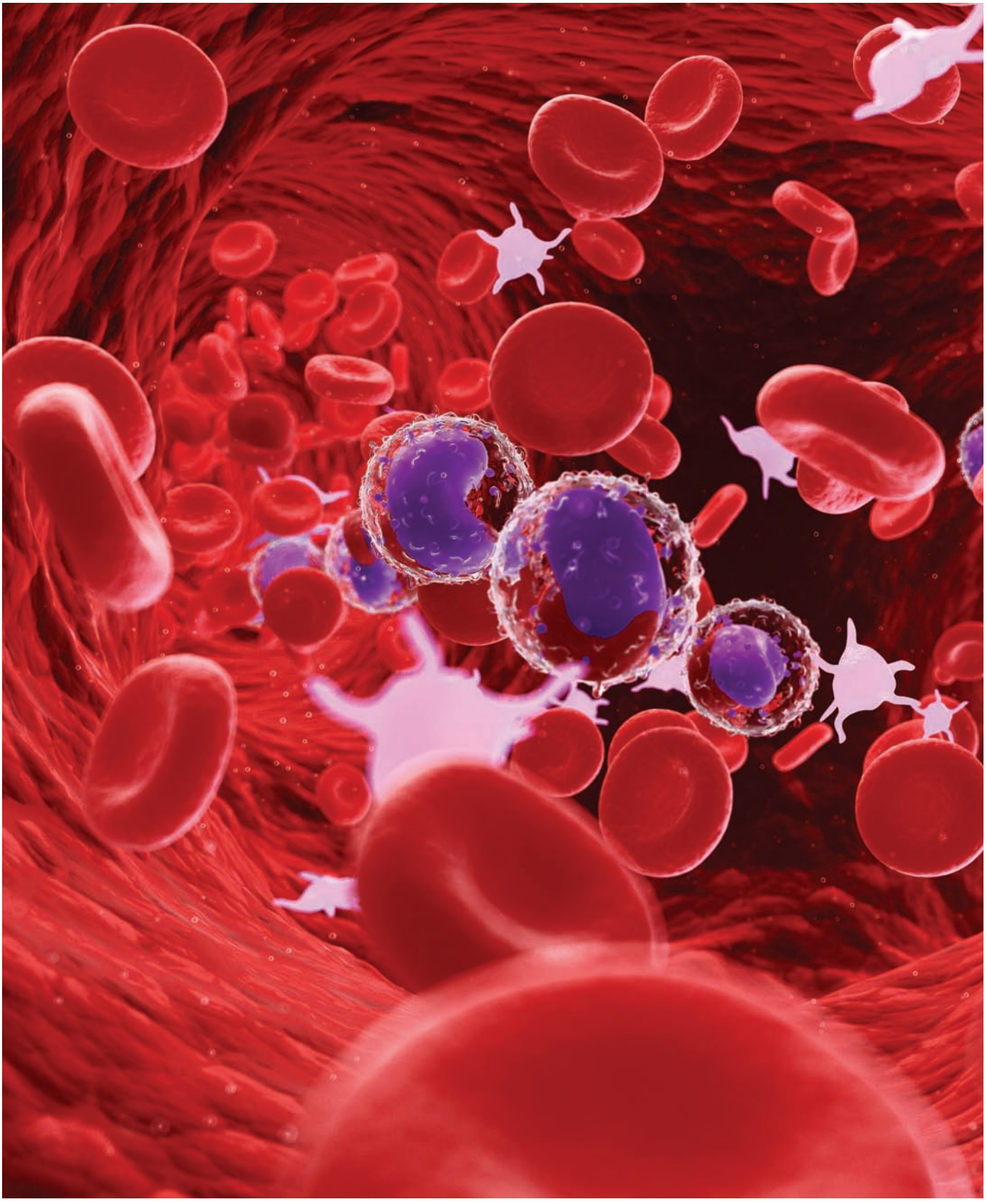

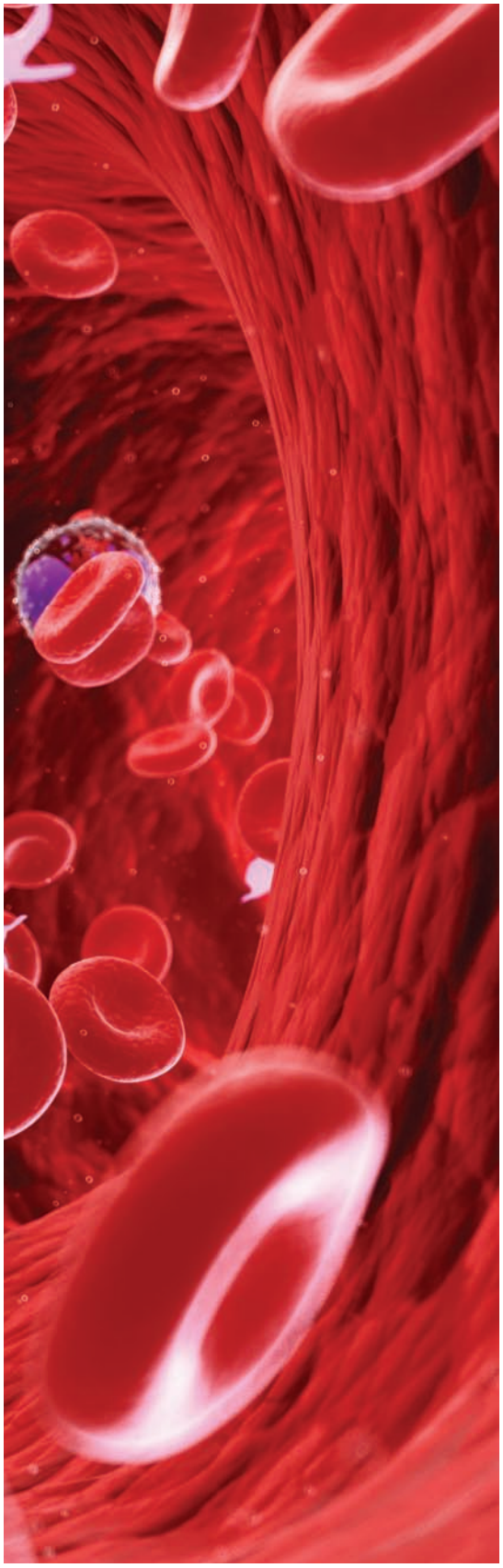

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Three myeloproliferative neoplasms: An overview

BY JILL BRENNAN-COOK, DNP, RN-BC, CNE

Abstract: A group of rare hematologic cancers, myeloproliferative neoplasms (MPNs) evolve when bone marrow dysfunction causes overproduction of one or more blood cell types. This article explores the diagnosis, treatment, and nursing care of patients diagnosed with one of three classic MPNs: essential thrombocythemia, polycythemia vera, and primary myelofibrosis.

Keywords: essential thrombocythemia, ET, HCT, hematologic cancer, hematopoietic cell transplantation, motivational interviewing, MPN, myelofibrosis, myeloproliferative neoplasm, phlebotomy, PMF, polycythemia vera, primary myelofibrosis, PV

SL, 48, HAD BEEN FEELING exhausted for several months but attributed it to the demands of her job and managing a stable single-parent home for her four children. Her health history included hypertension, diabetes, and overweight with a body mass index (BMI) of 29 (normal, 18.5 to 24.9). Her prescribed medications included hydrochlorothiazide and metformin. A routine physical exam revealed abnormal lab values, including a hematocrit of 58% (normal, 34% to 44%). Following a referral to a hematologist, SL underwent a bone marrow biopsy and more lab tests. Her diagnosis: polycythemia vera, one of the chronic myeloproliferative neoplasms (MPNs).

In the US, about 10,000 people are diagnosed with an MPN each year (see *Epidemiology of MPNs*).[1] Although patients with MPNs are largely in the care of hematologist-oncologists, nurses play a significant role in helping them understand and manage their disease and empowering them to advocate for themselves. This article provides an overview of three classic MPNs: essential thrombocythemia (ET), polycythemia vera (PV), and primary myelofibrosis (PMF).[4]

MPN pathophysiology

A group of rare hematologic cancers, MPNs evolve when bone marrow dysfunction causes overproduction of one or more blood cell types.[2] The primary cause is genetic mutations expressed in the bone marrow. The mutually exclusive Janus kinase 2 (JAK2), calreticulin (CALR), and myeloproliferative leukemia (MPL) gene mutations are present in approximately 90% of patients with MPNs.[2] The most common mutation

is JAK2-V617F, which is present in 50% to 60% of patients with ET, 95% of those with PV, and 50% to 60% of those with PMF. Causes of the gene mutations are not fully understood, but they are thought to play a significant role in disease progression.[2]

MPNs are progressive and may evolve over time from ET to PV to MF, or ET to MF, or PV to MF.[3] Chronic MPNs may also evolve into acute leukemia.[1]

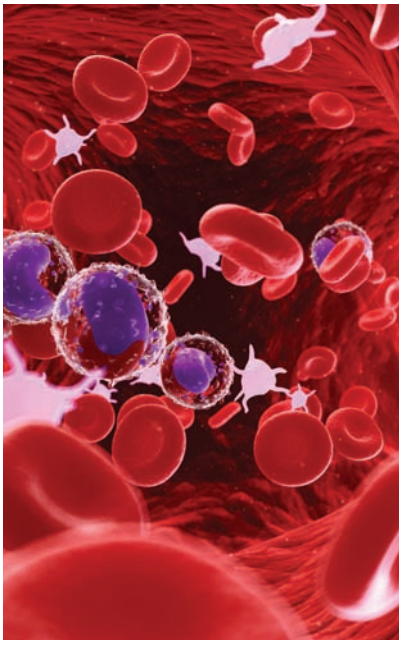
Clinical manifestations

The overproduction of red blood cells (RBCs), white blood cells (WBCs), and/or platelets is characteristic of MPNs. These lead to a wide range of signs, symptoms, complications, and quality-of-life changes.[4] Signs and symptoms are related to the type of blood cell being overproduced and associated inflammatory responses.

All three classic MPNs share certain signs and symptoms such as fatigue and headaches. The most common complications are hemorrhage and thrombosis.[5] Here is a closer look at how these disorders compare.

- In ET, the bone marrow makes too many platelets.[6] Excess platelets increase blood viscosity, raising the risk of thrombosis. Because patients may not experience signs or symptoms related to thrombocytosis, they may be unaware of the diagnosis until they present to their healthcare provider with a thrombotic complication.[5] Other common presenting findings include signs and symptoms of stroke, transient ischemic attack, myocardial ischemia, myocardial infarction, deep vein thrombosis, and pulmonary embolism.[5,7] If increased platelet activation and aggregation occlude small vessels in the brain, patients experience neurologic signs and symptoms such as headaches, ocular migraines, transient visual disturbances, and dizziness.[8]

  ET is more common in women than men.[9] Treatment goals focus on minimizing the risk of thrombosis.[10]



Classic MPNs share certain signs and symptoms such as fatigue and headaches. The most common complications are hemorrhage and thrombosis.

- In PV, the bone marrow makes too many RBCs. Some patients also experience overproduction of WBCs and platelets. Excessive blood cell counts lead to sluggish, thick blood that occludes blood flow through arteries and veins, increasing the risk of complications such as thrombosis and bleeding.[11] Common signs and symptoms include shortness of breath, abdominal pain, paresis or paralysis, pruritus, and chest discomfort.[5,11] PV is more common in men than women.[9] Treatment goals focus on maximizing quality of life, minimizing the risk of bleeding and thrombosis, and lowering hematocrit.[10]
- PMF is associated with bone marrow fibrosis and cytopenias, leading to anemia and thrombocytopenia. PMF is more common in men than in women.[9] Treatment goals focus on reducing signs and symptoms related to cytopenias and slowing disease progression.[12]

Diagnosis and prognosis

ET is a diagnosis of exclusion. PV is diagnosed when an otherwise unexplained increase in hemoglobin, hematocrit, and RBC mass is accompanied by a JAK2 mutation and a decreased erythropoietin level. PMF is characterized by leukoerythroblastic lab findings, splenomegaly, and bone marrow fibrosis that cannot be attributed to another myeloid disorder.[13] In light of the COVID-19 pandemic, patients presenting with deep vein thrombosis, pulmonary embolism, thrombotic stroke, or myocardial infarction should also be evaluated for COVID-19.[14,15]

The World Health Organization (WHO) diagnostic criteria is used as a guide to help the healthcare provider make a diagnosis.[16] For diagnostic findings for each of these MPNs, see *Key diagnostic criteria*.

The prognosis for patients with MPN is variable because each type

Epidemiology of MPNs

Worldwide, the most commonly occurring MPN is ET, followed by PV and PMF.[6] Incidence and prevalence of MPNs vary across countries due to wide-ranging registry data, variable time periods for determining prevalence detection rates, geographical location, and diagnostic and classification changes since 2005.[6] From 2001 to 2012, approximately 31,900 people had been diagnosed with MPNs in the US.[9] Prevalence (per 100,000) of ET is 38 to 57, PV is 44 to 57, and PMF is 4 to 6.[37]

progresses differently and patient comorbidities and age influence outcomes. A study of survival rates among 3,023 Mayo Clinic patients with MPN from 1967 to 2017 showed an average survival of 18 years for ET, 15 years for PV, and 4.4 years for PMF.[17] MPN survival rates increase in patients diagnosed before age 60, but survival for these patients is still below the average US age expectancy.[18]

Management goals

Therapies for patients with MPNs are prescribed to manage signs and symptoms, maintain quality of life, and prevent complications such as thrombotic events and bleeding. Therapies are highly individualized based on the diagnosis, assessment of symptom burden, and prognosis.[13] For example, phlebotomy to reduce RBC mass is the mainstay of PV management, but patients with PMF may require RBC transfusions to manage anemia. Allogeneic hematopoietic cell transplantation (HCT) is the preferred option for some patients with PMF.[19]

Pharmacotherapy for MPNs require close hematologic monitoring with clear provider and patient communication because of the potentially severe adverse reactions associated with some medications. Nurses can ease fears and concerns by helping the patient understand the rationale for prescribed medications and informing them about possible adverse reactions and long-term effects.

Nurses can also educate patients with PV about phlebotomy, which is commonly prescribed to lower hematocrit levels. Phlebotomy needs vary from patient to patient, but provider guidelines suggest maintaining hematocrit at <45% for men and <42% for women.[20,21] Phlebotomy may reduce risks for thrombosis and provide symptomatic relief for pruritus, night sweats, and headaches.[21]

Key diagnostic criteria[10,16]

The WHO specifies these diagnostic criteria for ET, PV, and PMF.

Essential thrombocythemia (ET)

Major criteria

- Platelet count ≥450 × 10^9/L
- Bone marrow biopsy showing proliferation mainly of the megakaryocyte lineage with increased numbers of enlarged, mature megakaryocytes with hyperlobulated nuclei. No significant increase or left shift in neutrophil granulopoiesis or erythropoiesis and very rarely minor (grade 1) increase in reticulin fibers.
- Not meeting WHO criteria for BCR-ABL1+ chronic myeloid leukemia (CML), PV, PMF, myelodysplastic syndromes, or other myeloid neoplasms
- Presence of JAK2, CALR, or MPL mutation

Minor criterion

- Presence of a clonal marker or absence of evidence for reactive thrombocytosis.

Diagnosis of ET requires meeting all four major criteria or the first three major criteria and the minor criterion.

Polycythemia vera (PV)

Major criteria

- Hemoglobin >16.5 g/dL in men
  Hemoglobin >16.0 g/dL in women
  or,
  Hematocrit >49% in men
  Hematocrit >48% in women
  or,
  Increased red cell mass
- Bone marrow biopsy showing hypercellularity for age with trilineage growth (panmyelosis) including prominent erythroid, granulocytic, and megakaryocytic proliferation with pleomorphic, mature megakaryocytes (differences in size)
- Presence of JAK2 V617F or JAK2 exon 12 mutation

Minor criterion

- Subnormal serum erythropoietin level.

Diagnosis of PV requires meeting either all three major criteria, or the first two major criteria and the minor criterion.

Primary myelofibrosis (PMF)

Major criteria

- Presence of megakaryocytic proliferation and atypia, accompanied by either reticulin and/or collagen fibrosis grades 2 or 3
- Not meeting WHO criteria for ET, PV, BCR-ABL1+ CML, myelodysplastic syndromes, or other myeloid neoplasms
- Presence of JAK2, CALR, or MPL mutation or, in the absence of these mutations, presence of another clonal marker, or absence of reactive myelofibrosis

Minor criteria

- Presence of at least one of the following, confirmed in two consecutive determinations:
  - Anemia not attributed to a comorbid condition
  - Leukocytosis ≥11.0 × 10^9/L
  - Palpable splenomegaly
  - Lactate dehydrogenase increased to above upper normal limit of institutional reference range
  - Leukoerythroblastosis.

Diagnosis of overt PMF requires meeting all three major criteria and at least one minor criterion.

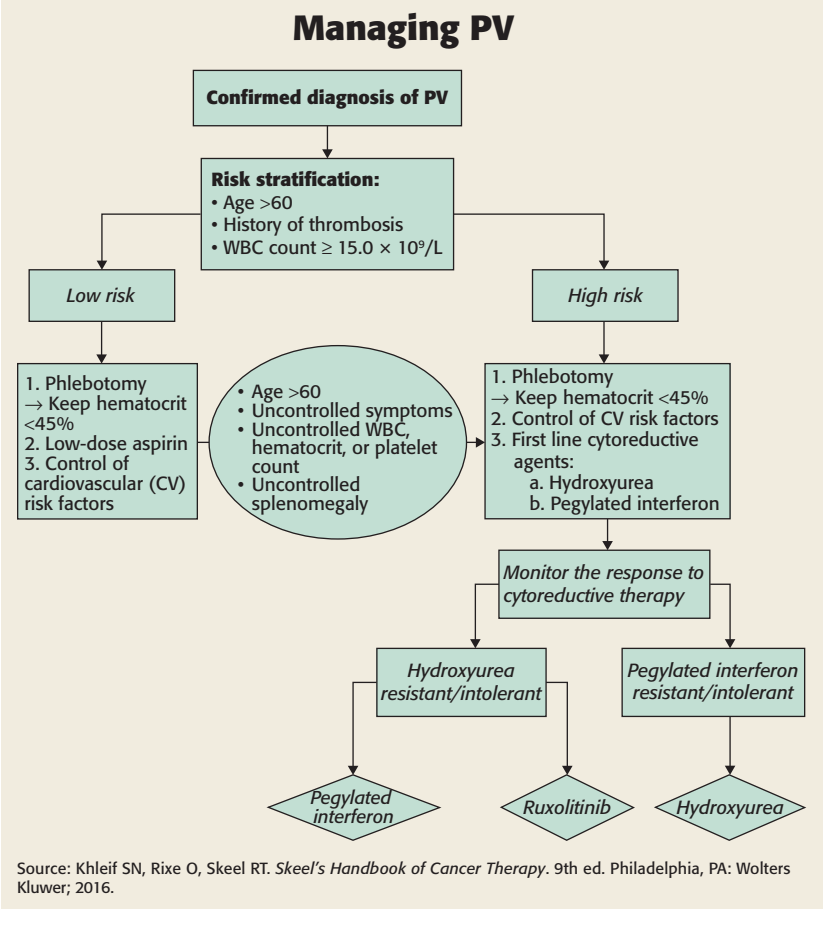
Pharmacotherapy for ET and PV

Medication regimens for ET and PV focus on preventing thrombotic complications (see *Managing PV*). Cytoreductive drugs such as hydroxyurea and pegylated interferon and low-dose aspirin are the most common medications prescribed for patients with either disorder.[10] Aspirin therapy must be adjusted if the patient is scheduled for elective surgery or has an increase in bleeding or continued vasomotor symptoms such as headache, lightheadedness, syncope, atypical chest pain, and transient vision disturbances.[21-23]

Teach patients taking hydroxyurea to report adverse reactions such as leg ulcers, mucocutaneous lesions, gastrointestinal upset, and fever.[21] Hydroxyurea may be discontinued if myeloproliferation is uncontrolled, platelets remain elevated, and/or the patient is experiencing intolerable adverse reactions.

Pegylated interferon may be administered if the patient is intolerant to hydroxyurea, is pregnant, or is a younger patient.[21] Pegylated interferon is administered subcutaneously once a week, and may cause flulike symptoms, fatigue, myalgia, and fever. Instruction on how to self-administer the injection, what expected benefits and potential adverse reactions to anticipate, and when to notify the provider about adverse reactions, are all included in pegylated interferon education.

Ruxolitinib, a JAK2 inhibitor, is an oral medication that can be used for patients with PV who are intolerant to hydroxyurea and interferons. Patients should be educated about adverse reactions to ruxolitinib, including neutropenia, anemia, and thrombocytopenia. Instruct them to report signs and symptoms such as bleeding, excessive fatigue, petechiae, and fever.[21] Warn patients not to adjust the ruxolitinib dose or discontinue the drug without notifying the provider.



Source: Khleif SN, Rixe O, Skeel RT. *Skeel's Handbook of Cancer Therapy*. 9th ed. Philadelphia, PA: Wolters Kluwer; 2016.

Therapies for PMF

Pharmacotherapy with ruxolitinib, fedratinib, or hydroxyurea has not been shown to improve survival in patients with PMF.[23] Lower-risk, asymptomatic patients with PMF may simply be monitored closely initially. Allogeneic HCT may be recommended for patients at higher risk, who generally have a poorer prognosis. Nursing education related to medications for stem cell transplant should be comprehensive due to the complexity and risks of the procedure, such as graft-versus-host disease and treatment-related mortality.[19]

Symptomatic patients who are not candidates for HCT may be encouraged to enter medication clinical trials, and treatment with ruxolitinib, fedratinib, or hydroxyurea may be considered for symptom relief.[12]

Transfusions may be indicated to treat anemia, which is a major cause of symptoms in patients with PMF.[19] Patients receiving chronic transfusions must be monitored for potentially serious complications such as iron overload.

Aligning nursing care with patient goals

Patient risk factors such as older age, history of thrombosis, cardiovascular risk factors, and JAK2V617F mutation are used to help estimate the risks of MPN complications such as bleeding and thrombosis.[10] Mitigating these complications is medically necessary for optimal outcomes. However, nursing management and goals of therapy may become misaligned with the patient's goals if the

nurse and patient do not communicate with one another.

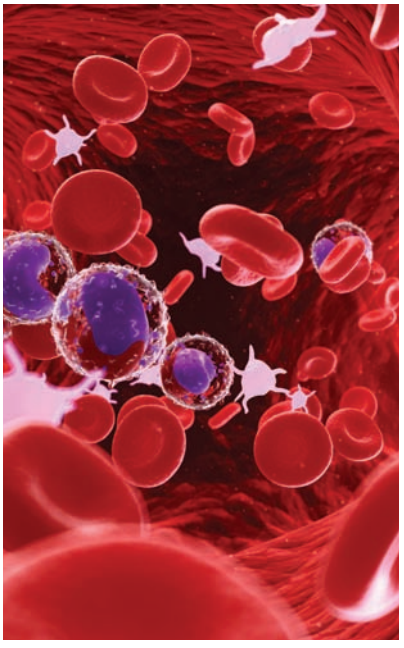
While carefully monitoring blood cell counts and assessing the risk of complications, nurses must also evaluate the patient's readiness to learn about self-care. Healthcare team members are rightly concerned about cardiovascular health, especially thrombosis prevention, but if they do not address patient concerns first, the patient may not "hear" important education about therapies and lifestyle modifications.

A landmark survey on the perceptions of patients with MPN and physicians who treat them found significant differences between provider and patient communication and perceptions. For example, while providers were focused on preventing thrombotic events, patients were more concerned about preventing disease progression.[24] Improved patient education with an accurate evaluation of symptom burden may help align overall treatment goals shared by provider, nurse, and patient.

Patient-centered nursing considerations

MPNs diminish quality of life because many patients experience various burdensome symptoms such as fatigue, headache, night sweats, and insomnia.[4] Nurses play a significant role in helping patients recognize and accept limitations to their activities of daily living, advising them to pace themselves and take rest periods as needed.

Motivational interviewing is an effective style of communication that nurses can use to educate patients about making healthy behavioral changes.[25] With this collaborative approach, nurses encourage patients to express their concerns and articulate their treatment preferences. Once patients understand the risks of their disease, motivational interviewing may help them identify their own goals for wellness and realistic steps they can take to modify behaviors and maintain optimum health.



Cardiovascular health should be addressed at each patient encounter because the risks of thrombotic vascular events with ET and PV are significant.

Patients with MPNs may also feel worried and anxious about their disease. Many experience depression, anger, and difficulty coping with stress.[4] Friends and family may not be fully aware of the patient's fears and anxiety level, especially if the patient appears outwardly healthy. Nurses can actively listen to the patient's concerns, validate fears, and provide emotional support.

After nurses explore concerns and validate the patient's feelings, cardiovascular health should be addressed at each encounter because the risks of thrombotic vascular events with ET and PV are significant.[26] Asking patients about steps they might take to improve their cardiovascular health is essential. Counseling to identify and decrease cardiovascular risk factors such as cessation of smoking, managing diabetes and hypertension, eating a healthy diet, and getting regular exercise are recommendations from clinical practice guidelines for MPNs.[21,27]

Techniques that increase aerobic activity may be considered jointly, with the nurse gently encouraging the patient to make lifestyle modifications to increase activity levels. For example, the patient may plan daily walks or try taking the stairs at work, parking farther away from a store, or scheduling walking breaks throughout the day. These behavior changes are easy and less complicated than embarking on a challenging new exercise routine that might not be sustainable. Small behavior changes help patients feel accountable for their own goals.

Fatigue is the most common symptom reported for all patients with MPNs.[24] Nurses can inform patients that fatigue does not necessarily reflect disease progression.[28] Helping patients accept and manage fatigue may help them to balance their activities and relieve frustration.

Although research that directly addresses fatigue associated with MPNs is limited, physically active persons who have MPNs experience less fatigue, and exercise reduces fatigue. However, while nurses should encourage daily activity and regular exercise, they must also remember that patient fatigue might pose a barrier to increasing activity levels. In addition, it is important for nurses to recognize the chronicity of MPNs, the multifactorial causes of fatigue, and the influence of fatigue on quality of life. No one solution works for all patients.[29]

Being physically active is not the only approach to managing fatigue. For example, smartphone meditation

interventions are easy to use and well accepted by patients as a means to reduce fatigue and relieve feelings of stress and anxiety.[30] Encourage patients to explore options to determine which intervention works best for them.

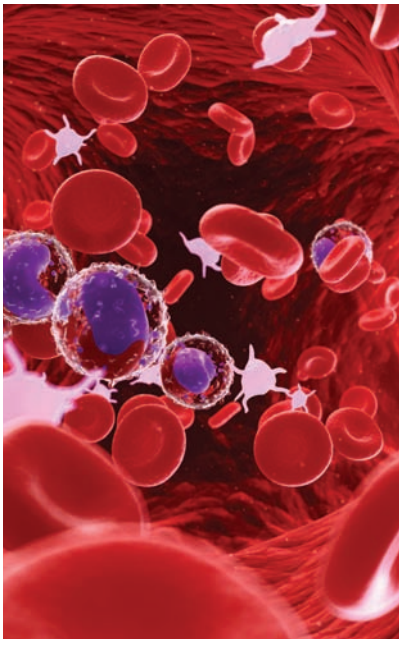
Self-care strategies

Scheduling and pacing activities, using labor-saving devices, setting priorities, and walking are the most beneficial self-care nonpharmacologic strategies used by patients with MPNs.[29] Referrals to physical therapy for an exercise program may provide structure and help the patient meet activity goals.[28] Nursing assessment and patient education should focus on the following:

• ***Lab testing.*** Patients with MPNs are followed closely by hematologists and often require frequent lab tests to monitor their disease. Supporting and educating the patient about routine and frequent lab tests and values may help them to better understand their specific disease and its manifestations. Learning what values are normal for them may lessen their anxiety.

• ***Sleep hygiene***. Many patients with MPNs experience night sweats, pruritus, and altered sleeping habits, which interfere with overall health.[4] Online yoga programs studied in patients with MPNs have demonstrated improved sleep patterns, including improved ease in falling asleep and better quality of sleep.[31,32]

A patient-centered approach involves a review of the patient's sleep hygiene practices. Using motivational interviewing, the nurse can ask the patient to suggest ways to change nightly routines to improve sleep quality. Good sleep hygiene practices include keeping regular bedtime hours, maintaining a restful sleep environment such as a dark and quiet bedroom, and limiting caffeine to mornings only.[28]



Advise patients to keep a water bottle handy. Dehydration complicates a disease in which fluctuations of blood cells and night sweats are common.

Screening for sleep concerns should be done routinely. If sleep hygiene education is unsuccessful, the nurse may need to alert the provider or request a referral to a sleep specialist.[33]

• ***Hydration***. Advise patients to keep a water bottle handy at all times to help maintain hydration, especially during warmer months. Although no available evidence directly supports the importance of maintaining hydration in patients with MPN, dehydration complicates a disease in which fluctuations of blood cells and night sweats are common.

• ***Nutrition***. Patients with MPNs often experience early satiety and abdominal discomfort, impacting nutrition.[4] Asking patients about their current dietary intake is a patient-centered first step to making dietary changes for a healthier lifestyle. No specific nutritional guidelines are recommended for patients with MPNs, but all patients with cancer should be asked about dietary intake and eating habits.[34] Encourage them to maintain a healthy diet that decreases cardiovascular risk factors. General recommendations are to eat a diet that is 50% plant based, avoid foods that are high in calories, and limit alcohol consumption, with the goal of maintaining a normal weight. Referrals to certified specialists in oncology nutrition are recommended.[33]

• ***Pruritus.*** Commonly experienced by patients with MPNs, pruritus is triggered by inflammatory cytokines. It causes severe symptomatic burden and reduces quality of life.[4,35] Currently no specific treatments are available to decrease pruritus.[35] Nurses can support patients by listening to their concerns and advise them on how to best maintain skin integrity with moisturizers and protection from the sun.

• ***Caregiver burden.*** Nurses may also address family caregiving if family members are present. Encouraging the caregiver to take breaks and to care for oneself facilitates caring for the patient. Supportive factors to decrease caregiver burden and improve mental well-being are having family and friends to discuss concerns and to help when needed.[36] Referrals to caregiver support groups and chronic disease support may also be helpful.

Education resources

The MPN Research Foundation website (www.mpnresearchfoundation.org) is dedicated to research for new treatments and patient education for people with these rare hematologic malignancies. It also offers information specific to each of the MPNs. The nurse can review the website with the patient and print patient educational materials specific to the patient's MPN. In addition, the

website offers free online and print newsletters, webinars, and contains patient stories so patients do not feel alone in their journey.

Teaching patients to monitor symptoms and when to notify their hematologist with concerns can help them self-manage their health. Symptom burden should be assessed routinely and patients should be educated on how to use the MPN Symptom Assessment Form Total Symptom Score (MPN-SAF TSS).[21] The MPN-SAF TSS asks patients about their fatigue, early satiety, abdominal pain, pruritus, night sweats, problems with concentration, and bone pain. Inform patients that significant changes in MPN-SAF TSS may indicate changes in disease progression or status.[21]

SL's case progression

Because SL is under age 60 and has no history of thrombosis, she is considered low-risk.[20] Her treatment regimen includes:

- phlebotomy to lower hematocrit levels.
- low-dose aspirin.
- management of cardiovascular risk factors, such as diabetes, hypertension, and excess weight.

Nursing interventions for SL should begin with an assessment of what she knows about her diagnosis and what concerns she may have. The nurse uses motivational interviewing techniques that encourage SL to make positive lifestyle changes, especially related to her fatigue and busy schedule. To ensure that nurse and patient goals are aligned, the nurse engages in active listening about SL's concerns and goals while emphasizing the importance of mitigating cardiovascular complications.

The nurse reviews information about PV on the MPN Research Foundation website and discusses the disease with SL. The nurse uses the teach-back method to verify SL's understanding of the health information provided. The nurse provides printed information for SL so she can review it later and share it with significant others.

The nurse assesses SL's symptom burden using the MPN-SAF TSS and bases nursing interventions on individual parameters and the total symptom score. The nurse learns that SL's primary concerns are her fatigue and insomnia. Together, the nurse and SL review ways for SL to balance her schedule, ask for assistance with routine tasks, and initiate self-care strategies, such as mild exercise and enrolling in an online yoga program, to improve sleep quality.

After reviewing symptom burden, the nurse discusses management of SL's hypertension and diabetes, and prevention of thrombotic and vascular events. SL plans to follow up with a certified diabetic educator and agrees to self-monitor her BP and follow up with her cardiologist.

Patient-centered nursing care also involves reviewing low-dose aspirin therapy and teaching the patient about therapeutic phlebotomy while supporting her concerns about family and work obligations. By carefully listening to her fears, the nurse provides validation and emotional support.

The nurse walks SL to the transfusion center to familiarize her with the phlebotomy procedure, including what it looks like and how long each procedure may take. SL will undergo lab tests and phlebotomy weekly for the next 3 to 6 weeks, or until her hematocrit is less than 42%.

SL will follow up with the nurse after each phlebotomy and schedule routine visits with the hematologist to monitor for disease progression. The nurse works closely with SL to provide support and education, enabling SL to self-manage her health, advocate for herself, and continue to learn about her disease. ■

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