Healthline VOLUME 25

Coram's Continuing Education Program

Pulmonary Arterial Hypertension

Pulmonary arterial hypertension (PAH) is a rare disease, with approximately 800 to 1,000 cases diagnosed in the United States each year.[1] It is characterized by elevated pressure in the pulmonary arteries, and has been classified into five groups by the World Health Organization (see Table 1). PAH is a serious condition for which there is no known cure, and the cause or causes are still not completely understood. It is progressive, with an approximate 30% mortality within five years and a median post-diagnosis life expectancy of approximately seven years.[2] Fortunately, there are treatments available that can improve length and, importantly, quality of life. Early diagnosis and intervention are extremely important for PAH patients. Unfortunately, since the initial symptoms mimic other disease states, it often takes years before a PAH diagnosis is obtained. Life expectancy for untreated patients is less than three years.[2]

Pulmonary Physiology

In normal pulmonary physiology, the pulmonary arteries carry oxygen-poor blood from the heart's right ventricle to the small arteries in the lungs. Normal pulmonary circulation is high volume at low pressure with low resistance. In a normal subject, the average pulmonary arterial pressure at rest is approximately 14 mmHg.

PAH Pathophysiology

In PAH, both arterial pressure and resistance are increased. While the pathophysiology of PAH is poorly understood, it is thought that a hormonal, mechanical, or toxic insult may occur in some patients, resulting in an injury to the arterial endothelium. Whatever the cause, pulmonary arteries narrow, stiffen, and may become blocked — a change referred to as *arterial remodeling*. Patients present with:

- Progressively elevated pulmonary resistance and pressure;
- The development of arterial plexiform lesions, the hallmark sign of morphologic changes in PAH;
- Increased risk of thrombus formation and arterial blockage; and, ultimately,
- Right-sided heart failure and death.

The narrowed pulmonary arteries cause the right side of the heart to work harder to pump blood through the lungs. The heart muscle weakens over time to the point that it loses the ability to pump enough blood through the body, resulting in severe hypoxia. The ensuing right-sided heart failure is the most common cause of death in persons with PAH.

Signs and Symptoms

The signs and symptoms of PAH are variable, depending on the cause of the PAH and the degree of progression. In the early stages of PAH, the symptoms mimic those of a number of health issues, such as asthma, chronic obstructive pulmonary disease (COPD), sleep apnea, heart disease, or pulmonary emboli. The signs and symptoms are related to the right ventricle working harder to pump blood into the highly resistant pulmonary blood vessels.

> With PAH, dysfunctional changes occur in the endothelial cells of the pulmonary arterial smooth muscle, leading to a persistent state of vasoconstriction, inflammation, and abnormal cell proliferation.

Patients typically present with:

- Progressive shortness of breath, especially with activity (the most common symptom)
- Dizziness
- Fatigue
- Progressive weakness
- Hemoptysis
- Hyperventilation
- Progressive cyanosis
- Progressive weakness
- Syncope

On physical examination, patients with PAH may present with:

- Hepatomegaly
- Neck venous distension
- Upper and lower extremity edema

Functional Classification

Patients with PAH are functionally classified according to the New York Heart Association (NYHA)

classification system (see Table 2). Functional class has been shown to be a strong predictor of survival; again, this emphasizes the importance of early diagnosis and intervention.

Unfortunately, most patients are not diagnosed until they reach Class III or IV. PAH is rarely identified in a routine medical examination and, even in its later stages, its signs are commonly confused with other cardiopulmonary diseases. The Registry to Evaluate Early and Long-term PAH Disease Management (REVEAL Registry), the largest registry of patients with PAH, found that the mean time from symptom onset to diagnosis by right heart catheterization (see *Diagnosis below*) was 2.8 years, at which time 73.6% of cases had progressed to advanced stages of the illness.[2]

Diagnosis

Initial testing is performed to assess heart and lung function. For example, an electrocardiogram and chest x-ray will demonstrate the presence, degree, and progression of right ventricular hypertrophy. Similarly, an echocardiogram will show enlargement of the right ventricle and can often be used to estimate the right ventricular and pulmonary artery pressures.

However, the gold standard for establishing a PAH diagnosis is via a *cardiac catheterization.* In fact, a cardiac catheterization is required in order to definitively establish a PAH diagnosis. Catheterization measures the pressures on the right side of the heart; from these pressures, the resistance of the blood vessels in the lungs can be calculated. Importantly, too, various drugs such as nitrous oxide, prostacyclin, or adenosine may be used during a cardiac catheterization to assess the lung blood vessels' response to those medication(s), thus helping to guide therapy decisions.

A PAH diagnosis is confirmed if the testing results show a:

- Mean PAP ≥25 mmHg at rest,
- Pulmonary vascular resistance >3 Wood units, and
- Pulmonary capillary wedge pressure/left ventricular end diastolic pressure ≤15 at rest.

In addition, the results of the cardiac catheterization help determine both disease stage and next steps. If the pulmonary artery systolic pressure is >35–40 and/or there is evidence of right ventricular dysfunction AND a common cause is not clearly present OR a common cause was treated and symptoms persist or worsen, additional tests are warranted.

As stated, if with invasive testing the PAP is ≥25, a diagnosis of pulmonary hypertension can be made. However, evaluation of the pulmonary capillary

Table 1. Pulmonary Hypertension (PH) Classification[3]

Group	Disease States
1	Pulmonary Arterial Hypertension (PAH) • Heritable: Disease is inherited; typically the most aggressive form of PAH • Drug and toxin-related: For example, Fen-Phen or other diet drugs • Associated with (disease related): » Connective tissue disease » Congenital heart disease » Portal hypertension » HIV infection » Schistosomiasis
1'	Disease state Pulmonary veno-occlusive disease and/or pulmonary capillary hemangiomatosis
1"	Persistent pulmonary hypertension of the newborn (PPHN)
2	PH related to left heart disease
3	PH associated with lung disease and/or hypoxemia
4	CTEPH (chronic thromboembolic pulmonary hypertension)
5	PH with unclear or multifactorial mechanisms

Table 2. Functional Classification According to the NYHA Classification System[4]

Class	Functional Symptoms
I	Patients have no symptoms with normal activities; the right-sided heart failure is not yet progressed to the point of symptoms.
II	Patients are comfortable at rest but have symptoms with less-than-ordinary physical activity, resulting in slight limitations on physical activity. Patients are also likely to have an elevated pulmonary artery pressure (PAP). As patients' ability to conduct activities of daily living worsens, the PAP rises. Cardiac dysfunction is evident.
III	Patients are comfortable only at rest. Symptoms present with less-than-ordinary effort, resulting in marked limitations on physical activity.
IV	Patients experience symptoms at rest, and manifest signs of heart failure.

Table 3. Concomitant Medications

Medication	Anticipated Benefit
Anticoagulants	Decrease risk of blood clots in the narrowed vessels
Calcium channel blockers	Cause vasodilation
Diuretics	Help manage heart failure-associated fluid overload
Digoxin	Improve right ventricular ejection fraction and help control heart rate in the presence of supraventricular tachycardia. PAH patients may have increased sensitivity to digoxin, requiring close monitoring for digitalis toxicity.
Nitric oxide	Relax smooth muscle, therefore causing vasodilation

Table 4. Goal-Oriented Therapy[5,6]

Variables	Goals
Functional class	I or II
Hemodynamics	Normalization of RV function • RAP <8 mmHg • CI <3L/Min/m2
ECHO/MRI	Normal/near normal RV size and function
BNP	Normal
6MWT	380–440 meters
Cardiopulmonary exercise test	Peak VO2 >15 VE/VCO2 <45

wedge pressure (PCWP) is then important to distinguish between pulmonary *venous* hypertension and pulmonary *arterial* hypertension. If the PCWP is ≤15, it is evidence of PAH. If it is >15, the diagnosis is pulmonary venous hypertension (PVH). PVH results from an increase in pressure in the pulmonary veins, usually as a result of left atrial hypertension, versus elevated pulmonary arterial pressure impacting the right side of the heart.

Functional testing is also valuable for staging the patient. The most commonly used test is the six-minute walk test (6MWT); this determines how far a patient can walk in six minutes. The 6MWT is also used for monitoring disease progression or response to treatment.

Once the diagnosis of PAH is established, additional tests such as pulmonary function tests (PFTs), liver function tests (LFTs), a ventilation/perfusion (VQ) scan, or sleep studies may be conducted to help determine a cause.

Concomitant Treatment

Presenting patients may be on, or may be placed on, a number of medications to help manage the symptoms and risks of PAH. Some of these medications are listed in Table 3.

Many PAH patients require oxygen, depending on their degree of lung dysfunction. Oxygen is generally administered at 1 to 4 L/min via nasal prongs and adjusted to maintain the oxygen saturation above 90% at rest and, if possible, with exercise and sleep. Exercise training is often a component of therapy.

Of note, select PAH patients in the WHO's group 4 (see Table 1) who are severely incapacitated due to their PAH may benefit from a thromboendarterectomy. Prior to proceeding with this invasive approach, a three-month period of anticoagulation therapy is required.

PAH Treatment

It is recommended that every patient diagnosed with PAH be treated. The most effective treatment is goal-directed and measured by symptom improvement, increased exercise capacity (6MWT), and improved hemodynamic measures. (See Table 4.) Medication recommendations and dosing options are impacted by the presence and severity of adverse effects and the patient's response to treatment.

There are currently four classes of drugs approved for the treatment of PAH: endothelin receptor antagonists (ERAs), prostacyclin analogues, phosphodiesterase type 5 inhibitors, and the newest —soluble guanylate cyclase stimulators. While no treatment has been demonstrated to be superior as first-line therapy, patients are typically initiated on an oral or inhaled form of therapy. There are also recommendations based on the patient's functional class.

Regardless of what is used as initial treatment, if there is inadequate improvement within two months, that particular drug should be discontinued and another therapy tried. It is important not to delay effective treatment, as the disease will progress and become less responsive. Combination therapy with two agents of different action is recommended in patients who are not responding adequately to monotherapy. These medications are available in various forms, depending on the medication, including oral, inhaled, intravenous, or subcutaneous. Very importantly, these medications are complex, and administration requires specialized training. These medications have specific handling, monitoring, and reporting requirements and can be dispensed only by select specialty pharmacies.

Endothelin Receptor Agonists (ERAs)

The three drugs currently available in this class are bosentan (Tracleer®), ambrisentan (Letairis®) and macitentan (Opsumit®). Each is an oral agent.

Black Box Warnings

Letairis and Opsumit have a Food and Drug Administration (FDA) black box warning regarding the likelihood of serious birth defects if used in pregnant women. Letairis is available only through a restricted distribution program for pharmacies, prescribers, and patients called the Letairis Education and Access Program (LEAP). Female patients can receive Opsumit only through the Opsumit Risk Evaluation and Mitigation Strategy (REMS) Program. The restricted-distribution REMS program requires: prescribers to be certified by enrolling in the program; all female patients to be enrolled in the program and comply with applicable pregnancy testing and contraception requirements before initiating treatment; and pharmacies to be certified and to dispense Opsumit only to patients who are authorized to receive it.

Tracleer has two black box warnings. It is also likely to cause major birth defects and is therefore considered teratogenic. Women of childbearing age should not become pregnant while using Tracleer, and female patients on Tracleer should receive monthly pregnancy tests. Tracleer is also hepatotoxic.

To understand how ERAs work, consider the pathophysiology of PAH. The endothelium is the thin layer of endothelial cells that line the interior surface of blood vessels. The endothelial cells produce several vasoactive chemical factors, one of which is endothelin. Endothelin not only causes vasoconstriction, it also promotes cell proliferation. Cell proliferation causes arterial wall smooth muscle overgrowth, narrowing the arteries and decreasing blood flow.

With PAH, endothelin balance is not maintained. There is either increased production and/or decreased inhibition, resulting in excess endothelin and its associated vasoconstriction, cell proliferation, and ultimately, increased arterial blood pressure. ERAs work by binding to the endothelin receptor sites, thus preventing the endothelin from binding at those sites. The result is arterial vasodilation.

Some of the potential adverse effects of ERAs are:

- Abdominal pain
- Birth defects
- Constipation
- Decreased Hgb/Hct
- Decreased sperm count
- Flushing
- Hepatic dysfunction
- Nasal congestion
- Palpitations
- Sinusitis

Prostacyclin Analogs

IV prostacyclin analogs tend to have the greatest efficacy as treatments for PAH and often are effective in patients who have failed other treatments. Currently available prostacyclins are epoprostenol sodium (Flolan®) continuous IV, epoprostenol (Veletri®) continuous IV, generic epoprostinil continuous IV, treprostinil (Remodulin®) continuous IV or subcutaneous (SC), treprostinil (Orenitram™) oral, selexipag (Uptravi®) oral, treprostinil (Tyvaso®) inhaled, and iloprost (Ventavis®) inhaled.

Prostacyclin is another vasoactive factor produced by the endothelial cells. Prostacyclin induces vasodilation of blood vessels and inhibits smooth muscle cell proliferation and platelet aggregation. In healthy vasculature, prostacyclin helps counterbalance the actions of endothelin. If production of prostacyclin by the endothelium is impaired, the deleterious effects of excessive levels of endothelin predominate, again causing vasoconstriction, cell proliferation, and elevated arterial pressure. Prostacyclin analogues essentially replace the patient's missing or insufficient prostacyclin, improving both symptoms and prognosis for many patients with PAH. Each of the medications in this category requires titration.

There are some important differences in the administration of these medications. Flolan and Veletri have a very short half-life of three to five minutes, and thus pose significant risk if the patient is detached from the IV infusion for any reason (such as kinked tubes or a malfunctioning pump). A back-up cassette should always be available. Dosing is based on weight and requires frequent titration based on the patient's response to therapy. First dose(s) must be given in the hospital. Administration for all doses requires a long-term venous access. In addition, Flolan must be kept at a constant and cool temperature, which can be logistically complicated for patients.

Remodulin can be administered either through a continuous intravenous (IV) or through continuous or intermittent subcutaneous (SC) routes. With a half-life of about four hours, Remodulin provides some protection should flow be compromised in any way. SC administration has the advantage that patients can discontinue the infusion long enough to shower, swim, or bathe. However, with SC administration, some patients experience significant pain at the infusion site. As with Flolan and Veletri, dosing of Remodulin is based on weight and titrated as per the patient's response to therapy. Remodulin is stable at room temperature, and patients can be inducted at home.

There are also two inhalation forms of prostacyclin analogs—treprostinil (Tyvaso) and iloprost (Ventavis). Tyvaso has a half-life of 4 to 4.5 hours and is inhaled four times a day, or every four hours while awake. Each treatment lasts about two to three minutes and is administered via an ultrasonic nebulizer. Ventavis has a half-life of 20 to 30 minutes, and its effects generally last for about 1.5 hours. Inhalation is therefore required six to nine times a day for six to ten minutes each time, depending on the patient's response, breathing pattern, and activity level. Ventavis is typically initiated at a dose of 2.5 mcg. If the 2.5-mcg dose is tolerated, the dose is increased to 5 mcg. The medication is inhaled via a handheld, battery-powered drug delivery system.

Potential adverse effects of prostacyclin analogs include:

- Bone pain
- Cough (w/ inhaled)
- Decreased appetite
- Diarrhea
- Flushing
- Headache
- Hypotension
- Jaw pain
- Palpitations
- Rashes

- Syncope

Phosphodiesterase Type 5 Inhibitors

Sildenafil (Revatio®, generic sildenafil) and tadalafil (Adcirca®) are the two oral agents in this category of medications. Revatio is also available for continuous IV. These drugs work by restoring nitric oxide/cGMP signaling.

Nitric oxide (NO) is one of the body's free radicals and a potent vasodilator. The blood vessel endothelium uses NO to signal the surrounding smooth muscle to relax, resulting in vasodilation. One of the major mechanisms through which the effects of NO are mediated is via the production of a second messenger called cyclic guanosine monophosphate (cGMP). Through a series of events, NO can stimulate production of cGMP. cGMP activates protein kinase, which also causes vasodilation and

> Cyclic guanosine monophosphate (cGMP) relaxes smooth muscle tissues, among other functions. Relaxation of vascular smooth muscles lead to vasodilation and increased blood flow.

relaxation of the smooth muscle cells. cGMP is converted back to guanosine-5'-triphosphate (GTP) by proteins known as phosphodiesterases. This conversion effectively blocks further NO signaling. In the presence of the vasoconstriction of PAH, it becomes important to inhibit the phosphodiesterases so that cGMP can again signal the NO, which will lead to vasodilation and decreased pressure.

Potential adverse effects of Revatio and Adcirca include:

- Bone pain
- Dyspepsia
- Extremity pain
- Enhanced nitrates
- Flushing
- Headache
- Hypotension
- Muscle aches
- Nasal congestion
- Nausea
- Nose bleeds
- Bleeding (rare)
- Priapism (rare)
- Sudden hearing loss (rare
- Sudden vision loss (rare)

Soluble Guanylate Cyclase Stimulator

Soluble guanylate cyclase (sGC) is an enzyme in the cardiopulmonary system and the receptor for NO. Riociguat (Adempas®) is the first sGC stimulator approved in the United States. Riociguat sensitizes sGC to endogenous NO by stabilizing the NO-sGC binding, and it directly stimulates sGC via a different binding site, independently of NO. This drug was approved by the FDA in October 2013 as an orphan drug for two indications:

- The treatment of adults with persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH) after surgical treatment, or inoperable CTEPH to improve exercise capacity and WHO functional class, or
- The treatment of adults with PAH to improve exercise capacity, improve WHO functional class, and delay clinical worsening.

Adempas is the first drug in its class approved to treat PAH and the first drug of any class to be shown to be effective for patients with CTEPH. It, too, will carry a black box warning alerting patients and health care professionals that the drug should not be used in pregnant women because of potential harm to a developing fetus. Women will be able to receive the drug only through the Adempas Risk Evaluation and Mitigation Strategy (REMS) program, which will require them to comply with pregnancy testing requirements and be counseled regarding the need for contraception.

Nitric Oxide

In addition to the four classes of medications described above, nitric oxide for inhalation (INOmax®) is a vasodilator that, in conjunction with ventilatory support and other appropriate agents, is indicated for the treatment of term and near-term (>34 weeks gestation) neonates with hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension. For these patients, INOmax improves oxygenation and reduces the need for extracorporeal membrane oxygenation. INOmax has been given orphan status for PAH in adults in the United States. INOMax is typically prescribed for 14 days, until oxygen saturation is normal, but must be tapered off as there is a risk of rebound of PAH if the drug is discontinued suddenly.

Combination Therapy

PAH treatment guidelines support combination therapy for patients exhibiting poor clinical response or deterioration on monotherapy. Clinical trials, research, registry data and expert consensus opinion have lead to combination therapy treatment recommendations targeting two to three of the PAH signaling pathways (endothelial, prostacycline and NO). Analysis of registry data illustrates greater than 50% of United States PAH patients are managed on combination therapy.[7]

Lung Transplantation

Lung transplantation is a viable, and ultimately the only, option for select patients with advanced PAH who are continuing to deteriorate despite optimal pulmonary vasodilator therapy. The typical PAH lung transplant candidate has exhausted his or her medical treatment options and presents with a persistent NYHA classification of III or IV. The patient's six-minute walk test is low or declining (which also impacts quality of life) and has significant right-sided heart dysfunction. Unfortunately, a majority of these patients do not survive the wait for an available lung. Based on Organ Procurement and Transplant Network data as of January 17, 2014, for those who are able to be transplanted, the survival rates for PAH at one, three, and five years are similar to success rates for other disease states and for lung transplant overall.[7] See Table 5.

Most patients with PAH who have a transplant undergo a double lung transplant. Approximately 10% of PAH patients require a heart/lung transplant, although in the majority of cases, the right ventricle is quickly able to recover after the lung transplant.

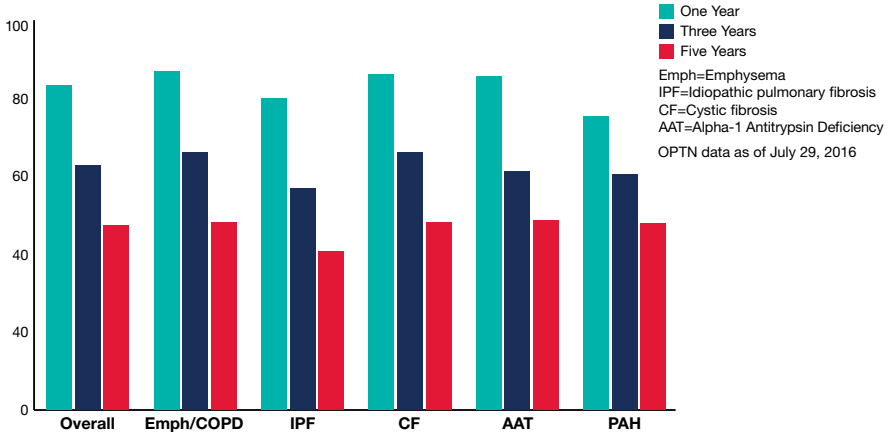
Atrial Septostomy

Atrial septostomy is used in cases of severe PAH when the right ventricular function continues to deteriorate despite optimal therapy or the patient experiences frequent exertional syncope; it is also used as a bridge to transplant. With this procedure, a small hole is made via a cardiac catheter between the right and left atria. This helps to reduce pressure in the right side of the heart, allow the heart to pump more efficiently, and improve blood flow to the lungs.

Extracorporeal Membrane Oxygenation (ECMO)

In extreme emergencies, ECMO may be required temporarily.

Table 5. Lung Transplant Survival[8]



ECMO is a procedure that circulates blood outside of the body through an ECMO machine. The goal is to take over the workload of the lungs and allow them to recover. As compared to cardiopulmonary bypass, which can be used for only a few hours, ECMO can be in place for several days. Thus, it can be used as the patient stabilizes and/or as a bridge to transplant.

Lung Assist Device (LAD)

A pumpless lung assist device (LAD) may be used for patients with acute decline and cardiogenic shock. The LAD connects the main pulmonary artery trunk and the left atrium, and can therefore help with gas exchange as well as emptying of the right ventricle.

Patient Education

Two key areas of education for PAH patients are lifestyle changes and medication. Patients with PAH often have to make lifestyle changes to better manage and enjoy their lives. Depending on the degree of symptomatology, lifestyle changes may be relatively simple or more complex. Some examples include:

- Make the kitchen, laundry, and other areas of the home—as well as the tools and supplies within—more accessible.
- Modify showers and baths for easy access and use.
- Limit the use of stairs.
- Limit heavy lifting and activities that cause straining.
- Limit activities at higher elevations.
- Avoid smoking or second-hand smoke.
- Obtain a handicap-parking permit.

Table 6.

Key Points for Medication-Related Patient Education
Long-term therapy requirements • Central line care • Risk of infection
Preparation • For immediate use • Prepare ahead and store • Diluent(s)
Infusion • Length • Temperature (ice packs needed?)
Infusion site reaction
Medication administration • Pump » Type: ambulatory or syringe » Troubleshooting • Inhalation » Effective technique » Dosing » Times per day » Number of cycles » Inhalations per cycle » Care of equipment
Potential adverse effects
Medication withdrawal

Medication-specific patient education depends on the type of medication and route of delivery, as well as the patient's unique symptoms and medication adverse effects. Key components of medication-related patient education plans are listed in Table 6. ♦

**Do not use the information in this article to diagnose or treat a health problem or disease without consulting a qualified physician. Patients should consult their physician before starting any course of treatment or supplementation, particularly if they are currently under medical care, and should never disregard medical advice or delay in seeking it because of something set forth in this publication.*

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Self-Assessment: Pulmonary Arterial Hypertension

LEARNING GOAL

To gain knowledge of the disease process, treatment, and outcomes of pulmonary arterial hypertension (PAH), as well as key components of patient education.

LEARNING OBJECTIVES

At the end of this program, the reader will be able to:

1. Describe the pathology of PAH.
2. Outline the typical progression of PAH from symptom presentation to right-sided heart failure.
3. List the four classes of drugs used to treat PAH and their primary mode of action.

SELF-ASSESSMENT QUESTIONS

In the Quiz Answers section on the next page, circle the correct answer for each question. To obtain two (2.0) contact hours toward CE credit, the passing score is 100%. Return your Self-Assesment Quiz to Coram via email, fax or mail. See the next page for details on how to return to your quiz. Please allow approximately seven days to process your test and receive your certificate upon achieving a passing score.

1. **The pathophysiology of PAH centers around pulmonary circulation that is high volume at low pressure with low resistance.**
   a. True.
   b. False.

2. **Arterial remodeling:**
   a. Occurs as pulmonary arteries narrow and stiffen.
   b. Leads to progressively elevated pulmonary resistance and pressure.
   c. Decreases the risk of thrombus formation.
   d. Increases the risk of right-sided heart failure.
   e. All of the above.
   f. A, B, and D.

3. **Right-sided heart failure is the most common cause of death in persons with PAH.**
   a. True.
   b. False.

4. **A PAH diagnosis is best determined from a right-sided cardiac catheterization.**
   a. True.
   b. False.

5. **A PAH diagnosis is confirmed if the:**
   a. Mean pulmonary artery pressure is ≥25 mmHg at rest.
   b. Pulmonary vascular resistance is >3 Wood units.
   c. Capillary wedge pressure is below normal.
   d. A, B, and C.
   e. A and B.
   f. B and C.

6. **Which of the following statements is (are) true? Endothelin receptor agonists (ERAs):**
   a. Cause vasoconstriction.
   b. Block endothelin receptor sites.
   c. Are administered intravenously.
   d. A and C.
   e. B and C.

7. **Which of the following statements is (are) true? A prostacyclin analog:**
   a. Counteracts the vasodilative properties of prostacyclin.
   b. Inhibits smooth muscle cell proliferation.
   c. Inhibits the effect of endothelin.
   d. May be in an intravenous, subcutaneous, or inhalation form.
   e. All of the above.
   f. A, B, and D.
   g. B and C.
   h. B, C, and D.

8. **Phosphodiesterase inhibitors:**
   a. Are oral agents.
   b. Maintain the vasodilatory effects of nitrous oxide.
   c. Cause vasoconstriction.
   d. All of the above.
   e. A and B.
   f. A and C.

9. **Lifestyle changes can positively impact symptoms and quality of life for patients with PAH.**
   a. True.
   b. False.

10. **The typical PAH lung transplant candidate will likely:**
    a. Have exhausted his or her medical treatment options.
    b. Present with a persistent New York Heart Association classification of III or IV.
    c. Have a low or declining six-minute walk test.
    d. Present with significant right-sided heart dysfunction.
    e. All of the above.
    f. B, C, and D.

Healthline VOLUME 25

Coram's Continuing Education Program

Pulmonary Arterial Hypertension

QUIZ ANSWERS

Circle the correct answers below to receive 2.0 Continuing Education credits.*

1. (a) (b)
2. (a) (b) (c) (d) (e) (f)
3. (a) (b)
4. (a) (b)
5. (a) (b) (c) (d) (e) (f)
6. (a) (b) (c) (d) (e)
7. (a) (b) (c) (d) (e) (f) (g) (h)
8. (a) (b) (c) (d) (e) (f)
9. (a) (b)
10. (a) (b) (c) (d) (e) (f)

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