



Patient Guide to The Philadelphia Chromosome Negative Myeloproliferative Disorders

- **Essential Thrombocythemia (ET)**
- **Polycythemia Vera (PV)**
- **Chronic Idiopathic Myelofibrosis (MF)**

MPD
FOUNDATION

Searching for a cure for Myeloproliferative Disorders
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What are myeloproliferative disorders?

The Philadelphia Chromosome Negative Myeloproliferative disorders (MPDs) are a closely related group of hematological malignancies in which the bone marrow cells that produce the body's blood cells develop and function abnormally. The disorders are progressive blood cancers that can strike anyone at any age, and for which there is no known cure.

They include Essential Thrombocythemia (ET), Polycythemia Vera (PV) and Chronic Idiopathic Myelofibrosis (MF). An MPD is featured by the proliferation of one, two or three hematopoietic cell lineages.

Until recently, these MPDs have been considered rare or orphan diseases with the prevalence of MPDs estimated at 1-2 per 100,000. Studies currently underway suggest a much higher prevalence.

What causes MPDs?

In MPDs, the stem cell in the bone marrow that is capable of producing all blood cell lines is abnormal and overproduces (proliferates) certain types of blood cells. Thus, the marrow becomes unable to keep the blood elements in proper balance. The exact cause of the abnormality is not known. In March 2005, researchers found that a single somatic mutation in the protein tyrosine kinase JAK2 appears responsible for many of the features of PV, ET and MF. The research also suggests the diseases are acquired rather than inherited.

This finding promises to impact the diagnosis and treatment of patients with these disorders and to spur additional research into the origins of dysregulated cell growth and function.



How are they diagnosed?

Diagnostic tests for these disorders include complete blood counts (CBC,) blood analysis, red blood cell mass studies, bone marrow biopsies (BMB,) cytogenetic studies, and ultrasound or CT scan to detect an enlarged spleen or liver. MF is characterized by bone marrow failure evidenced by falling blood counts and the amount of fibrosis (scarring) in the marrow. With the recent JAK2 discovery, the diagnostic process is expected to be simplified. Your doctor will order the tests he/she feels are necessary to adequately diagnosis a Ph negative myeloproliferative disorder.

Essential Thrombocythemia (ET)

Primary or Essential Thrombocythemia is a chronic myeloproliferative disorder characterized by an increased number of circulating platelets. This disorder is characterized by profound marrow megakaryocyte hyperplasia, splenomegaly and a clinical course punctuated by hemorrhagic or thrombotic episodes or both. Essential Thrombocythemia is a clinically heterogeneous disorder with up to two-thirds of patients being asymptomatic at presentation. Most patients present with symptoms related to small or large vessel thrombosis or minor bleeding. Clots in the small arteries of the toes and fingers are common leading to digital pain enhanced by warmth, distal gangrene and classic erythromelalgia. The incidence of thrombotic

and bleeding episodes is minimized but not eliminated with reduction of the platelet count to normal. Relatively rarely, primary thrombocythemia may evolve into acute leukemia or myelofibrosis. Usually patients with ET, if appropriately treated, live close to a normal life span.

The decision to use platelet lowering agents depends on a variety of risk factors including platelet count, history of bleeding or thrombosis, vascular risk, and severity of symptoms. Current treatment options include low dose aspirin, or platelet lowering agents such as anagrelide, interferon or hydroxyurea. The choice of treatment is based on a variety of risk factors including age, history of thrombotic events and drug tolerance.

Polycythemia Vera (PV)

Polycythemia Vera is a chronic progressive myeloproliferative disorder characterized by an elevated hematocrit, an increase in the red cell mass, and usually by an elevated leukocyte count, an elevated platelet count and an enlarged spleen. Polycythemia Vera differs from many other hematological malignancies in that prolonged survival is enjoyed by most patients if excessive production of red blood cells and platelets can be controlled. The clinical course can be characterized by episodes of thromboses, bleeding and excessive itching after exposure to water. Prolonged survival can be interrupted by the development of other syndromes including myelofibrosis and acute leukemia. The most common cause of morbidity and mortality is the predisposition of polycythemia vera patients to develop life threatening arterial (heart attacks, strokes, intestinal gangrene) and venous (thromboses of the portal and /or hepatic veins, pulmonary embolism) thromboses.

Treatment to return hematocrit to normal values is associated with a reduction of the number of throm-

botic events. Treatment options include: phlebotomy with low dose aspirin or myelosuppressive therapy. Maintaining a hematacrit below .45 and .42 for men and women respectively, along with low dose aspirin, is currently accepted as a nonleukemogenic approach and first choice treatment in newly diagnosed low risk PV patients. Current myelosuppressive options include hydroxyurea, inteferon or anagrelide. The choice of treatment is based on a variety of risk factors including age, history of thrombotic events and drug tolerance.

Chronic Idiopathic Myelofibrosis (MF)

Chronic Idiopathic Myelofibrosis (MF) is a chronic malignant hematological disorder characterized by an enlarged spleen, varying degrees of anemia and low platelet counts, red cells in the peripheral blood that resemble tear drops, the appearance of small numbers of immature nucleated red cells and white cells in the blood, varying degrees of fibrosis of the marrow cavity (myelofibrosis) and the presence of marrow cells outside the marrow cavity (extramedullary hematopoiesis or myeloid metaplasia). The syndrome ultimately leads to marrow failure characterized by severe anemia and frequently low platelet counts. Nonspecific symptoms include fatigue, weight loss and night sweats. Symptoms due to an enlarging spleen are also common as the disease progresses. Optimal care is at present supportive and palliative but new strategies including stem cell transplantation show promise.

Current treatment is directed at alleviation of constitutional symptoms, anemia and symptomatic splenomegaly. Treatment options include hydroxyurea, inteferon, thalidomide with prednisone, and oxymethalone. Other drugs are currently being tested. Depending on risk factors and disease progression, high dose chemotherapy and allogeneic stem cell transplant may be an option. Removal of the spleen may lead to resolution of pain and improvement of anemia.

About the MPD Foundation

The MPD Foundation is a not-for-profit organization whose primary mission is to fund original medical research for Myeloproliferative Disorders.

The MPD Foundation supports innovative efforts to advance scientific understanding of the causes and potential treatments for Ph negative MPDs.

The Foundation's esteemed Medical Advisory Board utilizes a rigorous selection process to ensure donations are allocated to the most innovative research projects. The medical advisory board includes highly regarded physicians from Mayo, Scripps, Harvard, Baylor and University of Illinois at Chicago.

The MPD Foundation produces several newsletters a year informing patients on key advances in MPD research, news from MPD conferences and progress with MPD Foundation supported grants. To register for our (free) newsletter, visit our website at **www.mpdfoundation.org**.

Where to get more information

The MPD Foundation website contains more information about the diseases, treatments available, links to informative articles and websites, and research grant awards.

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We would like to thank Dr. Ron Hoffman for preparing the information in this brochure.

Yes, I would like to receive periodic MPD Foundation newsletters with timely Myeloproliferative Disorder news.

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