Mrs C is a Hispanic woman who, at the age of 32, began experiencing increased shortness of breath with exercise and was being treated for asthma as an outpatient. She was referred to a cardiologist when her symptoms worsened with lower extremity edema and the inability to carry out most physical activities, as well as having increased symptoms at rest. An echocardiogram revealed severe elevation of pulmonary artery systolic pressure, with normal function of the left side of the heart. She was then admitted to acute care for a cardiac catheterization, which showed a pulmonary artery wedge pressure of 22 mm Hg and an elevated pulmonary artery pressure of 112/79 mm Hg with moderate to severe tricuspid valve regurgitation.

Mrs C underwent diuresis and her pulmonary wedge pressure decreased to less than 15 mm Hg.

Clinically, her shortness of breath improved and her peripheral edema decreased, but her pulmonary artery pressure remained nearly the same. A pulmonologist was consulted to begin a workup for pulmonary arterial hypertension (PAH). Idiopathic pulmonary arterial hypertension (IPAH) was diagnosed.

### PAH Overview

**Definition/Prevalence**

PAH has been classified by the World Health Organization into 5 groups (Table 1).

<table>
<thead>
<tr>
<th>Group</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pulmonary arterial hypertension (includes idiopathic pulmonary arterial hypertension)</td>
</tr>
<tr>
<td>2</td>
<td>Pulmonary hypertension with left-sided heart disease</td>
</tr>
<tr>
<td>3</td>
<td>Pulmonary hypertension associated with lung disease and/or hypoxemia</td>
</tr>
<tr>
<td>4</td>
<td>Pulmonary hypertension due to chronic thrombotic and/or embolic disease</td>
</tr>
<tr>
<td>5</td>
<td>Miscellaneous</td>
</tr>
</tbody>
</table>

Based on information from Simonneau et al.¹

affected by appetite suppressant drugs (anorexigens) and connective tissue disorders such as rheumatoid arthritis, systemic lupus erythematosus, or systemic sclerosis. Groups 2 through 5 have the diagnosis of pulmonary hypertension caused by or associated with other disease states or disorders.

The prevalence of PAH is 15 per million, and the prevalence of IPAH is only 6 per million.2,3 PAH predominately affects females of childbearing age with a female to male ratio of 1.7 to 1. The mean age at the time of diagnosis is 37 years. Despite modern treatment techniques, PAH mortality is approximately 15% in the first year of therapy.4

Pathophysiology

First reported in 1891, IPAH is a devastating, incurable syndrome characterized by progressive elevation of the pulmonary artery pressure and pulmonary vascular resistance.5 Restricted blood flow through the pulmonary arterial circulation leads to right ventricular failure.6 The development of PAH is believed to be caused by multiple pathogenic pathways. Many changes can occur at the molecular and genetic levels, including smooth muscle hypertrophy, endothelial cell dysfunction, in situ thrombosis, and adventitial and intimal proliferation.7

Vascular injury appears to result from a number of vasoactive mediators. For example, diminished prosta-
cyclin or nitric oxide production (vasodilators) affects endothelial cell proliferation.5 Enhanced production of thromboxane or endothelin 1 (vasoconstrictors) leads to vasoconstriction in the pulmonary artery.5 At this earlier stage, PAH is considered potentially reversible if identified. As the disease progresses, the vascular lesions become more advanced and irreversible, leading to thrombosis and extensive narrowing of the pulmonary vascular bed.8 This remodeling causes an increase in pulmonary vascular resistance leading to eventual right ventricular failure.4 Genetic mutations of bone morphogenetic protein receptor II (BMPR-2) have been identified in approximately 80% of families with PAH and 25% of families with IPAH.9 BMPR-2 has been identified as playing a role in regulating the growth and differentiation of bone, cartilage, and numerous types of cells.

Diagnosis

IPAH is a disease of exclusion. The diagnosis is determined by ruling out other causes of pulmonary hypertension such as those included in groups 2 through 5 of the World Health Organization’s classification system (Table 1). Patients undergo a number of tests such as pulmonary function testing, echocardiography, and ventilation perfusion scanning to rule out chronic embolic disease in an effort to identify a causative factor. Catheterization of the right side of the heart is the standard test used to identify PAH and exclude pulmonary venous hypertension.3 PAH is present if mean pulmonary artery pressures are 25 mm Hg or greater with a pulmonary artery wedge pressure of equal to 15 mm Hg or less.10

Clinical Course

A high percentage of patients with PAH will die of right ventricular failure after a life of progressive and crippling dyspnea.3 Most patients initially have dyspnea but may also experience other nonspecific signs and symptoms (Table 2). The mean

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Table 2
Clinical manifestations of pulmonary arterial hypertension

<table>
<thead>
<tr>
<th>Symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea</td>
</tr>
<tr>
<td>Chest pain</td>
</tr>
<tr>
<td>Exercise intolerance</td>
</tr>
<tr>
<td>Syncope</td>
</tr>
<tr>
<td>Peripheral edema</td>
</tr>
<tr>
<td>Abdominal distention</td>
</tr>
<tr>
<td>Decreased appetite</td>
</tr>
<tr>
<td>Abnormal heart sounds</td>
</tr>
<tr>
<td>Jugular vein distention</td>
</tr>
<tr>
<td>Raynaud phenomenon</td>
</tr>
</tbody>
</table>

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time from the onset of symptoms until diagnosis usually is about 2 years. Patients often visit several specialists and are misdiagnosed with asthma or chronic obstructive pulmonary disease before achieving an accurate diagnosis. Once the diagnosis of PAH is identified, determining the patient’s prognosis through a risk assessment will guide the patient’s treatment plan (Table 3).

Management/Treatment

Current treatment methods focus on blocking vasoconstriction and replacing deficient vasodilators. Often, treating PAH with a combination of medications is necessary. As outlined by the American College of Cardiology Foundation/American Heart Association 2009 Expert Consensus Document on Pulmonary Hypertension, the treatment goals for PAH patients are numerous. The most important goal is to improve the patient’s dyspnea and other symptoms to enhance quality of life. Other treatment objectives include preventing disease progression, lowering pulmonary artery pressure, and normalizing the cardiac output, enhancing functional capacity, and improving survival.

Oxygen Therapy

Supplemental oxygen therapy is often needed because of impaired pulmonary oxygen transport due to the pathological changes in the lungs. Hypoxemia is a potent pulmonary vasoconstrictor that requires many patients to be on home therapy to maintain oxygen saturation above 90%. Patients may also have a continuous positive airway pressure (CPAP) machine for use while sleeping if obstructive sleep apnea is a secondary diagnosis.

Diuretics

Diuretics are another frequently used medication for PAH patients to manage right ventricular volume overload. Diuresis will diminish hepatic congestion and peripheral edema. However, administering diuretics should be done with caution to avoid decreasing the cardiac output or inducing arrhythmias due to electrolyte imbalances.

Anticoagulants

PAH patients are at increased risk for thrombosis formation because of abnormalities in the coagulation cascade, platelet dysfunction, and changes that occur in the vascular endothelium. IPAH patients are recommended to receive warfarin anticoagulation treatment to potentially improve survival rates. Warfarin is used with a goal of maintaining the international normalized ratio (INR) at a therapeutic level of 1.5 to 2.5.

Calcium Channel Blockers

IPAH patients should receive acute vasodilator testing during the right-sided heart catheterization unless right-sided heart failure or hemodynamic instability exists. Those patients who have an acute response to vasodilator administration during testing will show a decrease of at least 10 mm Hg in mean pulmonary artery pressure to an absolute level of less than 40 mm Hg without a decrease in cardiac output. Long-acting calcium channel blockers such as nifedipine, diltiazem, or amlodipine are the most commonly used. However, because of their pure vasodilator response without antiproliferative effects, calcium channel blockers benefit a small minority of PAH patients because very few of these patients have vasoconstriction alone as their predominant abnormality.

### Table 3 Risk assessment for pulmonary arterial hypertension

<table>
<thead>
<tr>
<th>Determinants of risk</th>
<th>Lower (good prognosis)</th>
<th>Higher (poor prognosis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical evidence of right ventricular failure</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Progression</td>
<td>Gradual</td>
<td>Rapid</td>
</tr>
<tr>
<td>World Health Organization class</td>
<td>II, III</td>
<td>IV</td>
</tr>
<tr>
<td>6-Minute walk distance</td>
<td>Longer (&gt;400 m)</td>
<td>Shorter (&lt;300 m)</td>
</tr>
<tr>
<td>Brain natriuretic peptide</td>
<td>Minimally elevated</td>
<td>Very elevated</td>
</tr>
<tr>
<td>Echocardiographic findings</td>
<td>Minimal right ventricular dysfunction</td>
<td>Pericardial effusion Significant right ventricular dysfunction</td>
</tr>
<tr>
<td>Hemodynamics</td>
<td>Normal/near normal right atrial pressure and cardiac index</td>
<td>High right atrial pressure, low cardiac index</td>
</tr>
</tbody>
</table>

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Endothelin-1 Receptor Antagonists

Endothelin-1 is a vasoconstrictor that stimulates proliferation of the smooth muscle cells of the pulmonary artery. Endothelin levels are increased and correlate with the severity and prognosis of PAH. Bosentan is a nonselective oral endothelin-1 receptor antagonist (ETRA) that blocks endothelin receptors. Studies with bosentan have shown improved pulmonary artery pressures and a decrease in clinical worsening defined as death, initiation of intravenous (IV) epoprostenol, hospitalization for worsening PAH, lung transplant, or atrial septostomy. Ambrisentan is another drug in this class but is a selective antagonist of the ETA receptor. The major advantage of ETRAs is that they are dosed orally once daily. These drugs can improve the cardiac and pulmonary pressures as well as exercise capacity.

Phosphodiesterase Type 5 Inhibitors

Phosphodiesterase type 5 inhibitors are another drug class administered orally and are given to patients with mild to moderate PAH who are unable to tolerate or do not respond to ETRAs. These medications are similar to ETRAs in improving hemodynamics and exercise capacity. Sildenafil and tadalafil are phosphodiesterase type 5 inhibitors that are approved by the Food and Drug Administration for the treatment of PAH.

Prostanoids

Prostanoids are prostacyclins that act as vasodilators and inhibit platelet aggregation. All prostanoid formulations have the limitations of a short half-life. Prostanoids include epoprostenol, treprostinil, and iloprost. Iloprost is administered through a highly specialized inhalation device and requires frequent administration of 6 to 9 nebulizer treatments daily. It is a computerized inhaler device that has a memory to help specialty pharmacies track the medication delivered and ensure that the patient is using it correctly. The advantage of this inhalation administration is that it limits the need for an indwelling central venous catheter. Results of long-term outcome research studies are somewhat in conflict with iloprost therapy, and further research is needed.

Epoprostenol (Flolan) has been indicated as the only therapy to increase life expectancy in patients with severe PAH and is the recommended medication for World Health Organization functional class IV (Table 4). It is a continuous IV infusion with a 6-minute half-life and has a stability of only 8 hours at room temperature. This medication must be mixed daily and kept on ice to increase stability to 24 hours.

Treprostinil (Remodulin) can be administered intravenously or subcutaneously, has a half-life of 3 to 4 hours, and is stable for 72 hours at room temperature. When administered subcutaneously, advantages include elimination of a central venous catheter, thus decreasing the potential for infection. The medicine is administered through a subcutaneous infusion pump that is small and lightweight. The pump is about the size of a cellular phone and can be easily concealed. Unfortunately, 85% of patients treated with subcutaneous treprostinil report pain at the pump site and may experience a hematoma at the site. The cost of treprostinil is 3 to 4 times the cost of epoprostenol. Subcutaneous treprostinil maintains the functional status of patients with PAH who were treated with epoprostenol and subsequently transitioned to subcutaneous treprostinil.

Surgical Options

Despite maximal medical therapy, the disease can progress and function of the right side of the heart can worsen, making patients critically ill. Other treatment options for these PAH patients may include atrial septostomy, pulmonary thromboendarterectomy, or lung and combined heart and lung transplantation at specialized centers.

Evaluation and Management of Mrs C

After the cardiac catheterization, Mrs C was admitted to the medical intensive care unit (MICU) with a pulmonary artery catheter for initiation of a vasodilator trial. She started receiving IV epoprostenol to...
evaluate her response and establish a starting dose for treatment. While titrating the drug, the MICU nurses frequently monitored the patient’s vital signs, pulmonary artery pressure, and cardiac output. They also treated adverse effects of the medication such as headache, hypotension, nausea, and vomiting. Once the vasodilator trial was completed, Mrs C was transferred from the MICU to the cardiac intermediate (progressive) care unit, where the nurses also have specialized training in the care of patients with PAH. The training addresses the pathophysiology of PAH, medication administration including specialized infusion pumps, and how to access support from appropriate pharmaceutical companies. This encompasses a 24-hour hotline to answer questions and troubleshoot problems that arise. The pharmaceutical companies and specialty pharmacies work together to educate nurses and patients about administration of the medication and assist with infusion pump problems.

A central venous catheter was established for continuous infusion of the epoprostenol, which became Mrs C’s lifeline for the next 7 years. Before being discharged to home, Mrs C and her family received extensive teaching about how to care for her central venous catheter and the IV infusion of epoprostenol. Another person, a significant other, always must be identified to provide care in case of an emergency. Unfortunately, during the 7 years with the catheter, Mrs C was readmitted multiple times to the MICU with catheter-associated sepsis that required IV antibiotic therapy, which is not uncommon for patients caring for a central catheter at home.

Medication Transition

Because of the frequency of her infections, it was determined that Mrs C’s treatment needed to be changed from IV epoprostenol to subcutaneous treprostinil. Guidelines for transition indicate starting the treprostinil dose at 10% of the epoprostenol dose.24 Treprostinil is commonly initiated in the acute care setting at a dose of 2 ng/kg per minute.24 The optimal dose range for adult monotherapy is between 25 and 40 ng/kg per minute but may be individualized to the patient depending on the symptoms of the disease and the adverse effects.6 At the time of the next admission to the cardiac progressive care unit, Mrs C’s epoprostenol dose had been increased to 57 ng/kg per minute. The nurse worked closely with the pulmonologist and pharmacist to ensure correct calculations and dosing. The Figure shows a summary of Mrs C’s transitional rates.

Mrs C was successfully transitioned to subcutaneous treprostinil over a 28-hour time frame. Nursing care provided during the transition included hourly noninvasive monitoring of the patient. Signs and symptoms of increasing PAH that were monitored during the transition were shortness of breath and objective assessment data including pulse oxygen saturation, blood pressure, and heart rate. Monitoring for adverse effects of prostacyclin included assessment of flushing, rash, site pain, and nausea. Table 5 summarizes the most frequent adverse effects of
epoprostensol and treprostinil. Frequent monitoring allowed the progressive care nurses the opportunity to educate Mrs C on the administration of her medications.

**Coordination of Care**

Insurance qualification for the medication transition began in the physician’s office before Mrs C’s hospitalization. A care coordinator in the hospital performed a clinical review of her chart to obtain additional information needed for her insurance company. The care coordinator had frequent communication with the insurance case manager to obtain continued approval for Mrs C’s inpatient stay. It is important for the nurse in this role to be familiar with the needs of IPAH patients to prevent barriers with the insurance companies and discharge planning. For example, the insurance company negotiated rates with a specialty pharmacy that would provide Mrs C’s costly medications. The care coordinator continued to work with the insurance company when Mrs C was transferred from intensive care to progressive care for transitioning from epoprostensol to treprostinil. While awaiting insurance approval for her treprostinil, Mrs C was discharged to spend time at home with her family over the Christmas holiday. A date was arranged for her to return for the medication transition, which was completed without complications during the approved 2-day stay.

Home health care also plays an important role in the continuum of care for patients being treated with epoprostensol and treprostinil. Home health agencies must employ highly trained nurses to manage the complexity of care needed for PAH patients. Intensive patient and family teaching (Table 6) is started in the hospital and continues in the home setting with the ultimate goal for the patient and family to become independent with care.

**Nursing Implications**

Mrs C is a wife, mother, and a patient. Many mothers can relate to the pressure of balancing home, work, and children. She expressed that her primary concern was the daily challenges she faced raising her 6 children while dealing with a life-threatening disease that has no cure. These difficulties included physical limitations, psychosocial issues, and alterations in body image.

**Physical Limitations**

The symptoms of IPAH limit what patients can do physically. The fatigue, dyspnea, and exercise intolerance that Mrs C experiences with her IPAH is chronic and limits many aspects of her life. She must accomplish meal preparations, laundry for a family of 8, doctor and dentist visits, school routines with early morning chaos, lunch preparation, and homework assistance. Specifically, Mrs C indicates that her fatigue interferes most with her ability to participate in field trips, playing catch, swimming, or bike riding with her children. She requires someone with her to shop for groceries because of her severe fatigue and dyspnea. Social and extracurricular activities are also limited by her IPAH.

### Table 5 Most frequent adverse effects of epoprostensol and treprostinil

<table>
<thead>
<tr>
<th>Epoprostenol</th>
<th>Treprostinil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flushing</td>
<td>Pain and redness at site of subcutaneous infusion</td>
</tr>
<tr>
<td>Headache</td>
<td>Headache</td>
</tr>
<tr>
<td>Dizziness</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>Nausea</td>
<td>Rash</td>
</tr>
<tr>
<td>Musculoskeletal pain</td>
<td>Nausea</td>
</tr>
<tr>
<td>Skin rash</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td></td>
</tr>
</tbody>
</table>

### Table 6 Patient and family education

- Basic disease pathophysiology and process
- Recognizing early symptoms of a change in condition
- Recognizing signs and symptoms of infection in upper part of respiratory tract
- Care of infusion sites and/or central venous catheter site
- Operation of infusion pump and/or other equipment
- Preparation and administration of medications; sterile technique when required
- Obtaining required laboratory tests
- Safe use of oxygen
- Smoking cessation and the need to prevent second-hand smoke
- Avoiding overexertion by spacing activity and rest
- Keeping vaccinations up to date
Psychosocial Issues
For many years, Mrs C and her family’s lives were driven by an epoprostenol clock. She had to be home at a certain time to mix the IV medication and to change and load the cassette, ice packs, and batteries. This time was written in stone. Because the medicine had a 6-minute half life, it had to be mixed at the same time every day. She and her family had grown very comfortable with epoprostenol. Their anxiety increased when it became necessary to switch to treprostinil. Financial concerns related to the cost of specialized medications, durable medical equipment, and the fear of an insurance cap all added to the stress of dealing with Mrs C’s IPAH.

Mrs C’s frequent hospitalizations also compounded the stress and anxiety. Activities that most families take for granted are anything but routine for Mrs C. To provide some comfort and support during one hospitalization, Mrs C’s family chose to move a preplanned party (to watch the Ohio State University versus University of Michigan rivalry football game) to her hospital room. The nurses and other health care providers helped to participate in the festivities. Encouraging open communication for the patient to feel comfortable in sharing their experiences or concerns is crucial. Support groups for patients with PAH are also an invaluable resource.25

Alterations in Body Image
For about 6 years, Mrs C had a central venous catheter. Her last catheter was placed near her left breast due to scar tissue from the old infected catheter sites. This was difficult for her to accept in regard to her sexuality. It made her feel uncomfortable and self-conscious. With her IPAH, she also suffered from a lack of energy and fatigue that further interfered with intimacy. The presence of a central venous catheter was a constant physical reminder to Mrs C that she was ill. Mrs C also loved to swim, and the placement of a catheter along with symptoms of IPAH made swimming impossible for her.

Adverse effects of the medications affected Mrs C’s body image. She had an intense rash on her legs and face caused by the epoprostenol. In the summer, wearing shorts and dealing with stares and questions about the rash proved challenging in addition to coping with feelings related to her perceived disfigurement. Unfortunately, after initiation of the treprostinil, Mrs C had subcutaneous hematomas that were tender, which further altered her appearance.

Education of Patients
With this complex disease, as with others, it is important for progressive and critical care nurses to provide patients with education and emotional support. It is imperative for PAH patients to be proactive in communicating problems to their health care providers and working as part of a team to manage their disease. PAH comes with important lifelong patient responsibilities that require intensive education of patients and their families (Table 6).

Conclusion
Presenting Mrs C’s story at nursing grand rounds with more than 125 nurses in attendance gave the staff nurses from the MICU and the cardiac progressive care unit the opportunity to share their expertise in the care of this IPAH patient. The complexity of her illness required nurses with special training in the care of PAH patients. Although each nurse was specially trained to care for a patient with PAH in their own unit, working together to prepare for this presentation broadened their knowledge of care over the continuum. It was also rewarding to see Mrs C in attendance at nursing grand rounds, where she reported that she was less short of breath and believed the medication was working well for her. She was no longer experiencing site hematomas and felt it was easier to be compliant with her care.

Although PAH patients can be very difficult to manage, transitioning from epoprostenol to treprostinil was successfully completed in our cardiac progressive care unit. However, some PAH patients may need to be managed at a PAH Center of Excellence owing to the complexity of the disease and its treatment.4 These centers provide a multidisciplinary approach that includes specialized physicians, nurses, psychologists, and social workers and clinical trials of investigational agents. Regardless of the setting, it takes a team approach and solid understanding of the disease process to care for patients with PAH.
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