



Polycythemia Vera

No. 13 in a series providing the latest information on blood cancers

Myeloproliferative disorders are diseases in which certain types of blood cells are overproduced in the marrow. The different types of myeloproliferative disorders include idiopathic myelofibrosis, essential thrombocythemia and polycythemia vera. In polycythemia vera, blood cell production, notably red cells, is increased as a result of an acquired stem cell mutation.

Another type of polycythemia is called secondary polycythemia. This disorder is not a myeloproliferative disease and generally only red cell production is increased. Secondary polycythemia is caused by lower blood oxygen saturation, which might occur at high altitudes, with certain heart and lung diseases, or from an abnormal increase in the secretion of erythropoietin, a hormone that stimulates marrow to make red cells.

This fact sheet discusses polycythemia vera and its causes, diagnosis, symptoms, and current and emerging treatments.

What is polycythemia vera?

Polycythemia vera begins with an acquired, abnormal change to a single hemopoietic (blood-forming) stem cell in the marrow, where blood cells are made. Abnormal cell production gradually dominates normal cell production and too many red cells are produced. In many patients, white cell and platelet counts are also elevated. The increase in red cells leads to hyperviscosity (blood that is thicker than normal).

How common is polycythemia vera?

The average age at which polycythemia vera is diagnosed is 60 years. It is rarely diagnosed in people younger than 20 years of age. The incidence varies worldwide, ranging from 5 to 26 out of 1,000,000 people. It is more prevalent among Jews of Eastern European descent than other Europeans or Asians.

What are the causes and risk factors associated with polycythemia vera?

The cause of polycythemia vera is unknown. Polycythemia vera is called a clonal disorder because it begins with a change to the DNA in a single cell: all the cells that will dominate blood cell production are the offspring of the one mutant cell.

The gene that causes the acquired genetic mutation responsible for polycythemia vera has not been identified. The change to the DNA in the cell has not been linked to any environmental cause.

Most patients with polycythemia vera do not have a family history of the disorder. However, there are reports of familial incidence.

How is polycythemia vera diagnosed?

The diagnosis of polycythemia vera may be considered in certain patients when either a periodic physical examination, or a medical examination related to a blood clot, uncovers a high red cell count. The diagnosis is made from a physical examination in combination with lab tests to look at cells in blood and marrow.

Significant diagnostic features of polycythemia vera generally include:

From physical exam:

- Enlarged spleen.
- Reddened (or purplish) appearance of the skin.

From blood tests:

Blood cell counts are determined by a complete blood cell count (CBC), a standard test that measures the concentration of red and white cells and platelets in the blood.

- Elevated hematocrit (the percentage of red blood cells in the total blood volume).
(In healthy individuals: red cell count is about 4.0 to 6.0 million cells per microliter of blood, and the average red cell count is about 5.2 million red cells for men and about 4.6 million for women; hematocrit averages 42% in women and 47% in men; hemoglobin (the iron-containing protein in red cells that carries oxygen from the lungs to the body's tissues) concentration averages about 14 grams per 100 milliliters of blood in women and about 16 grams per 100 milliliters of blood in men.)

- Elevated white count, especially neutrophils, a type of white blood cell.

The white cell count is increased mildly in most polycythemia vera patients. The increase usually does not progress.

- Elevated platelet count, which occurs in at least 50% of patients.

The increased platelet count can progress, causing an increased risk of blood clot formation that may require treatment.

Other diagnostic features from blood tests are:

- Elevated serum B12 level.
- Elevated serum uric acid level.
- Normal or near-normal arterial oxygen saturation.
- An erythropoietin (EPO) assay, to measure of the blood level of EPO.

Blood levels of EPO may be extremely low in polycythemia vera, but are normal or high in secondary polycythemia.

Patients may also have a bone marrow analysis as part of their diagnostic testing. With a diagnosis of polycythemia vera, 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.

Certain biomarkers including c-Mpl and PRV-1, have been identified on the cells in association with polycythemia vera. These may play a role in the development of diagnostic tests in the future.

What are the symptoms and complications of polycythemia vera?

People with polycythemia vera may have no symptoms for years, or may experience only vague and non-specific symptoms.

The most common symptoms, experienced by at least 30 percent of polycythemia vera patients, are headaches, weakness, itching, dizziness and sweating.

Thrombotic episodes (blood clots) occur in about 30 percent of patients before the diagnosis of polycythemia vera is made. During the first 10 years after diagnosis, 40 to 60 percent of polycythemia vera patients have blood clots. The clots may cause serious or fatal problems, such as stroke, heart attack, deep vein thrombosis or pulmonary embolism.

Skin. The skin may appear reddened or purplish, especially, palms, ear lobes, and cheeks. This occurs as a result of the high concentration of red cells in the blood. In addition, patients may experience a burning sensation in the hands and feet. Itching after a bath or shower, a symptom that is very specific to polycythemia vera, occurs in about 40 percent of patients.

Neurologic symptoms. These may include visual disturbances, such as double vision or blind spots and vertigo (a spinning feeling.)

Complications of polycythemia vera result mainly from the increase in red cells and platelets:

- Too many red blood cells make it difficult for the blood to flow smoothly.
- Too many platelets can lead to the formation of clots.
- Underlying vascular disease, commonly found in older persons with the disease, can increase the risk of clotting complications, such strokes or heart attacks.

Peptic ulcers may be associated with polycythemia vera; angina or congestive heart failure; gout (a painful inflammation of certain tissue, the big toe or foot, caused by increased levels of uric acid); and bleeding or bruising, usually minor, occurs in about 25% of polycythemia vera patients.

Surgery. Untreated patients who undergo surgery have increased risk for bleeding complications.

Associated diseases. Polycythemia vera may evolve into a syndrome simulating another myeloproliferative disorder, idiopathic myelofibrosis, or another blood disorder called myelodysplastic syndrome and much less commonly into acute leukemia.

What are the current treatments for polycythemia vera?

Treatment goals for polycythemia vera are:

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

Therapies are aimed at:

- Lowering the number of red cells to normal or near normal levels.
- Lowering the platelet count if it is high or becomes high over time.

Decisions about the types of therapy for polycythemia vera are based on:

- The symptoms and rate of progression of the disease.

- The patient's age.
- The patient's overall health, including any other chronic diseases.

The two main types of treatment for polycythemia vera are phlebotomy, the removal of blood from a vein in a manner similar to a blood donation, and drug therapy.

Phlebotomy. Phlebotomy is the usual starting point of treatment for most patients. A volume of blood is drawn at regular intervals to decrease the number of red cells to normal red cell counts within a period of weeks or months. The immediate effect of phlebotomy is to reduce the hematocrit, which results in the improvement of certain symptoms, such as headaches. The usual consequence of phlebotomy is 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.

Hydroxyurea (Hydrea[®]). The most commonly used myelosuppressive agent for polycythemia vera, hydroxyurea is given in pill form. It has few side effects, and helps to reduce both the red cell and platelet counts. Hydroxyurea is thought to have much less potential for causing leukemic changes than other myelosuppressive agents.

Other myelosuppressive agents. In some patients, phlebotomy alone cannot control the overproduction of red cells and can accentuate the overproduction of platelets. In such cases, drugs may be used to suppress the marrow production of red cells and platelets. A single drug or combinations of drugs may be administered. Drug therapy may be the only treatment or it may be combined with phlebotomy. Myelosuppressive agents are associated with some increased risk for development of leukemia. However, in certain cases, this risk must be weighed against the need to treat extremely high platelet counts to prevent serious or fatal complications.

Patients with an extremely high platelet count, complications from bleeding or blood clots or severe systemic complaints not responding to low-dose aspirin or phlebotomy, may also be treated with myelosuppressive agents. These drugs include hydroxyurea, interferon-alpha, anagrelide, busulfan and chlorambucil.

- Radioactive phosphorus (³²p) is an option for patients who are unable to have frequent follow-up because longer-lasting control is possible with one or two doses given intravenously.
- Anagrelide is another drug that can be used if platelet numbers are too high. The drug can blunt the rate of platelet formation in the marrow.

- Interferon-alpha and other chemotherapy agents are available in special cases but are not used in most patients because they are not as effective, are inconvenient to administer, or may have more severe effects.

Other Treatments

- Low-dose aspirin is sometimes prescribed to help reduce the risk of blood clots. The drug acts on the platelets to decrease their tendency to form clots.
- Antihistamines may be prescribed to relieve itching.

What is the spent phase of polycythemia vera?

About 15 percent of patients have further disease progression despite the treatment they receive. After years of disease, their stem cells undergo further mutations 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 (myelofibrosis.) The platelet count may fall to low levels. Immature white cells may be released from the marrow into the blood.

Therapy at this time may include blood transfusions as needed, pain control and careful myelosuppression. In some cases, the massive enlargement of the spleen may require splenectomy (surgical removal of the spleen). In patients unable to tolerate surgery, low-dose radiation therapy (to the spleen) may be used.

What is the prognosis for polycythemia vera?

Polycythemia vera is a chronic disease; it is not curable. The median survival of patients treated for polycythemia vera exceeds 10 years.

Careful medical supervision and therapy to keep the red count near normal are important. People with polycythemia vera who receive treatment often have a normal or near-normal quality of life. Their disease usually does not interfere significantly with everyday activities and employment.

Some patients may have disability from blood clots or other symptoms. People with polycythemia vera are at slightly greater risk for developing leukemia than the general population. Treatment with certain drug therapies increases this risk. However, the degree of increased risk has not been determined.

What are the emerging treatments for polycythemia vera?

Researchers continue to look for more effective ways to treat polycythemia vera by conducting clinical trials (research studies) of new therapies or combinations of therapies. Some treatments under examination for polycythemia vera in clinical trials include:

- *Imatinib mesylate* (Gleevec[®]). This drug, approved for use in the treatment of chronic myelogenous leukemia, is currently being studied in the treatment of polycythemia vera to evaluate its effectiveness in reversing the overproduction of red cells. It is possible that this drug may be able to inhibit the process responsible for the overproduction by blocking certain enzymes need for cell growth.
- *Allogenic stem cell transplantation*. Small numbers of polycythemia vera patients with myelofibrosis, splenomegaly (enlarged spleen), or progressed disease including myelodysplastic syndrome or acute myeloid leukemia, may be candidates for allogenic stem cell transplantation. This treatment may help patients by replacing immune cells that were destroyed by radiation therapy and chemotherapy. One clinical trial currently underway is studying the effectiveness of combining low-dose total-body radiation therapy and fludarabine with alemtuzumab (Campath[®]) followed by allogenic stem cell transplantation in treating patients who have polycythemia vera, other myeloproliferative disorders or myelodysplastic syndrome. Alemtuzumab is a type of monoclonal antibody therapy.

For more information about polycythemia vera speak to your physician or a hematologist (a physician who specializes in blood disorders). You can also contact The Leukemia & Lymphoma Society.

Resources

The Leukemia & Lymphoma Society

The Leukemia & Lymphoma Society is a national voluntary health agency with 63 chapters serving all 50 states. It provides education and support services for the public and for cancer treatment professionals. To find the Society chapter nearest you, visit our online chapter finder or contact:

The Leukemia & Lymphoma Society
1311 Mamaroneck Avenue
White Plains, NY 10605
(800) 955-4572 or www.LLS.org

Through the Society's Information Resource Center, callers may speak directly with an Information Specialist, Monday-Friday, 9 - 6 p.m., ET (800) 955-4572. To contact an Information Specialist, click on Live Help (10 a.m. - 5 p.m.) on the Society's Web site or email us at infocenter@LLS.org .

Information Specialists can answer general questions about diagnosis and treatment options, offer guidance and support, and assist with clinical trial searches for leukemia, lymphoma and myeloma.

The Society's Web site features a link to the clinical trial search service of the National Cancer Institute. Clinical trials listings for blood cancers, including abstracts of clinical trial protocols and contact information, are available.

The Society provides fact sheets and booklets that can be ordered via the 800 number or through the Free Materials section on the Web site, www.LLS.org.

Understanding Blood Counts

http://www.leukemia-lymphoma.org/all_mat_toc.adp?item_id=9452&cat_id=1215

Idiopathic Myelofibrosis

http://www.leukemia-lymphoma.org/all_mat_toc.adp?item_id=9962&cat_id=1214

Facts about Leukemia

http://www.leukemia-lymphoma.org/all_mat_toc.adp?item_id=154758

Acute Myelogenous Leukemia

http://www.leukemia-lymphoma.org/all_page?item_id=8459

Myelodysplastic Syndrome

http://www.leukemia-lymphoma.org/all_mat_toc.adp?item_id=54083

The Association of Cancer Online Resources

www.acor.org/diseases/hematology/mpd

A web site that discusses polycythemia vera

References

Beutler E. *Polycythemia*. Williams Hematology, 6th edition, Beutler E, et al. New York City: McGraw-Hill Book Co. 2003: 689-699.

Gruppo Italiano Studio Policitemia. “ Polycythemia vera: The natural history of 1213 patients followed for 20 years.” *Ann Intern Med*. 123:656, 1995.

Diagnostic criteria and prognosis in polycythemia vera and essential thrombocythemia. Seminars in Hematology, 1999: Vol. 36 (Supplement 2):9-13.

Gilbert HS. *Modern Treatment Strategies in Polycythemia Vera*. Seminars in Hematology, 2003: Vol. 40, No.1 (Supplement 1): 26-29.

Golden C. *Polycythemia Vera: A Review*. Clinical Journal of Oncology Nursing, 2003, Vol. 7, No. 5: 553-556.

Pahl HL. Diagnostic approaches to polycythemia vera in 2004. Expert Review of Molecular Diagnostics, 2004, Vol. 4, No. 4: 495-502.

Oehler L, Jaeger E, Eser A, et al. *Imatinib mesylate inhibits autonomous erythropoiesis in patients with polycythemia vera in vitro*. Blood, 2003:Vol. 102, No. 6: 2240-2242.

This publication is designed to provide accurate and authoritative information in regard to the subject matter covered. It is distributed as a public service by The Leukemia & Lymphoma Society, with the understanding that The Leukemia & Lymphoma Society is not engaged in rendering medical or other professional services.