

**“What is Polycythemia vera?” Amber Vinchesi. April 24, 2007.**

### **Other names**

“Primary polycythemia; Polycythemia rubra vera; Myeloproliferative disorder; Erythremia; Splenomegalic polycythemia; Vaquez's disease; Osler's disease; Polycythemia with chronic cyanosis - Myelopathic polycythemia; Erythrocytosis megalosplenica; Cryptogenic polycythemia” (4). Myeloproliferative refers to the overproduction of cells by the bone marrow.

### **Overview**

Polycythemia vera, or PV, is a rare blood disease where too many red blood cells are produced. Basically, the bone marrow is producing too many blood cells (4). The increase in red blood cell production leads to thick blood. The thicker blood moves slowly through the body, leading to less oxygen transport. The oxygen in the blood cannot reach the places of the body as fast as it needs to, which can lead to many of the symptoms of PV (5). The thick, slow-flowing blood can form clots, which is a major complication of PV since it can lead to heart attack or stroke (4).

### **Cause**

The cause of PV is unknown. It is a disorder that begins with a single mutation in one cell. The all the offspring of this one cell and will then dominate blood production. The gene that causes the mutation has not been discovered yet. PV is not genetic but there have been some incidences of family history (3). The mutation occurs in the JAK2 gene. This provides an important protein that is involved in blood production. The

mutation occurs after fertilization and is not passed from parent to child. Unfortunately, the mutation is irreversible (5). The JAK2 gene is very crucial to signaling “by the receptors for erythropoietin, thrombopoietin, interleukin-3, granulocyte colony-stimulating factor (G-CSF), and granulocyte–macrophage colony-stimulating factor (GM-CSF)” (Myeloproliferative). JAK2 takes a signal and converts it to another signal therefore making it instrumental in binding erythropoietin with its receptor (1)

“Polycythemia vera represents an accumulation of abnormal hemopoietic progenitors that arise from a single clone, grow autonomously, and retain the capacity to differentiate into mature blood cells. A defect in programmed cell death may make these precursors slow to die; hence, they pile up and proliferate without a need for growth factors (or growth factor receptors)” (2). Basically, there is an aggregation of blood-forming stem cells that come from a single mutated cell and grow independently from growth factors. They die slowly, adding to the accumulation and the amount of the blood cells in the body. This ultimately leads to the complication of PV.

## **Who**

PV affects men more than it affects women and is rarely found in patients under forty years old (4). There are only about five cases per year for every one million people. It is more common in adults older than sixty years (5). “It is more prevalent among Jews of Eastern European descent” (3).

## **Symptoms**

It is possible for PV patients to have no symptoms, or at least be asymptomatic for the first few years of the disease. Many patients, when diagnosed, find out they have had

the disease for years without representing any symptoms. Thirty percent of those affected by PV experience headaches, weakness, itching, dizziness and sweating. Thirty percent may also experience blood clots before they are even diagnosed with Polycythemia. Forty to sixty percent of patients will experience blood clots in the first ten years after diagnosis. Forty percent experience intense itching after water contact, such as a warm shower or bath. This is a specific sign of PV. Other symptoms include red or purple skin (due to high number of blood cells) and burning in the hands and feet. Neurological symptoms of PV include blind spots, visions problems, and vertigo (3). “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” (3). Shortness of breath, reddened face, difficulty breathing while lying down are also common symptoms (4). Due to the slow flow of oxygen in the thick blood, many functions of the body may not work properly. An enlarged spleen and bleeding from the gums are also common symptoms of PV according to the National Heart Lung and Blood Institute (5). PV can also lead to other diseases. These other diseases include “myeloproliferative disorder, idiopathic myelofibrosis, or another blood disorder called myelodysplastic syndrome and much less commonly into acute leukemia” (3).

## **Diagnosis**

You may have Polycythemia vera long before you are diagnosed due to the possibility of being asymptomatic. Most PV cases are found through routine blood tests.

Doctors will diagnose PV based on symptoms, age, physical exam, test results and the patient's overall health. Erythropoietin (EPO) levels are checked if there is difficulty in determining whether it is primary or secondary Polycythemia. Primary PV will present low levels of EPO. After diagnosis, the patient may be referred to a hematologist. Blood tests will show levels of all types of blood cells to give a better picture of whether the patient has PV. A CBC count may be used. This is a complete blood count. It will count the number of red blood cells that carry oxygen, the white blood cells that fight infection, and the platelets that clot the blood. If these counts are high, then PV is a likely diagnosis. If hemoglobin is high or if the hematocrit, measures the percent of red blood, is high, then it is also likely for PV. To confirm a potential diagnosis, a blood smear may be made. The doctor will look under a microscope at the patient's blood sample, and look for a high concentration of RBCs and for abnormal cells seen in myelofibrosis. An arterial blood gas test is used to see if blood from the arteries has low oxygen. A red blood cell mass is done by mixing a blood sample with a small amount of radioactive dye and injecting it back into the bloodstream. Then another blood sample is taken from the patient and special cameras that can see the dye count the total number of RBCs. A bone marrow biopsy may be done too (5). Healthy individuals should have an **EPO level** between four to six million per micro liter. Fifty percent of PV patients have an elevated platelet count, elevated serum B12 level, or an elevated serum uric acid level. Biomarkers such as cMpl and PRV-1 cells may help with PV in the future.

### **Treatment**

PV cannot be cured. It is a chronic disease that is fatal, but treatments are very successful in improving longevity of life. By reducing the number of red blood cells,

itching, vision problems and headaches can be reduced as well (5). Treatments of PV are dependent on symptoms and the rate of progression, age, and the patient's overall health (3). The most common treatment for PV is a phlebotomy. A phlebotomy is a pint of blood taken each week until the hematocrit level is back to normal. It is an efficient way to lower the number of red blood cells and may need to be repeated every few months (5). Iron deficiency is a consequence of phlebotomy (3). Medicines can also help keep the bone marrow from producing too many RBCs. Hydroxyurea is a chemotherapy medicine and reduces platelets and RBCs. Aspirin can also reduce the chance of clotting and relieves the burning in hands and feet (5). Aspirin can be a controversial drug because it may cause stomach bleeding in some PV patients (4). Interferon-alpha is an immunotherapy substance that is already naturally produced in our bodies. It reduces production of RBCs in the bone marrow as well (5) but can have bad side effects and not be very effective (3). Prescription medicines can help relieve the itching and allopurinol is used for gout (4). "Since JAK2 inhibitors reduce the growth of *JAK2* V617F-positive cell lines and primary cells in vitro,<sup>8,12</sup> there is considerable interest in developing compounds for clinical use" (1).

## Works Cited

1. Campbell PJ, Green AR. The Myeloproliferative Disorders. *NEJM* [serial online].

2006; 355:2452-2466. Available at

[http://content.nejm.org/cgi/content/full/355/23/2452?andorexacttitleabs=and&search\\_tab=articles&tocsectionid=Original+Articles&tocsectionid=Special+Reports&tocsectionid=Special+Articles&tocsectionid=Videos+in+Clinical+Medicine&tocsectionid=Clinical+PracticeAORBClinical+Therapeutics&tocsectionid=Review+ArticlesAORBClinical+PracticeAORBClinical+Implications+of+Basic+ResearchAORBMolecular+MedicineAORBClinical+TherapeuticsAORBVideos+in+Clinical+Medicine&tocsectionid=EditorialsAORBPerspectiveAORBOutlookAORBBehind+the+Research&tocsectionid=Sounding+BoardAORBClinical+Debate&tocsectionid=Clinical+Implications+of+Basic+Research&tocsectionid=Health+Policy+ReportsAORBHealth+Policy+2001AORBQuality+of+Health+Care&searchtitle=Articles&sortspec=Score+desc+PUBDATE\\_SORTDATE+desc&excludetag=TWEEK\\_element&hits=20&where=fulltext&andorexactfulltext=and&fyear=1996&fmonth=Nov&sendit=GO&searchterm=polycythemia+vera&searchid=1&FIRSTINDEX=0&resourcetype=HWCIT](http://content.nejm.org/cgi/content/full/355/23/2452?andorexacttitleabs=and&search_tab=articles&tocsectionid=Original+Articles&tocsectionid=Special+Reports&tocsectionid=Special+Articles&tocsectionid=Videos+in+Clinical+Medicine&tocsectionid=Clinical+PracticeAORBClinical+Therapeutics&tocsectionid=Review+ArticlesAORBClinical+PracticeAORBClinical+Implications+of+Basic+ResearchAORBMolecular+MedicineAORBClinical+TherapeuticsAORBVideos+in+Clinical+Medicine&tocsectionid=EditorialsAORBPerspectiveAORBOutlookAORBBehind+the+Research&tocsectionid=Sounding+BoardAORBClinical+Debate&tocsectionid=Clinical+Implications+of+Basic+Research&tocsectionid=Health+Policy+ReportsAORBHealth+Policy+2001AORBQuality+of+Health+Care&searchtitle=Articles&sortspec=Score+desc+PUBDATE_SORTDATE+desc&excludetag=TWEEK_element&hits=20&where=fulltext&andorexactfulltext=and&fyear=1996&fmonth=Nov&sendit=GO&searchterm=polycythemia+vera&searchid=1&FIRSTINDEX=0&resourcetype=HWCIT). Accessed April 19, 2007.

2. Chance, Death and Mutability. *NEJM* [editorial serial online]. 1998; 338:613-615.

Available at

[http://content.nejm.org/cgi/content/full/338/9/613?andorexacttitleabs=and&search\\_tab=articles&tocsectionid=Original+Articles&tocsectionid=Special+Reports&tocsectionid=Special+Articles&tocsectionid=Videos+in+Clinical+Medicine&tocsectionid=Clinical+PracticeAORBClinical+Therapeutics&tocsectionid=Review+ArticlesAORBClinical+Practice](http://content.nejm.org/cgi/content/full/338/9/613?andorexacttitleabs=and&search_tab=articles&tocsectionid=Original+Articles&tocsectionid=Special+Reports&tocsectionid=Special+Articles&tocsectionid=Videos+in+Clinical+Medicine&tocsectionid=Clinical+PracticeAORBClinical+Therapeutics&tocsectionid=Review+ArticlesAORBClinical+Practice)

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3. The Leukemia and Lymphoma Society Web site. Available at [http://www.leukemia-lymphoma.org/all\\_mat\\_toc.adp?item\\_id=9955](http://www.leukemia-lymphoma.org/all_mat_toc.adp?item_id=9955). Accessed March 31, 2007.

4. MedlinePlus Web site. Medical Encyclopedia. Available at <http://www.nlm.nih.gov/medlineplus/ency/article/000589.htm>. Accessed March 31, 2007.

5. National Heart Lung and Blood Institute Web site. Diseases and Conditions. Available at [http://www.nhlbi.nih.gov/health/dci/Diseases/poly/poly\\_what.html](http://www.nhlbi.nih.gov/health/dci/Diseases/poly/poly_what.html). Accessed April 16, 2007.