detect higher-risk mutations, such as *ASXL1*, *EZH2*, and *RAS*. These mutations suggest that the myelofibrosis is likely to progress and a transplant may be needed.

If myelofibrosis worsens but doesn't progress, the next treatment is based on the current risk level and prior treatment. New anemia may be treated with medications that improve blood counts.

Key points

- Myelofibrosis is a blood cancer that results in scarring of the bone marrow (fibrosis). How quickly it worsens greatly differs between people.
- The first step of treatment planning is to assess the prognosis using a risk stratification system. NCCN recommendations for treatment are based on two risk levels—lower and higher.
- If you don't have anemia, watch-and-wait is an option for lower-risk myelofibrosis that isn't causing symptoms. Symptoms and higher-risk myelofibrosis are often treated with a JAK inhibitor. Some people are healthy enough to get an allogeneic hematopoietic cell transplant (HCT) .
- If you have anemia, treatment may include a JAK inhibitor, medication that increases red blood cell counts, or both. Standard treatment of anemia that's causing symptoms is a red blood cell transfusion.
- Advanced phases of myelofibrosis are often treated with chemotherapy, which can vary in intensity. Chemotherapy may be followed by an allogeneic transplant for some people.
- NCCN experts recommend clinical trials for people with MPNs. A clinical trial tests new ways of stopping cancer or reducing symptoms in people. Ask your care team if there are clinical trials that are a good fit for you.
- You will meet with your care team often after diagnosis. During visits, the status of the cancer will be checked as well as how you feel.

The initial diagnosis and new reality can be very overwhelming since not much is known about MPNs. While myelofibrosis is very rare, there are helpful resources from MPN research and education organizations as well as informal patient networks that provide the opportunity to share questions, fears, symptoms, and treatments. It is comforting to know there is new research and potential treatment options emerging that should help improve and extend our lives."

6
Supportive care

The goal of supportive care is to maintain or improve your quality of life. This chapter discusses some of the supportive needs of people with myeloproliferative neoplasms (MPNs).

Supportive care is very important for all people with myeloproliferative neoplasms (MPNs). It is not just for people at the end of life who need hospice.

Supportive care is sometimes called palliative care since symptom relief is a main goal. But supportive care addresses many other needs. You can get help with food, financial aid, or family counseling.

Tell your care team about your symptoms and other needs to get the best supportive care. A palliative care specialist may be a member of your cancer care team. This specialist has received specific training to provide additional support to you. Some cancer centers have palliative care programs.

Bleeding

People with MPNs are at increased risk for bleeding. Also called hemorrhaging, bleeding is often mild and occurs when platelet counts are high or low.

Bleeding occurs most often in myelofibrosis compared to polycythemia vera (PV) and essential thrombocythemia (ET). It can be severe, especially in people who have anemia or low platelets.

Bleeding events differ between people. Some people bruise easily while others get nose bleeds. Menstrual periods may be heavier than normal. Bleeding may occur in your digestive tract. You may see blood in your urine.

"Please ensure that your hematologist/MPN specialist listens and actually hears what you're saying. It doesn't matter what the symptoms are. You could be the first to experience something 'outside of the radar.' They're there for you."

Ask your care team which types of bleeding events need immediate medical attention.

Causes of bleeding

Normally, bleeding is stopped when cells called platelets plug the hole in blood vessels with help from clotting factors. A lot of bleeding may occur when the blood doesn't clot properly.

There are several causes of bleeding in PV and ET:

- Platelets may not work correctly.
- The number of platelets may be very high. High levels of platelets may lower a clotting factor called von Willebrand.
- Prevention of blood clots with aspirin may thin the blood too much.
- Prevention of blood clots with antiplatelet or cytoreductive therapy may reduce blood counts to very low levels.
- Treating blood clots with anticoagulants may slow down clotting time too much.

The cause of bleeding is simpler in myelofibrosis. Bleeding is typically caused by a low number of platelets.

Bleeding in myelofibrosis

You may receive a platelet transfusion to prevent bleeding if your platelet count is lower than 10,000 m^3. Platelet transfusions are also used for the treatment of bleeding. Most white blood cells should be removed from the donated blood. This will help prevent the blood from attacking your body. It also prevents you from getting infected with cytomegalovirus (CMV).

Transfusions may not stop bleeding. In this case, antifibrinolytic agents may be used. These drugs help your blood to clot.

Bleeding in PV and ET

Your health care provider will identify and treat all causes of bleeding. Coagulation tests to assess for acquired von Willebrand Syndrome (aVWS) may be done. Levels of von Willebrand factor may be low due to high platelet counts.

Aspirin will be stopped until the platelet count is normal. Treatment to reduce platelet counts may be given. If you have ET, you may receive plateletpheresis if bleeding is severe but this is rare.

Blood clots

You may get a blood clot even though you took steps to prevent it. Many blood clots are safely managed with anticoagulants. Coagulation is another word for blood clotting. Despite being called blood thinners, anticoagulants slow down the clotting of blood.

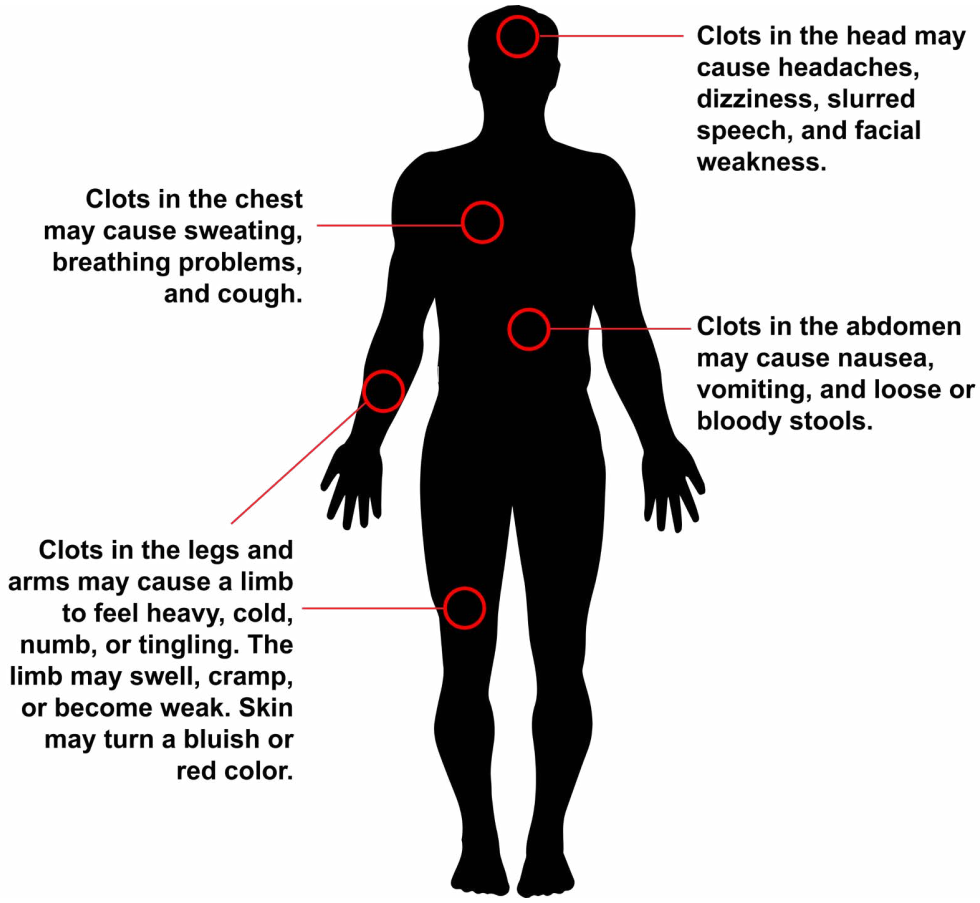
Anticoagulants

Research has shown that anticoagulants help treat blood clots in general practice. But there is little to no research on anticoagulants in people with an MPN. It is unknown if one anticoagulant works better than another. It is also unknown exactly how long an anticoagulant is needed.

Your health care provider will decide how long you'll take an anticoagulant based on the severity of the blood clot. Three common types of anticoagulants are:

- **Low-molecular-weight heparin (LMWH)** – This medicine enhances the effect of a natural anticoagulant in your body. It is injected into the skin and can be taken at home.
- **Direct oral anticoagulants** – These pills disable proteins that help the blood to clot. They include apixaban (Eliquis), betrixaban (Bevyxxa), dabigatran (Pradaxa), edoxaban (Savaysa), and rivaroxaban (Xarelto).
- **Vitamin K blockers** – Among these medicines, warfarin (Coumadin, Jantoven) is the most often used. It is a pill taken at home. Warfarin stops the liver from using vitamin K, which is needed to make clotting proteins. When taking warfarin, regular testing will be necessary to measure how quickly or slowly your blood is clotting.

Warning signs of blood clots



Anticoagulants increase the risk of bleeding. The risk is higher when taking aspirin or treatment that lowers platelet counts. Your health care provider may stop these treatments while you're on an anticoagulant. People with cardiovascular risk factors may stay on aspirin, but this may change depending on the situation.

Plateletpheresis

If you have a sudden life-threatening clot, you may receive plateletpheresis. This procedure withdraws your blood and removes platelets. Your platelet-reduced blood will then be returned to your body.

Plateletpheresis is rarely done as it only slightly decreases platelets and for a short time. It's useful in ET when people have life-threatening bleeds or clots or are not responding to medication.

Bone pain

Your health care provider will evaluate if any bone pain is caused by the MPN. This is needed because treatment of MPN-related bone pain differs from treatment of joint pain.

In one MPN study, ruxolitinib stabilized bone and muscle pain. For some people, loratadine and non-steroidal anti-inflammatory drugs (NSAIDs) may provide relief. A low dose of radiation may provide short-term relief of bone pain.

Headaches and tinnitus

You may have a blood clot if you start to have headaches. Also, sounds made by the body and not heard by others (tinnitus), such as high-pitch ringing, may be a symptom of a blood clot. Tell your health care provider if you have these symptoms.

Headaches as well as other vascular symptoms may be relieved with low-dose aspirin. If symptoms persist, taking aspirin twice a day or taking an antiplatelet agent (clopidogrel) may have better results. Aspirin may be taken with an antiplatelet agent. Taking an NSAID with aspirin should be done with caution and not without your physician's knowledge. Always tell an urgent care or emergency care practitioner if you are taking daily aspirin.

There are several options in addition to aspirin. Headaches in people with PV may be relieved with phlebotomy or ruxolitinib. For all MPNs, cytoreduction therapy reduces headaches and other vascular symptoms. Migraine headaches may be prevented as well as treated with triptans or topiramate.

Itching

Itching (pruritus) is a common problem among people with MPNs. It can be severe, even life-altering.

The first approach to relieve itching is to practice sensitive skin care. This care includes taking short showers, using mild soap, and moisturizing your skin. Antihistamines (cetirizine, diphenhydramine) and topical steroids may also be helpful.

If needed, the next step to relieve itching will be based on the benefits and downsides of treatments. Ruxolitinib relieves itching. Early research on selective serotonin reuptake inhibitors (SSRIs) and narrow-band ultraviolet B shows promise.

Other medicines that may be tried include peginterferon alfa-2a, gabapentin, aprepitant, and immunosuppressant agents, such as cyclosporine, methotrexate, azathioprine, mycophenolate mofetil, or dupilumab.

Infections

You may be prone to infections because of myelofibrosis or its treatment. Ask your health care provider which vaccinations are safe for you. They may prescribe the recombinant (killed) zoster vaccine if taking a JAK inhibitor.

If you get infections often, your health care provider may prescribe antibiotics for prevention. Instead of antibiotics, you may receive granulocyte colony-stimulating factor (G-CSF) or granulocyte-macrophage colony-stimulating factor (GM-CSF) if you have low neutrophil counts. These medicines should be used with caution because, though rare, enlarged spleens can rupture.

Tumor lysis syndrome

Tumor lysis syndrome (TLS) occurs when the waste released by dead cells is not quickly cleared out of the body. The waste can cause kidney damage and severe blood electrolyte disturbances. TLS can be life-threatening.

Induction chemotherapy may cause TLS. Induction chemotherapy is a treatment for advanced myelofibrosis or acute myeloid leukemia (AML). This treatment kills many cancer cells and results in too much waste too quickly.

TLS may be prevented by high amounts of fluids during chemotherapy. Fluids may help clear out the cell waste. Decreasing uric acid levels with allopurinol or rasburicase is another option. Rasburicase may be given as the first treatment if you have high uric acid or if it's affecting your kidneys.

Iron overload

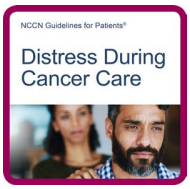
Iron overload is a term for too much iron in your body. It can occur if you've had many red blood cell transfusions. Iron chelation is a type of drug that removes extra iron from your body. It is an option at times for lower-risk myelofibrosis. Your health care provider may prescribe iron chelation if you've had more than 20 transfusions or your blood ferritin level is greater than 2500 ng/mL.

Supportive care guidelines

The library of NCCN Guidelines for Patients has several books on supportive care. These books focus on the treatment of common physical and emotional effects of many cancers. One book is about healthy living and shares recommendations for exercise, food and supplements, and vaccines.

Supportive care guidelines

Distress



Everyone with cancer feels distress at some point. It is normal to be worried, sad, helpless, or angry. Distress can become severe and affect the way you live.

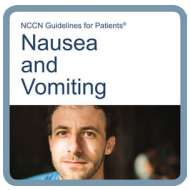
Fatigue

Cancer-related fatigue is not the typical tiredness that follows an active or long day. It is a lack of energy that is distressing, does not improve with normal resting or sleep, and disrupts life.

Palliative care

Palliative care is an approach to health care for people living with serious illnesses, including cancer. It focuses on providing relief from the symptoms and stress of having cancer.

Nausea and vomiting

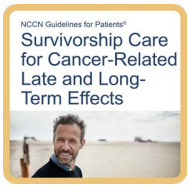


Chemotherapy can cause nausea and vomiting. Nausea is the feeling that you are going to throw up. Vomiting is forcefully throwing up what's in your stomach.

Graft-Versus-Host Disease

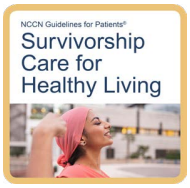
A side effect of allogeneic hematopoietic cell transplants is graft-versus-host disease. This side effect is caused by donor cells attacking your healthy cells.

Late and long-term effects



Cancer and its treatment can cause long-term and late effects. Long-term effects start during treatment and persist after treatment is done. Less often, effects start long after treatment has ended. Late and long-term effects include heart disease, fatigue, poor sleep, pain, and depression.

Healthy living



It's important to start or keep a healthy lifestyle. Healthy living may help prevent disease and improve well-being. Topics covered include physical activity, food, and vaccinations.

The full library of NCCN Guidelines for Patients is available at
NCCN.org/patientguidelines

Key points

- Supportive care is health care that improves quality of life. It provides symptom relief and help for other needs.
- Bleeding is most common in myelofibrosis compared to PV and ET. Treatment options vary between MPN types to target the cause of bleeding.
- Blood clots are a focus of treatment for PV and ET, but also occur in people with myelofibrosis. They are treated with anticoagulants and antiplatelet medicines.
- Bone pain, headaches, tinnitus, and itching occur across all MPNs and greatly impact quality of life. More research is needed to find the best treatment of these symptoms among people with MPN.
- People with myelofibrosis may develop frequent infections, tumor lysis syndrome, and high levels of iron. Vaccinations may be your best defense against infections. Fluids to clear out cell waste may prevent TLS. Iron chelation is a treatment for high levels of iron.
- The library of NCCN Guidelines for Patients includes books on supportive care. These books focus on common effects of cancer and its treatment, such as distress, fatigue, nausea and vomiting, and poor sleep.

"Living with an MPN diagnosis can be challenging. It's not a life-defining condition but a life altering experience. It requires understanding and managing the physical symptoms, such as fatigue and pain, as well as the emotional impact of living with a chronic condition."

7
Making treatment decisions

It is important to be comfortable with the cancer treatment you choose. This choice starts with having an open and honest conversation with your care team.

It's your choice

In shared decision-making, you and your care team share information, discuss the options, and agree on a treatment plan. It starts with an open and honest conversation between you and your team.

Treatment decisions are very personal. What is important to you may not be important to someone else. Some things that may play a role in your decision-making:

- What you want and how that might differ from what others want
- Your religious and spiritual beliefs
- Your feelings about certain treatments
- Your feelings about pain or side effects
- Cost of treatment, travel to treatment centers, and time away from school or work
- Quality of life and length of life
- How active you are and the activities that are important to you

Think about what you want from treatment. Discuss openly the risks and benefits of specific treatments and procedures. Weigh options and share concerns with your care team. If you take the time to build a relationship with your team, it will help you feel supported when considering options and making treatment decisions.

Second opinion

It is normal to want to start treatment as soon as possible. While cancer should not be ignored, there is time to have another care provider review your test results and suggest a treatment plan. This is called getting a second opinion, and it's a normal part of cancer care. Even experts get second opinions!

Things you can do to prepare:

- Check with your insurance company about its rules on second opinions. There may be out-of-pocket costs to see health care providers who are not part of your insurance plan.
- Make plans to have copies of all your records sent to the health care provider you will see for your second opinion.

Support groups

Many people diagnosed with cancer find support groups to be helpful. Support groups often include people at different stages of treatment. Some people may be newly diagnosed, while others may be finished with treatment. If your hospital or community doesn't have support groups for people with cancer, check out the websites listed in this book.

Questions to ask

Possible questions to ask your care team are listed on the following pages. Feel free to use these or come up with your own.

Questions about cancer testing

1. What tests will I have? What is involved if I need a biopsy?
2. Do the tests have any risks?
3. Do I need to do anything to prepare for testing?
4. Should I bring someone with me to the appointments?
5. Where do I go for testing, and how long will it take?
6. If any of the tests will hurt, what will you do to make me comfortable?
7. How soon will I know the results and who will explain them to me?
8. How can I get a copy of the pathology report and other test results?
9. Is there an online portal with my test results?

Questions about MPN

1. What type of MPN do I have?
2. Is this a fast- or slow-growing MPN?
3. What are the possible complications of MPN?
4. How do I find an MPN specialist?
5. What are the goals of treatment?
6. What are my chances that the MPN will become myelofibrosis or leukemia?
7. What are the symptoms and signs that the MPN may be changing?

Questions about treatment options

1. What are my treatment options?
2. What will happen if I do nothing?
3. Are you suggesting options other than what NCCN recommends? If yes, why?
4. How do my age, sex, overall health, and other factors affect my options?
5. What if I am pregnant, or planning to become pregnant?
6. Does any option offer a cure or long-term cancer control?
7. How do I get a second opinion?
8. How long do I have to decide about treatment, and is there a social worker or someone who can help me decide?
9. What are my options if the MPN progresses?

Questions about clinical trials

1. Do you recommend that I consider a clinical trial for treatment?
2. How do I find clinical trials that I can participate in?
3. What is the study drug used in the clinical trial and will everyone get it?
4. Has the study drug been used for other types of cancer?
5. What are the risks and benefits of this drug?
6. What side effects should I expect and how will they be managed?
7. How long will I be in the clinical trial?
8. Will I be able to get other treatment if this doesn't work?
9. How will you know if the treatment is working?
10. Will the clinical trial cost me anything?

Questions about what to expect

1. Does this hospital or cancer center offer the best treatment for me?
2. Do I have a choice of when to begin treatment?
3. How long will treatment last?
4. How might the recommended treatment interact with other medications that I am already taking?
5. Who should I call if I have concerns or questions about my treatment after I start taking it?
6. Who should I contact with questions or concerns if the office is closed?
7. How will you know if treatment is working?
8. What are the chances of the cancer worsening?
9. What follow-up care is needed after treatment?

Questions about side effects

1. What are the possible complications and side effects of treatment?
2. Does the cancer itself cause any side effects?
3. Which side effects are most common and how long do they usually last?
4. Which side effects are serious or life-threatening?
5. Are there any long-term or permanent side effects?
6. What symptoms should I report right away, and who do I contact?
7. What can I do to prevent or relieve the side effects of treatment?
8. Do any medications worsen side effects?
9. Do any side effects lessen or worsen in severity over time?
10. Will you stop or change treatment if there are serious side effects?

Questions about resources and support

1. Who can I talk to about help with housing, food, and other basic needs?
2. What assistance is available for transportation, childcare, and home care?
3. Who can tell me what my options for health insurance are and assist me with applying for insurance coverage?
4. How much will I have to pay for my treatment? What help is available to pay for medicines and other treatment?
5. Who can help me with my concerns about work or school?
6. How can I connect with others and build a support system?
7. Who can I talk to if I don't feel safe at home, at work, or in my neighborhood?

Resources

AnCan Foundation
ancan.org

Be The Match
BeTheMatch.org/one-on-one

CancerCare
cancercare.org

Imerman Angels
imermanangels.org

MPN Cancer Connection
mpncancerconnection.org

MPN Research Foundation
mpnrf.org

National Coalition for Cancer Survivorship
canceradvocacy.org

The Leukemia & Lymphoma Society (LLS)
LLS.org/PatientSupport

Triage Cancer
triagecancer.org

We want your feedback!

Our goal is to provide helpful and easy-to-understand information on cancer.

Take our survey to let us know what we got right and what we could do better.

NCCN.org/patients/feedback

Words to know

acute myeloid leukemia (AML)
A blood cancer of young white blood cells called myeloblasts.

allogeneic hematopoietic cell transplant (HCT)
A cancer treatment that replaces blood stem cells with donor stem cells, which in turn make a new, healthy bone marrow.

anemia
Low levels of healthy red blood cells that cannot provide enough oxygen to tissue.

anticoagulant
A treatment that slows down the clotting of blood.

artery
A blood vessel that moves blood away from the heart to the rest of the body.

BCR-ABL1
An abnormal gene that is the hallmark of chronic myeloid leukemia.

biomarker test
A lab test of a molecule in your body to assess your health.

blast
An early form of a blood cell that is unable to function like a mature blood cell.

blood clot
A gel-like clump of blood. Also called thrombus.

blood smear
A test that involves viewing a drop of blood with a microscope to assess features of blood cells.

bone marrow
A soft, spongy material inside of bones where most blood cells are made.

bone marrow aspiration
The removal of a small amount of liquid bone marrow to test for disease.

bone marrow biopsy
The removal of a small amount of solid bone and bone marrow to test for disease.

chromosome
A long but tightly coiled structure within cells that contains coded instructions for cell behavior.

chronic myeloid leukemia (CML)
A blood cancer that causes too many white blood cells called granulocytes to form.

clinical trial
Research on a test or treatment to assess its safety or how well it works.

CMV
cytomegalovirus

coagulation test
A test of the proteins that cause blood to clot.

complete blood count (CBC)
A test of the number of blood cells in a sample.

comprehensive metabolic panel
Tests of up to 14 chemicals in your blood.

constitutional symptom
A physical condition that is a general effect of a disease.

Words to know

cytogenetics
The study of chromosomes using a microscope.

cytokine
A protein that boosts or activates the immune system.

cytoreductive therapy
A treatment that reduces the number of blood cells.

diabetes
A disease that causes high levels of blood sugar.

diagnosis
The identification of an illness based on tests.

differential
Measurement of the different types of white blood cells in a blood sample.

DIPSS
Dynamic International Prognostic Scoring System

embolus
A blood clot that is not attached to a base and moves through the bloodstream.

erythropoiesis-stimulating agent
A drug that helps bone marrow to make more red blood cells.

erythropoietin (EPO)
A hormone made by the kidneys.

essential thrombocythemia (ET)
A cancer of blood stem cells that make too many platelets. Also called essential thrombocytosis.

fatigue
A feeling of extreme tiredness, even with enough sleep, that limits a person's functioning.

fibrosis
The scarring of supportive fibers in tissue.

fluorescence in situ hybridization (FISH)
A lab test that uses special dyes to look for abnormal changes in a cell's genes and chromosomes.

G-CSF
granulocyte colony-stimulating factor

gene
A set of coded instructions within cells that control cell behavior.

GM-CSF
granulocyte-macrophage colony-stimulating factor

graft-versus-host disease (GVHD)
An attack on normal cells by blood stem cells from a donor.

granulocyte
A type of white blood cell.

hematocrit
The percentage of red blood cells in blood.

hematologist
A health care provider who's an expert in diseases of the blood.

hematopoietic stem cell
A cell from which all other types of blood cells are made. Also called blood stem cell.

hemoglobin
A protein in red blood cells that carries oxygen.

hemorrhage
Blood loss inside or on the outside of the body. Also called bleeding.

human leukocyte antigen (HLA)
Special proteins on the surface of cells that help the body to tell its own cells apart from foreign cells.

Words to know

hypercellularity
A high number of cells.

hypertension
High blood pressure.

IPSET-thrombosis
International Prognostic Score of Thrombosis.

iron
A mineral needed to make new red blood cells.

karyotype
A test that uses a microscope to examine a cell's chromosomes.

lactate dehydrogenase (LDH)
A protein that helps to make energy in cells.

leukocyte
A type of white blood cell.

liver function tests (LFTs)
Tests that measure chemicals made or processed by the liver.

LMWH
low-molecular-weight heparin

MDS
myelodysplastic syndromes

medical history
A report of all your health events and medications.

megakaryocyte
A bone marrow cell that makes blood-clotting platelets.

MIPPS
Mutation-Enhanced International Prognostic Score System

molecular test
A lab test of an abnormal gene inside cells.

MPN-SAF TSS
MPN Symptom Assessment Form Total Symptom Score

mutation
An abnormal set of coded instructions in cells (gene).

myeloproliferative neoplasm (MPN)
A cancer of blood-forming cells that causes an excess of blood cells or bone marrow scarring.

MYSEC-PM
Myelofibrosis Secondary to PV and ET-Prognostic Model

NGS
next-generation sequencing

NOS
not otherwise specified

NSAID
non-steroidal anti-inflammatory drug

paresthesia
A burning or prickling sensation in the body.

pathologist
A doctor who's an expert in testing cells and tissue to find disease.

peripheral smear
The study of a drop of blood using a microscope.

phlebotomy
Withdrawal of blood.

physical exam
A review of the body by a health expert for signs of disease.

platelet
A type of blood cell that helps control bleeding. Also called thrombocyte.

plateletpheresis
A procedure that withdraws blood, removes platelets, and then returns your altered blood to your body.

polycythemia vera (PV)
Cancer of blood-forming cells that causes too many red blood cells.

post-ET myelofibrosis
Advanced essential thrombocythemia with scarring in the bone marrow.

post-PV myelofibrosis
Advanced polycythemia vera with scarring in the bone marrow.

pre-PMF
Prefibrotic primary myelofibrosis.

primary myelofibrosis (PMF)
Scarring of the bone marrow not due to other bone marrow problems.

prognosis
The likely course and outcome of a disease based on tests.

progression
A worsening of cancer.

pruritus
Itchy skin.

reverse transcription polymerase chain reaction (RT-PCR)
A lab test that detects a cancer marker even if it's in a few cells.

risk stratification
An assessment of the likelihood of an event based on proven predictors.

satiety
A feeling of fullness from eating.

SM-AHN
systemic mastocytosis with an associated hematologic neoplasm

spleen
A small organ to the left of your stomach that is part of the immune system.

splenomegaly
An abnormally large spleen.

SSRI
selective serotonin reuptake inhibitor

supportive care
Treatment for the symptoms or health conditions caused by cancer or cancer treatment.

thrombosis
A blockage of blood flow in blood vessels caused by a blood clot.

tinnitus
Sounds that are produced by the body and not heard by others, such as high-pitched ringing.

tumor lysis syndrome (TLS)
A health condition caused by the rapid death of many cancer cells.

uric acid
A chemical that is in most cells.

vein
A blood vessel that moves blood back to the heart.

venous thromboembolism (VTE)
A blood clot that formed in a deep vein and may now be stuck in a lung artery.

von Willebrand syndrome (VWS)
A blood disorder that causes blood not to clot.

NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Myeloproliferative Neoplasms, Version 1.2024. It was adapted, reviewed, and published with help from the following people:

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Notes

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Nanavati Max Hospital (Vile Parle):
10 am to 12 pm (Monday to Saturday)
S. L. Raheja Hospital (Mahim):
12 pm to 4 pm (Monday to Saturday)
Suvarna Hospital (Borivali):
5 pm to 6 pm (Monday and Friday)
Sushrut Hospital (Chembur):
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Hinduja Hospital (Khar): By appointment
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#Reference From NCCN Guidelines