Polycythemia vera (PV) is the only known primary acquired polycythemia (Pearson, 2001). This chronic myeloproliferative disorder is characterized by the insidious onset of erythroid proliferation (erythrocytosis) and secondary platelet proliferation. PV can progress from a proliferative stage to a metastatic phase and develop into a malignant phase (Gilbert, 2003). If the excessive proliferation of erythrocytes or platelets is controlled, patients can live for prolonged periods of time with this chronic disorder. However, the clinical course of PV can be complicated by a variety of events, such as bleeding, thrombosis, weakness, weight loss, and neurologic impairment. Life-threatening consequences of disease progression, including myelofibrosis or acute leukemia, also may occur (Hoffman, 1995). PV is a rare disorder with an incidence of 2.3 per 100,000 and occurs more frequently in men (Tefferi, 2001). Although rarely seen in individuals younger than age 40, the disorder can occur in children and young adults (Hoffman & Boswell, 1995). The disease develops slowly, usually after age 50–60. Risk factors are unknown, but the incidence is highest among people of eastern European Jewish ancestry (Lynch, 2000). Unfortunately, PV prevention is unknown.

Signs and Symptoms

The evolution of PV begins with an asymptomatic phase that can include the clinical findings of splenomegaly, erythrocytosis, and thrombocytosis (Bilgrami & Greenberg, 1995). Patients begin to exhibit symptoms during the erythrocytotic phase secondary to the excessive proliferation of red blood cells and platelets (Hoffman & Boswell, 1995). Symptoms may include pruritus (especially after a hot bath), headache, weakness, dyspnea, visual disturbances, paraesthesias, and epigastric complaints (Knoop, 1996). In a study conducted by Merup et al. (2002), the most frequently reported pretreatment symptoms were fatigue, headache, and muscle pain. Figure 1 lists the clinical and pathologic criteria for diagnosing PV.

PV can progress to an inactive phase in which patients may not require phlebotomy or chemotherapy for a period of time. Postpolycythemic myeloid metaplasia (PPMM) follows the inactive phase, which is characterized by splenomegaly, anemia, thrombocytopenia or thrombocytosis, and systemic symptoms such as fever and weight loss (Rosenthal & Murphy, 1995). Treatment of patients in the PPMM phase can include steroids, myelosuppressive agents, or splenectomy. Supportive measures also may require transfusion of packed red blood cells and platelets (Berlin, 2002). Myelofibrosis associated with the PPMM phase and myelosuppressive therapy may cause patients to develop acute myeloid leukemia or acute promyelocytic leukemia (Kajiguchi, Simokawa, Saito, & Takeyama, 2000). However, the risk of leukemic transformation is considered low (i.e., less than 5%) (Fenaux et al., 1990).

Treatment

Treatment of PV must be individualized according to age, gender, clinical status, disease manifestations, and hematologic findings (Spivak, 2002). Phlebotomy is integral to the management of PV. In a study conducted by Merup et al. (2002), the most frequently reported pretreatment symptoms were fatigue, headache, and muscle pain. Figure 1 lists the clinical and pathologic criteria for diagnosing PV.
therapy and may be the only treatment needed. This initial therapy commonly is administered to patients younger than age 50 and at lower risk for thrombosis (Gilbert, 2001). Initially, 450–500 mL of blood are removed every two to four days until the hematocrit level is 42%–47%. The frequency of phlebotomy can vary based on the rate of red blood cell regeneration but can be required every two to three months (Lynch, 2000). Acute changes in blood volume after phlebotomy may cause weakness and headache. Patients should be instructed to increase fluid intake the day prior to and for two days after the procedure. Thrombotic episodes may occur secondary to a high platelet count induced by phlebotomy; therefore, aspirin can be used to lower platelet levels (Gilbert, 2001). Iron deficiency is associated with phlebotomy and cannot be treated by supplementation because it increases the phlebotomy requirement by raising hematocrit and red blood cell mass (Fruchtman & Berk, 1995). Phlebotomies should be performed cautiously in elderly patients and those with cardiac or cerebrovascular disease. Phlebotomy reduces the overall volume of blood in the vessels and can lead to hypotension, mild vasovagal reactions, angina, and cardiac arrest.

Risks associated with pregnancy for women with PV include hypertension, perinatal death, and placental infarction. Pregnant women with PV should be monitored closely by a hematologist because of increased maternal blood volume, and they may require empirical treatment with phlebotomy, low-molecular-weight heparin, and low-dose aspirin (Subtil, Deruelle, Trillot, & Jude, 2001).

Phlebotomy is the preferred treatment for women of childbearing age because of myelo-suppressive agents that cause infertility and are unsafe for use during pregnancy (Tefferi, Solberg, & Silverstein, 2000). Biologic response modifiers such as interferon alfa have an unknown pregnancy safety profile (Altman, 2002).

Myelosuppressive therapy, including alkylating agents (busulfan, chlorambucil), nonalkylating agents (hydroxyurea), and radioactive phosphorus, also are used in the treatment of PV. Busulfan and chlorambucil can produce long-lasting depression of the bone marrow and increase the risk of leukemic transformation (Gilbert, 2001). As a result, the PV study group did not recommend chlorambucil (Berk et al., 1986). Patients who have experienced a previous thrombotic event, require frequent phlebotomies (more than once every two months), and have poorly controlled systemic syndromes (pruritis, weight loss) may benefit from myelosuppressive treatment (Lynch, 2000).

Treatment with radioactive phosphorus can be considered for patients older than age 70 who have not responded to other standard modalities, such as hydroxyurea. This treatment is convenient and given initially as one IV dose, which requires minimal patient compliance and monitoring (Berlin, 2000). Radioactive phosphorus is considered leukemogenic and is not recommended for long-term use. Hydroxyurea is the most common nonalkylating myelosuppressive agent used to treat PV. Given orally at a dose of 500 mg twice to three times daily, the short duration of hydroxyurea’s suppressive effect requires continuous therapy (Tefferi et al., 2000). Patients must have their blood counts monitored every two to four weeks for the dose-related side effects of thrombocytopenia and leukopenia (Knoop, 1996).

Interferon alfa, a biologic response modifier, also has been used to treat patients with PV who have not responded to myelosuppressive treatments. In addition, this therapy has been combined with others, such as phlebotomy and aspirin (Silver, 2002). Interferon alfa is indicated particularly for patients with myeloid metaplasia with splenomegaly (Gilbert, 2003). In usual dosing regimens, three to five million units are administered subcutaneously three to five days per week. Flu-like symptoms, fatigue, anorexia, and weight loss commonly occur (Tefferi et al., 2000).

Low-dose aspirin therapy (30–75 mg per day) has been combined with treatments such as interferon alfa and phlebotomy (Tefferi et al., 2000). Aspirin has antithrombotic effects through platelet aggregation inhibition and has been shown to be safe and effective in alleviating microvascular symptoms associated with PV, including headaches and erythromelalgia (i.e., paroxysmal throbbing and burning pain in the skin affecting one or both legs, feet, or hands) (Tefferi, 2003). Possible side effects include gastrointestinal toxicity and bleeding; however, these toxicities generally occur in patients receiving higher doses (Berk et al., 1986).

In younger patients, the safest and most effective combination treatment appears to be anagrelide plus interferon alfa; in older patients, anagrelide plus hydroxyurea is most effective. Hydroxyurea is used sparingly in younger patients because of the long-term increased risk of mutagenicity and leukemia (Gilbert, 2003). Anagrelide, which acts on the mature megakaryocyte to prevent platelet budding, requires individualized dosing. The adult dose is 0.5 mg four times daily or 1 mg twice daily for 7–10 days. The dosage then is adjusted in accordance with the patient’s platelet count. Anagrelide is provided in capsule form and must be taken on an empty stomach. Sucralfate interferes with absorption of anagrelide and should not be taken concurrently (Gilbert, 2003; Physicians’ Desk Reference, 2003).

In an anecdotal report, two patients with PV who were unable to tolerate either hydroxyurea or interferon alpha responded clinically to imatinib mesylate. The responses were attributed to the drug’s inhibitory effect on tyrosine kinase activity (Jones & Dickin- son, 2003).

Another newer treatment modality used to manage PV is hematopoietic stem cell transplantation (HSCT). The indications to perform HSCTs in 12 patients with PV were myelofibrosis with splenomegaly or the development of myelodysplastic syndrome or acute myeloid leukemia. Three-year survival was reported at 64% (Platzbecker et al., 2002).

**Nursing Care**

The chronic and unpredictable nature of PV combined with distressing associated symptoms often negatively impacts patients’ quality of life (Hoffman, 2002). Nurses play an important role in enhancing quality of life through the development of plans of care that empower patients and encourage self-care. Patients should receive education regarding the disease process, side effects, toxicities of current treatment regimens, and signs and symptoms of thrombosis and bleeding. Patients, physicians, and nurses should work in a collaboration to ensure compliance with therapy and observation.

Pruritus affects approximately 50% of pa-
tients with PV (Diehn & Tefferi, 2001); even when the underlying disease is controlled adequately, 20% of patients with PV continue to experience the symptom (Hernandez-Nunez, Dauden, Cordoba, Aragues, & Garcia-Diez, 2001). Pruritus can be an agonizing aspect of the PV disease continuum, depriving patients of restful sleep and interrupting social and physical activities. Ichthyosis generally occurs after bathing in hot water and vigorously using a towel on the skin (Knoop, 1996). Patients should be instructed to take tepid showers and dry the skin gently. Sodium bicarbonate dissolved in a lukewarm bath may improve pruritus. However, topical treatments and nonpharmacologic measures can be of limited value compared to systemic treatment with antihistamines, cimetidine, cyproheptadine, cholestyramine, antidepres-
sants, oral opioid antagonists, and myelo-
suppressive therapy (Casciato, 2000; Krajnik & Zylicz, 2001). Although these treatments may alleviate pruritis, many patients do not experience prolonged symptom relief.

Thrombosis is the most common cause of death in patients with PV (Bilgrami & Greenberg, 1995). Thrombosis is present in 20%–50% of patients with PV at the time of diagnosis and may involve major vessels and microvasculature (Pearson, 2002). Patients who are aged 60 or older or who have a history of thrombosis are at risk for these blood clots. Smoking and obesity also have been implicated in thrombosis risk (Solberg, 2002).

Thrombocytosis combined with an increased hematocrit level may cause thromboembolic events. Thrombotic complications can include erythromelalgia (vasodilation with burning pain), cerebral thrombosis, deep-vein thrombosis of the extremities, pulmonary embolus, peripheral vascular disease, and coronary thrombosis (Bromdaw, Passweg, Gratwohl, Tichelli, & Skoda, 2000). Thrombotic complications can be prevented by educating patients to avoid tight or restrictive clothing, elevate their legs while sitting or lying in bed, avoid crossing or dangling their legs while sitting, and perform range-of-motion exercises while sitting (Knoop, 1996). Healthcare providers also should educate patients and family members about recognizing possible thrombotic complications. Patients and families should be familiar with the signs and symptoms associated with thrombosis: weakness, headache, dizziness, visual disturbances, fatigue, dyspnea, chest pain, skin temperature or color changes, extremity pain, and extremity edema (Tefferi, et al., 2000).

Hemorrhage in PV is caused by abnormal platelet function and commonly occurs in the gastrointestinal tract, brain, mucocutaneous membranes (e.g., oral bleeding, epistaxis), bladder, and skin (petechiae). Patients need to be instructed to use only electric razors and soft toothbrushes, and patients and family members should be instructed to report any signs of bleeding.

Median survival of patients with PV who receive treatment can exceed 10 years. Patients who receive no treatment have a median survival of approximately 18 months. The most common cause of death is thrombosis, followed by the complication of hemorrhage (Bilgrami & Greenberg, 1995). Phase I and II clinical trials involving stem cell transplantation and tipifan (an enzyme inhibitor) are ongoing (National Cancer Institute, 2003). Although new cytoreductive regimens are being developed increasingly to treat PV, transformation of PV into either myelofibrosis or acute leukemia remains a challenge to manage and treat (Tefferi, 2002).

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References


### Rapid Recap

#### Polycythemia Vera: A Review

- Polycythemia vera (PV), the only known type of primary acquired polycythemia, is characterized by the insidious onset of erythroid proliferation.
- Early signs and symptoms of PV include headache, weakness, dyspnea, fatigue, muscle pain, and pruritus, which is most intense when the skin is submerged in warm water.
- Phlebotomy often is the only treatment needed for PV and usually is required at two- to three-month intervals.
- Myelosuppressive therapies, including the alkylating agent busulfan, the nonalkylating agent hydroxyurea, and radioactive phosphorus, are used to treat PV in addition to biotherapy with interferon alfa.
- Pruritus and thrombosis commonly occur among patients with PV, and thrombotic events are the leading cause of death in patients with PV.
- Patient education and support are integral in helping patients with PV to cope with this unpredictable and chronic disease.