Introduction

Polycythemia vera (PV) is one of several "myeloproliferative neoplasms" (MPNs), a term used to group a number of blood cancers that share several features, especially the "clonal" production of one or more blood cell lines. All clonal diseases (cancers) begin with one or more changes to the DNA in a single cell: the cells that are in marrow or blood are the offspring of that one mutant cell.

Other MPNs include essential thrombocythemia and myelofibrosis.

PV results from uncontrolled blood cell production, especially red cells, as a result of acquired mutations in an early blood-forming cell. Because this early cell has the capability to form not only red cells, but also white cells and platelets, any combination of these cell lines may be affected.

This fact sheet about PV provides information about diagnosis, treatment, new treatments being investigated in clinical trials and support resources.

Causes

The cause of PV is not fully understood. Almost all patients with PV have a mutation of the JAK2 (Janus kinase 2) gene. This mutated gene likely plays a role in the onset of PV. However, its precise role as the cause of the disease is still under study.

Most patients with PV do not have a family history of the disorder. However, occasionally there is more than one family member with the disease. PV is more prevalent among Jews of Eastern European descent than other Europeans or Asians. The incidence (newly diagnosed cases) of PV for all races and ethnicities is approximately 2.8 per 100,000 population of men and approximately 1.3 per 100,000 population of women. The prevalence (estimated number of people alive on a certain date in a population with a diagnosis of the disease) is approximately 22 cases per 100,000 population. This prevalence has been shown in several small studies. The average age at which PV is diagnosed is about 60 to 65 years. It is uncommon in individuals younger than 30 years.

PV can usually be managed effectively for very long periods. People with PV who receive treatment often have a normal
or near-normal quality of life. With careful medical supervision and therapy, PV does not usually interfere significantly with everyday activities and employment.

**Signs, Symptoms and Complications**

The signs, symptoms and complications of PV occur because there are too many red cells and, often, too many platelets in the blood. An increase in the number of white cells does not predispose the patient to an increased risk of infection or cause other significant effects.

Too many red blood cells can make the patient’s blood more viscous (thick) so the blood does not flow efficiently. High platelet counts can contribute to the formation of clots (thrombi). Underlying vascular disease, common in older persons with PV, can increase the risk of clotting complications. The clots may cause serious problems, such as stroke, heart attack, deep vein thrombosis or pulmonary embolism. Blood clots occur in about 30 percent of patients before the PV diagnosis is made. During the first 10 years after their diagnosis, 40 to 60 percent of untreated PV patients may develop blood clots.

Some people have few troublesome symptoms and PV may only be discovered when blood counts are done during a periodic health examination. However, signs, symptoms and complications of PV that patients may experience include:

- Headaches, exaggerated sweating, ringing in the ears, visual disturbances, such as blurred vision or blind spots, dizziness or vertigo (a more severe spinning feeling) may occur. These symptoms are presumed to be related to the effects of the engorged blood vessels with slower blood flow.
- Itchy skin called “pruritus,” especially after warm baths or showers, occurs in some patients.
- A reddened or purplish appearance of the skin, especially on the palms, ear lobes, nose, and cheeks may occur as a result of the high concentration of red cells in the blood. Some patients may experience a burning sensation in the feet.
- Peptic ulcers may be associated with PV and can lead to gastrointestinal (GI) bleeding.
- An enlarged spleen may be noted on physical examination or by ultrasound studies.
- Angina or congestive heart failure may be a harmful effect of the viscous blood and tendency of platelets to clump in the coronary blood vessels and lead to clots called “thrombi.”
- Gout, a painful inflammation of the joints caused by increased levels of uric acid (associated with PV), may occur or become worse.
- Bleeding or bruising, usually minor, occurs in about 25 percent of PV patients.

People with PV are at slightly greater risk than the general population for developing leukemia as a result of the disease and/or certain drug treatments.

**Diagnosis**

A diagnosis of PV is considered if the patient’s red cell counts are elevated. Three measures of the concentration of red cells in the blood can be used to diagnose PV: the hematocrit, the hemoglobin concentration and the red cell count. These measurements are included in a standard blood test called a “complete blood count” (CBC). Blood counts are usually measured in a machine that simultaneously measures the hematocrit, hemoglobin concentration and red cell count and these three measures closely parallel each other.

In a patient with PV, if a normal hematocrit concentration of 45 percent is increased by one-third to 60 percent, the corresponding normal hemoglobin concentration of 150 grams/liter (g/L) of blood would also be increased by one-third to 200 g/L of blood. The corresponding red cell count would be increased by one-third as well. Thus, for diagnostic purposes, any of the three measurements could be used.

**Hematocrit**

Generally, the hematocrit concentration is used to diagnose PV and measure the patient’s response to therapy.

Hematocrit is the proportion of red blood cells in a volume of blood, usually expressed as a percent or an increase in hemoglobin concentration in the blood. In healthy individuals, hematocrit concentration ranges from about 36 to 46 percent in women and 42 to 52 percent in men.

Other diagnostic features from the results of blood tests that will confirm the diagnosis of PV include:

- An elevated white cell count, especially the neutrophil (a type of white blood cell) count—the white cell count is increased mildly in most PV patients. Usually the increase does not progress.
- An elevated platelet count, which occurs in at least 50 percent of patients—the increase in the platelet count can progress.
- The presence of JAK2 mutation in blood cells
- Elevation of the red cell mass (Usually only measured
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if the hematocrit or hemoglobin concentration is not elevated decisively.)

- Normal or near-normal arterial oxygen saturation
- A low erythropoietin (EPO) assay in the blood. (Blood levels of EPO are usually low in PV patients, but are normal or high in those with secondary polycythemia. Secondary polycythemia is discussed briefly on page 4.)

Marrow Examination

Although not required to make the diagnosis, patients may also have a bone marrow analysis as part of their testing. With a diagnosis of PV, marrow contains more than the normal number of cells as a result of the overexpansion of the blood-forming cells and is lacking iron, which has been used up making the additional red cells. Chromosome analysis can also be done on marrow cells. The growth of marrow red cell precursors can also be studied to examine their ability to grow in the absence of added erythropoietin, a feature of PV.

For more information about bone marrow tests and other lab tests, please see the free LLS publication Understanding Lab and Imaging Tests.

Treatment Planning

Treatment decisions are based on the patient’s risk for clotting complications (thrombosis). Risks for thrombosis include

- A history of a clot
- Advanced age (over 60 years)
- Cardiovascular risk factors, such as high cholesterol levels, diabetes, smoking, obesity or hypertension—all considered by many doctors as additional risk factors for thrombosis.

Every patient’s medical situation is different and should be evaluated individually by a hematologist/oncologist who specializes in treating blood cancers. It is important for you and members of your medical team to discuss all treatment options, including treatments being studied in clinical trials.

For more information about choosing a doctor or a treatment center, see the free LLS publication Choosing a Blood Cancer Specialist or Treatment Center.

Treatment

PV is a chronic disease; it is not curable, but it usually can be managed effectively for very long periods. Careful medical supervision and therapy to keep the hematocrit concentration near normal are important.

Treatment goals for the disease are

- To control symptoms
- To decrease the risk of complications.

Therapies are aimed at

- Lowering the hematocrit concentration to normal or near-normal values
- Lowering the platelet count if the numbers are high or become high over time.

A troublesome symptom that occurs in many PV patients is itchy skin (pruritus). To help prevent pruritus, it is suggested that patients bathe less frequently. Aspirin and antihistamines may benefit patients. Other treatment options include light therapy (phototherapy) using psoralen and ultraviolet A light. Interferon alpha or pegylated interferon may be effective.

Patients with low-risk PV are usually phlebotomized and given low-dose aspirin. Patients with high-risk PV require medical therapy to decrease hematocrit concentration permanently, eliminate a need for phlebotomy and decrease the risk of clotting. All patients are given low-dose aspirin.

Phlebotomy

Phlebotomy is the removal of blood from a vein. It is the usual starting point of treatment for most patients. A volume of blood is drawn at regular intervals and the hematocrit concentration is brought down to normal values within a period of weeks to months. The procedure is identical to that used for donating blood to a blood bank. The immediate effect of phlebotomy is to reduce the hematocrit concentration, which usually results in the improvement of certain symptoms such as headaches, ringing in the ears and dizziness. Eventually, phlebotomy results in iron deficiency.

Phlebotomy may be the only form of treatment required for many patients, sometimes for many years. Acceptable disease control may be achieved with withdrawal of a volume of blood every few months. Patients may feel tired afterward and need to rest for a short time.

Drug Therapy

Aspirin therapy—Low-dose aspirin should be used to lessen the risk of thrombosis in an artery. It acts by making platelets less likely to adhere to the wall of an artery and aggregate. Aspirin is given by mouth and the most common side effects include upset stomach and heartburn.
Anagrelide (Agylin®)—This drug, given by mouth, can be used if platelet numbers are too high. The drug can reduce the rate of platelet formation in the marrow. It does not have an effect on the other blood cells. Patients taking anagrelide may experience side effects, including fluid retention, heart and blood pressure problems, headaches, dizziness, nausea and diarrhea.

Antihistamines or related drugs—These drugs may be prescribed to relieve itching and are given by mouth. Side effects include dry mouth, drowsiness, dizziness and restlessness. Some antihistamines can impair a person’s ability to drive or operate heavy machinery.

Myelosuppressive drugs (agents that can reduce red cell or platelet concentrations)—In some patients, phlebotomy alone cannot control the overproduction of red cells and can accentuate the overproduction of platelets. Patients who have an extremely high platelet count, complications from bleeding, blood clots or severe systemic complaints and are not responding to low-dose aspirin or phlebotomy, may also be treated with myelosuppressive agents. Drug therapy to suppress the marrow production of red cells and platelets is given as a replacement for phlebotomy.

Hydroxyurea (Hydrea®)—The most commonly used myelosuppressive chemotherapeutic agent for PV is hydroxyurea, given by mouth. It helps to reduce both the hematocrit concentration and the platelet count. Rare side effects are mouth ulcers, change in the sense of taste, skin ulcers or rash. There is some controversial evidence that, after long-term therapy, hydroxyurea is associated with an increased risk for patients to develop acute leukemia, so is frequently avoided as therapy for younger patients. However, it is thought to have much less potential for causing leukemia than other myelosuppressive agents, such as radiophosphorus and alkylating agents, which include melphalan (Alkeran®), busulfan (Myleran®), chlorambucil (Leukeran®) and others. Radiophosphorous and alkylating agents are reserved for patients with short life expectancy.

Interferon alfa (immediate-release preparations Intron® A [alfa-2b] and Roferon-A®[alfa-2a] and sustained-release preparations PEG-Intron® [peginterferon alfa-2b] and Pegasys® [peginterferon alfa-2a])—These agents are used to lower hematocrit concentration. However, they are not used for most patients because, in comparison with other treatments for PV, they are less convenient to administer (they are given by intramuscular or subcutaneous injection), and may cause troublesome side effects. Some patients experience moderately severe flu like symptoms, confusion, depression or other complications. Development of sustained-release preparations provides a new option for patients; injections would be weekly, a regimen patients tend to tolerate better (particularly in the case of Pegasys).

For specific drug information, see the free LLS publication Understanding Drug Therapy and Managing Side Effects and the Food and Drug Administration (FDA) drug information website at www.fda.gov/drugs/resourcesforyou/consumers/default.htm.

Special Considerations

Untreated patients have increased risk for bleeding complications after surgery. Thus, if surgery is needed for any reason, treatment should be put in place to bring the hematocrit to a normal concentration before surgery.

Some PV patients have further disease progression despite treatment. After years of disease, their cells undergo further changes and no longer overproduce red cells. For a time, the red cell count may stay near-normal without treatment or drop below normal, resulting in anemia. The spleen may become further enlarged, and the marrow may become fibrous or scarred, reducing its ability to make red cells and platelets. This condition of the marrow is called “myelofibrosis.” The platelet count may fall to low levels. Immature white cells may be released from the marrow into the blood. Treatment for myelofibrosis is described in the free LLS publication Myelofibrosis Facts.

PV can also transform into other blood cancers such as acute leukemia or myelodysplastic syndromes, but this is a very uncommon occurrence.

Secondary Polycythemia

Secondary polycythemia (also called “secondary erythrocytosis”) is not a myeloproliferative neoplasm. This may occur as a result of four principal situations: ascent to high altitude, diseases that lead to low oxygenation of the blood, tumors that secrete the hormone erythropoietin (e.g., kidney tumors) or inherited disorders that result in overproduction or exaggerated action of erythropoietin. (Erythropoietin is the principal hormone that stimulates red cell formation in the marrow.) Secondary polycythemia is limited to overproduction of red cells. In the case of high altitude or heart and lung diseases that lead to low blood oxygen content, secondary polycythemia is a physical response that the body makes to improve the oxygen-carrying capacity of the blood.

Talking to Your Doctor About Side Effects of Treatment

Management of side effects is important. If you are having any concerns about your side effects, talk to your doctor to get help. Most side effects are temporary and resolve when
treatment is completed.
The individual side effects of specific drugs are discussed in the treatment section on pages 3 and 4.

**Treatments Undergoing Investigation**

LLS invests research funds in PV and other blood cancers.
LLS is funding research related to identifying and effectively attacking targets in PV and other MPNs for new drug therapies, new approaches to classification, diagnosis and therapy. Research is also being funded to investigate the mechanism of action of pegylated interferon. The goal is to develop specific and more effective therapy for patients who have MPNs.

Clinical trials are carefully controlled research studies, conducted under rigorous guidelines, to help researchers determine the beneficial effects and possible adverse side effects of new treatments. Studies are also conducted to evaluate new indications for therapies that are already approved for other cancers or types of diseases. Patient participation in clinical trials is important in the development of new and more effective treatments for PV and may provide patients with additional treatment options. Patients interested in participating in clinical trials are encouraged to talk to their doctors about whether a clinical trial would be appropriate for them. For more information about clinical trials, see the free LLS publication *Understanding Clinical Trials for Blood Cancers* or visit www.LLS.org/clinicaltrials.

**Some research approaches under investigation include**

- **Ruxolitinib (Jakafi®)**—This drug is a JAK2 inhibitor that is taken by mouth twice a day. Ruxolitinib is approved by the FDA to treat symptoms and signs of myelofibrosis, including an enlarged spleen, night sweats, itching and bone or muscle pain. It is indicated for treatment of patients with intermediate- or high-risk myelofibrosis, including primary myelofibrosis, post polycythemia vera myelofibrosis and post essential thrombocythemia myelofibrosis. It is being tested in a study in which patients are randomized between ruxolitinib and best available therapy (the traditional medication that a doctor determines is the best treatment choice for a given patient). Ruxolitinib is being studied for possible approval as new therapy for PV patients who have failed or are unable to tolerate treatment with hydroxyurea.

- **Possible genetic origin of MPNs**—There is a theory that MPNs may occur in families; if so, they are a group of genetic diseases passed on from one generation to another. This idea is being studied to discover if abnormal genes cause MPNs.

We encourage you to contact an Information Specialist and visit www.LLS.org for more information about specific treatments under study in clinical trials.

**Treatment Outcomes**

The likely outcome of a disease, called the “prognosis,” varies in patients with PV. Each patient’s prognostic risk factors are evaluated individually. In people with PV, median survival approaches or exceeds 20 years. Some people may survive longer after diagnosis, perhaps achieving a near-normal life expectancy. It is important to know that outcome data can show how groups of people with PV responded to treatment, but cannot determine how any one person will respond. For these reasons, patients are advised to discuss survival information with their doctors.

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**We’re Here to Help**

LLS is the world’s largest voluntary health organization dedicated to funding blood cancer research, education and patient services. LLS has chapters throughout the country and in Canada. To find the chapter nearest you, enter your ZIP code into “Find your Chapter” at www.LLS.org or contact

**The Leukemia & Lymphoma Society**
1311 Mamaroneck Avenue
White Plains, NY 10605
Information Specialists: (800) 955-4572
Email: infocenter@LLS.org

Callers may speak directly with an Information Specialist Monday through Friday, from 9 a.m. to 6 p.m. ET. You may also contact an Information Specialist between 10 a.m. and 5 p.m. ET by clicking on “Live Chat” at www.LLS.org or by sending an email. Information Specialists can answer general questions about diagnosis and treatment options, offer guidance and support and assist with clinical-trial
searches for leukemia, lymphoma, myeloma, myelodysplastic syndromes and myeloproliferative neoplasms. The LLS website has information about how to find a clinical trial, including a link to TrialCheck®, a clinical-trial search service.

LLS also provides fact sheets and booklets that can be ordered via the 800 number or through the “Free Education Materials” option at www.LLS.org/resourcecenter.

**Other Resources**

**MPN Education Foundation**

www.mpdinfo.org

The MPN Education Foundation provides information, education and support and looks to advance research and develop drugs to improve the quality of life and care of patients with myeloproliferative neoplasms (MPNs). The foundation provides patient and doctor conferences and facilitates patient participation and accrual in clinical studies and surveys.

**The MPN Research Foundation**

www.mpnresearchfoundation.org

The MPN Research Foundation is a nonprofit organization whose primary mission is to promote, fund and support the most innovative and effective research into the causes, treatments and potentially the cure of essential thrombocytopenia, polycythemia vera and myelofibrosis. The organization also provides information and support to people who have myeloproliferative neoplasms.

**The Myeloproliferative Disorders Research Consortium (MPD-RC)**

www.mpd-rc.org

The MPD-RC is an international, multi-institutional nonprofit consortium funded by the National Cancer Institute. It is set up to coordinate, facilitate and perform basic and clinical research on Philadelphia chromosome-negative myeloproliferative neoplasms (Ph-MPNs).

**The National Organization for Rare Disorders (NORD)**

(800) 999-6673/(203) 744-0100

www.rarediseases.org

NORD is a unique federation of voluntary health organizations dedicated to helping people with rare “orphan” diseases and assisting the organizations that serve them. NORD is committed to the identification, treatment, and cure of rare disorders through programs of education, advocacy, research and service.

**The National Cancer Institute (NCI)**

(800) 422-6237

www.cancer.gov

The National Cancer Institute, part of the National Institutes of Health, is a national resource center for information and education about all forms of cancer, including polycythemia vera (PV). The NCI also provides a clinical-trial search feature, the PDQ® Cancer Clinical Trials Registry, at www.cancer.gov/clinicaltrials, where PV patients can look for clinical trials.

**References**


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