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TREATMENT UPDATE

Polycythemia Vera

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TREATMENT UPDATE

Polycythemia Vera

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New strategies and new knowledge continue to improve treatment.

Polycythemia vera (PV) is a rare, chronic (long-term) disease in which the bone marrow overproduces red blood cells and, in many cases, white blood cells and platelets as well. Red blood cells carry oxygen throughout the body, white blood cells fight infection and platelets are involved in clotting the blood to stop or slow bleeding and help heal wounds.

When too many red blood cells circulate, the blood thickens and may not flow properly through the blood vessels. This raises the risk of blood clots in major arteries and veins, which can lead to a stroke or heart attack. These clots can affect other vital organs as well. Smaller blood vessels also can be blocked by clots and lead to symptoms such as headache;

changes in vision; lightheadedness; and numbness, burning, redness and swelling of the hands.

Because PV is characterized by uncontrolled cell growth, it is considered a blood cancer. It is usually a long-term illness, and it can change into myelofibrosis—scarring of the bone marrow—and acute myeloid leukemia. The spleen may enlarge when extra blood cells collect in that organ. (The spleen filters the blood, stores blood cells and destroys old blood cells.)

PV must be carefully and routinely monitored by a hematologist/oncologist. These doctors specialize in diagnosing and treating blood disorders and blood cancers.

Because many PV symptoms could be caused by other medical conditions, it's important that doctors correctly diagnose PV. They do this by examining the blood and bone marrow to count the numbers of different blood cells and determine the level of erythropoietin, a hormone that stimulates the production of new red blood cells. A blood test also is used to determine whether certain gene mutations (changes) are present. About 95 percent of people with PV have a gene mutation called JAK2 V617F. Up to four percent of patients have a different type of JAK2 mutation (JAK2 exon 12). Usually, people are not born with these mutations; the gene changes typically occur in adulthood, for unknown reasons. A JAK2 mutation is a kind of switch that turns on and stays on, sending a constant signal to the bone marrow to produce blood cells.

Through research in clinical trials, treatment of PV keeps improving. In this booklet, we'll discuss the important parts of a treatment plan, new treatments being studied and tips for coping with symptoms. We'll also review some frequently asked questions about PV and highlight the resources available to you through Cancer*Care*® and other organizations.

Treatment

The goal of treating PV is to control symptoms, lower the number of blood cells and reduce the thickness of the blood. That's important because blood with normal thickness flows better and is less likely to cause blood clots. Blood with normal thickness also ensures that the body gets enough oxygen.

Current Treatments

A number of treatments are used to control PV symptoms:

Low-dose aspirin. In the 1960s, clinical trials showed that a single low-dose (81 milligrams, or mg) of aspirin daily helps reduce the risk of blood clots and stroke. Not only is low-dose aspirin beneficial for heart disease, it also can help people with PV. Taking low-dose aspirin is one of the first steps doctors advise when creating a treatment plan for people with PV.

Hydroxyurea (Hydrea and others) and busulfan (Myleran). These medicines are usually used to treat cancer. They can reduce the number of red blood cells, white blood cells and platelets, which helps improve blood flow and reduce the thickness of the blood.

Interferon alfa (Intron A, Roferon-A). Interferon alfa prompts the immune system to tamp down overactive bone marrow cells. This lowers the red blood cell count and keeps the blood thickness and blood flow closer to normal.

Phlebotomy *(fle-BOT-o-me).* This procedure removes some blood from the body to reduce the volume of circulating blood cells so that blood can flow and function correctly. A needle is inserted into a vein in a process similar to donating blood. Usually a pint of blood is removed each week until

the hematocrit level approaches normal. (Hematocrit is the measure of how much space red blood cells take up in the blood.) Some people with PV need to have phlebotomy done every few months. For many people, it is the only treatment they will need for years to come.

Radiation (radioactive phosphorus-32). Radiation treatments help subdue overactive bone marrow cells. This also helps lower the red blood cell count. But doctors use radiation rarely and with caution because it can raise the risk of developing leukemia and other blood diseases.

New Treatments

Researchers are learning more about treating PV and are developing new strategies, especially for people whose PV

The Importance of Clinical Trials

All of the advances that have been made in the treatment of polycythemia vera have been the result of clinical trials. These carefully controlled studies are the standard by which we measure the effectiveness of new treatments and their impact on patients' quality of life. Clinical trials also offer an additional treatment option. For these reasons, doctors and researchers urge people with PV to take part in clinical trials.

Your doctor can guide you in making a decision about whether a clinical trial is right for you. Here are a few things you should know about clinical trials:

- People who take part in clinical trials often gain access to (and may be the first to benefit from) new treatments.
- Before you take part in a clinical trial, you will be fully informed about the possible risks and benefits.
- Some studies show that patients get higher quality care simply by taking part in a clinical trial, because most trials require that doctors and nurses watch patients extremely carefully, and this extra attention may be beneficial by itself.
- You can choose to stop taking part in a clinical trial at any time for any reason—you are always in control of your voluntary participation.

cannot be well controlled by standard treatments. One focus of clinical trials is to target the genetic mutations in PV, also called the JAK (or JAK-STAT) pathway. These types of medication may prove to be a more effective way to treat PV for some patients. Here are some of the treatments being studied in clinical trials now:

JAK inhibitors. The U.S. Food and Drug Administration has approved ruxolitinib (Jakafi) for treating myelofibrosis. This oral medication and other JAK inhibitors such a momelotinib and NS-018 are being studied in clinical trials for people who have advanced PV. These drugs work by blocking the JAK-STAT pathway, which leads to production of too many blood cells.

HDAC inhibitors. This relatively new class of drugs has been shown to slow down the overproduction of red blood cells and PV symptoms. Two HDAC inhibitors currently being studied in patients with PV are givinostat and panobinostat.

Peginterferon alfa (Pegasys). In one clinical trial, this long-acting form of interferon is being compared with hydroxyurea in people with newly diagnosed PV to see which is the better treatment to use first. In another clinical trial, researchers are trying to learn whether peginterferon alfa can benefit people whose PV was previously treated but did not respond well.

Coping With Symptoms

It's important for people with PV to keep track of their symptoms. Over time, this is the best way for doctors to know what needs to be done to better manage this long-term illness. By keeping a detailed diary of the nature of your symptoms and how they affect your daily activities, you can make an accurate report to your physician or nurse during your next office visit.

The following list of the most common symptoms includes some practical steps that you can take to cope with them:

Fatigue. Start a gradual exercise program. Walking can improve your strength and energy level and can also improve blood flow, which decreases the risk of blood clots. Exercising and stretching the legs and ankles improves blood circulation.

People who have regular phlebotomy procedures may feel tired and tempted to use iron supplements. But increasing the iron in the blood stimulates the bone marrow to produce more red blood cells, which is not advised.

Gout. Signs of gout include swelling in one or many joints or pain in the big toe. Your doctor can prescribe various medications to control a flare-up of gout; allopurinol (Zyloprim and others) is often prescribed to prevent future attacks. (Allopurinol lowers the amount of uric acid in the blood, which can be raised by increased blood cell production.) It's important to check your feet regularly and report any changes to your doctor.

Itching. To keep your skin from drying out and becoming itchy, lower the temperature of your shower or bath water, especially in the winter. After bathing, pat yourself dry and use lotion to keep your skin moist. Try not to scratch; scratching can damage the skin and increase the risk of infection. Over-the-counter antihistamines like diphenhydramine (Benadryl and others) can help with severe itching. Talk with your doctor before taking any medications to make sure they won't interfere with your treatment. He or she may consider other ways to help with itching if you don't find relief from these simple measures.

Headaches and vision problems; burning, redness or swelling of the hands and feet. Aspirin may help with these symptoms. Your doctor can determine the dosage that is best for you.

Emotional distress. Sometimes, just talking with a sympathetic friend or loved one can help. But you may also benefit from the help of a professional counselor such as an oncology social worker, therapist or psychiatrist.

These are just some of the symptoms you may want to discuss with your health care team during routine visits. But there are other symptoms that you should report to your doctor immediately. They may suggest a disturbance in a blood vessel such as a blood clot or a change in your PV:

- Persistent changes in vision or difficulty with speech
- Weakness or numbness on one side of the body
- Chest discomfort or difficulty breathing
- Severe pain or swelling in the stomach
- Swelling, tightness or redness in a limb, particularly the leg
- Change in color of the fingers or toes
- Bleeding or blood in the stool
- Unintended weight loss

- New fevers or drenching sweats that prompt you to change sheets or pajamas
- Pain in the area of your spleen (below the ribs on the left side of the body)
- Feeling full before finishing a meal or needing to eat smaller meals
- Symptoms of severe anemia such as lightheadedness or an increase in fatigue

If you experience side effects from medication, it's also important to alert your doctor. For example, some people taking hydroxyurea develop ulcers in their ankles. If this happens, your doctor may want you to stop using this medication. Interferon can also cause side effects such as mood changes, rash, joint pain or changes in vision or the thyroid, for example. Aspirin can irritate the lining of the stomach.

It's important to focus on your overall health, which will affect your PV:

Exercise and eat a healthy diet to maintain your weight. In general, the guidelines for people with PV are the same as for everyone else: eat a lower fat diet in sensible portions and plenty of fruits, vegetables, grains and legumes.

Drink plenty of fluids. Especially in warm weather, it's important to stay well hydrated to keep your blood from thickening. Plain water, non-alcoholic drinks and sugar-free beverages are among the best choices. Try to drink six to eight eight-ounce glasses of fluids each day. It's fine to sip them slowly throughout the day. Part of your daily water intake can come from foods. Fruits and vegetables that have a high percentage of water include cucumber, celery, iceberg lettuce, broccoli, spinach, watermelon, strawberries and cantaloupe.

Your Support Team

When you are diagnosed with PV, you're faced with a series of choices that will have a major effect on your life. Your health care team, family members and friends will likely be an invaluable source of support at this time. You can also turn to these resources:

Oncology social workers provide emotional support for people with cancer and their loved ones. These professionals can help you cope with the challenges of a cancer diagnosis and guide you to resources. Cancer*Care*® offers free counseling from professional oncology social workers who understand the challenges faced by people with cancer and their caregivers. We can work with you one-on-one to develop strategies for coping with treatment and its side effects.

Oncology social workers can also help you communicate with your doctor and other members of your medical care team about the health care issues that are important to you.

Support groups provide a caring environment in which you can share your concerns with others in similar circumstances. Support group members come together to help one another, providing insights and suggestions on ways to cope. At Cancer*Care,* people with PV and their families can participate in support groups in person, online or on the telephone.

Financial help is offered by a number of organizations to help with cancer-related expenses such as transportation to treatment, child care or home care.

To learn more about how Cancer*Care* helps, call us at 800-813-HOPE (4673) or visit www.cancercare.org.

Stay active. Find an activity such as walking or biking that you like to do. Talk to your doctor about the kinds of activities that would be best for you. Yoga or dancing may be enjoyable as well as beneficial for you.

Stay up-to-date on screenings for breast, cervical and colon cancers. Men should discuss the value of prostate cancer screening with their primary doctor.

Avoid tobacco products. Smoking can cause the blood vessels to narrow, increasing the risk of heart attack or stroke due to blood clots. Smoking also can lead to lung and many other cancers, as well as the chronic lung disease emphysema.

Protect yourself from the sun. Exposure to ultraviolet rays (UVA and UVB) from the sun, tanning beds and sun lamps can damage your skin. Avoid the sun during the peak hours of 10 a.m. to 4 p.m. and use sunscreen with an SPF (sun protection

factor) of 30 or higher. Be sure to apply it at least 30 minutes before sun exposure, and reapply it every two hours, sooner if you've been swimming or are perspiring heavily. When you are outdoors, wear protective clothing, a broad-brimmed hat and UV-blocking sunglasses.

Maintain a normal blood pressure, cholesterol level and blood sugar level. Taking these steps will also reduce your risk of heart disease and stroke.

Take extra care of your hands and feet. People with PV who have poor circulation may be more prone to injuries from cold and heat. Wear warm gloves, socks and shoes during the winter months. Avoid hot tubs and heated whirlpools.

Guard against physical trauma. Because of the increased risk of bleeding and clotting, doctors caution people with PV to avoid high-risk situations that could lead to injury. If you are injured, seek treatment right away. Tell the person treating you that you have PV.

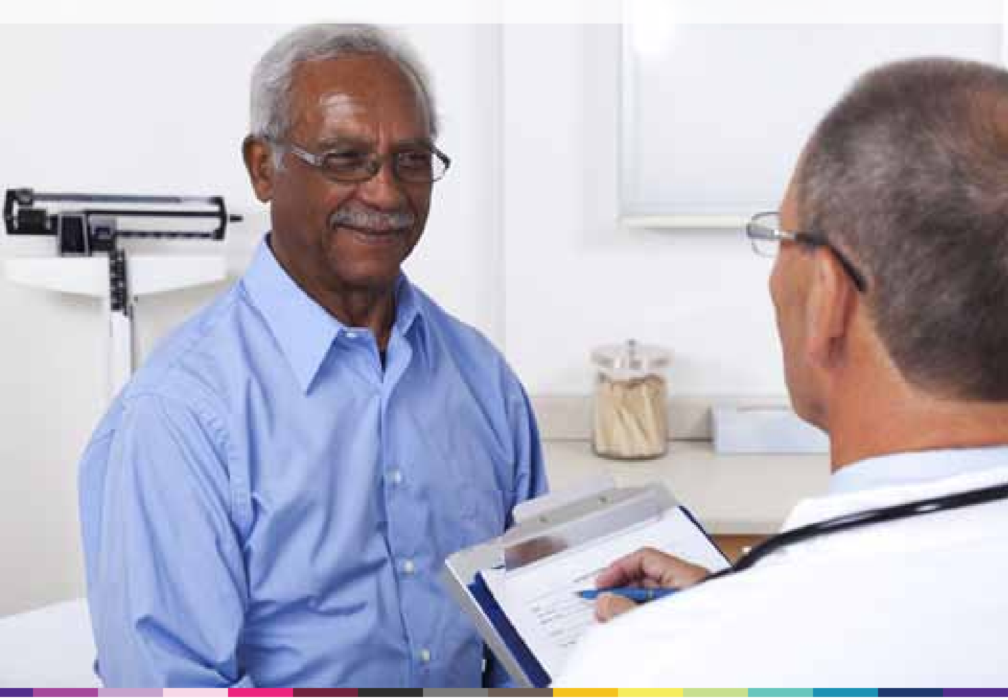
Stay in close touch with your health care team. Your doctor has created a detailed treatment plan that will allow you to live a healthier and more productive life. To maintain your health, you need to report to your health care team any new symptoms you are feeling as well as any other medications you are taking—whether those drugs are bought over-the-counter or were prescribed by another doctor for a different medical condition.

Stick with your treatment plan. Be sure to keep all your appointments for blood tests, doctor's visits and treatments such as phlebotomy or interferon injections. Adhering to the plan is the best way to improve your health and quality of life.

Frequently Asked Questions

Q. What is the role of phlebotomy, and is it a safe procedure?

A. The purpose of phlebotomy is to lower the red blood cell count and the amount of iron in the blood. It is very safe and is an important part of PV treatment. But phlebotomy can cause some side effects that vary from person to person. For example, some patients feel much better after the procedure, and others feel more fatigued. Some patients experience changes in their nails and hair due to low iron levels. Some people cannot tolerate the procedure, and others find it relatively painless. If you are receiving this



treatment and have any side effects that concern you, talk with your doctor. He or she may be able to change strategies or medications to improve your quality of life.

Q. What is the latest research on the most effective medication for the first treatment of PV?

A. Now underway is a clinical trial specifically for people who have been recently diagnosed with PV. Researchers are comparing the standard drug hydroxyurea to peginterferon alfa-2a as a first treatment. They want to find out how these two medications compare in terms of controlling the blood cell count and affecting quality of life. They also want to know which drug might be better at changing the bone marrow and controlling the number of cells with the JAK mutation. It's vital to find the answers to these and other questions about PV, which is why doctors encourage people with PV to consider taking part in clinical trials.

Q. If the spleen is enlarged or causing discomfort, should it be removed? Are there other options?

A. Doctors try to avoid removing the spleen. Usually they recommend using medications first. If the spleen enlarges, doctors may prescribe hydroxyurea and gradually increase the dose. Pegylated interferon is another option that is being used more often.

Resources

Cancer*Care*®
800-813-HOPE (4673)
www.cancercare.org

American Cancer Society
800-227-2345
www.cancer.org

Cancer.Net
Patient information from the American Society of Clinical Oncology
888-651-3038
www.cancer.net

Cancer Support Community
888-793-9355
www.cancersupportcommunity.org

Leukemia & Lymphoma Society
800-955-4572
www.lls.org

MPN Education Foundation
www.mpninfo.org

MPN Research Foundation
312-683-7249
www.mpnresearchfoundation.org

National Cancer Institute
800-422-6237
www.cancer.gov

CLINICAL TRIALS WEBSITES

Coalition of Cancer Cooperative Groups
877-227-8451
www.CancerTrialsHelp.org

EmergingMed
877-601-8601
www.emergingmed.com

National Cancer Institute
800-422-6237
www.cancer.gov/clinicaltrials

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