

What is pulmonary arterial hypertension?

Pulmonary arterial hypertension (PAH) is a rare, chronic (lifelong) disease that affects both the heart and lungs.¹ PAH occurs when the arteries that bring blood from the heart to the lungs become blocked by the tightening of the arterial wall, the growth and thickening of cells in the arterial wall, or the formation of blood clots (known as thrombosis).²

As the arteries begin to narrow, it becomes harder for blood to reach the lungs and for oxygen to be circulated throughout the body.² As a result, people living with PAH become breathless and fatigued more quickly, and can even have trouble breathing after walking for only a few minutes.² PAH also puts extra stress on the heart because it is forced to pump harder to circulate blood.²

People with PAH develop high blood pressure in the arteries leading from the heart to the lungs² and the disease can ultimately lead to heart failure if the heart is unable to keep up with its extra load, as PAH worsens over time.² The exact cause of PAH is unknown and there is no cure.² However, treatments are available to help ease symptoms.

How common is it?

Pulmonary arterial hypertension is a relatively rare disease that is estimated to affect between 2,000 and 10,000 Canadians.³ As physicians and researchers have learned more about PAH and awareness of the disease has spread, its prevalence has increased.

PAH affects males and females of all ethnicities and ages.⁴ However, some research suggests that genetics may play a role in determining who gets PAH,⁵ and that the disease is more common among women and people between the ages of 20 and 40.⁵ Certain groups of people also have a higher risk of developing PAH, such as those who have taken certain diet drugs or who have particular heart, connective tissue, or liver disease, or certain other medical conditions.⁶ See the “risk factors” section for more detail about people whose risk of developing PAH tends to be greater.

What are the risk factors?

Although the cause of PAH is unknown, research has begun to uncover some of its risk factors, which may influence the development of this disease alone or in combination. Some of the most common risk factors for PAH include:

- Genetics⁵
- HIV⁶
- Use of specific diet drugs⁶
- Congenital heart and liver diseases⁶
- Connective tissue disease (CTD), especially scleroderma⁶
- Amphetamine or cocaine use⁶

Can it be prevented?

Maintaining a healthy lifestyle that includes eating well and exercising could reduce the chances of developing certain risk factors for PAH, such as liver disease, but it does not guarantee prevention of PAH.

What are the symptoms?

People affected by PAH usually develop non-specific symptoms—in other words, symptoms that aren't specific to any particular disease.¹

The most common symptoms of PAH are related to the heart and lungs having to work harder. These include shortness of breath, laboured breathing (dyspnea) upon exertion, fatigue, and fainting (syncope). PAH may also cause weakness, swollen ankles and feet, or chest pain due to the physical stretching of their arteries or a lack of oxygen in the heart.¹ Less common symptoms include coughing up blood, which is known as hemoptysis.⁷

How is it diagnosed?

A PAH diagnosis is based partially on the presence of its most common symptoms—shortness of breath, fatigue, and fainting—in the absence of obvious signs of heart or lung disease.⁶

Tests that can be done to help diagnose PAH include an electrocardiogram, a chest x-ray, and a transthoracic Doppler-echocardiography.⁶ However, a definitive PAH diagnosis can only be made following a diagnostic test known as a right heart catheterization.⁸

An electrocardiogram (ECG) is a test that measures the electrical activity of the heart through electrodes placed on the different areas of the body. An ECG can tell a physician if the heart is under strain, possibly due to narrowing arteries that are typical of PAH. However, because people with PAH can still have normal ECG results, other tests may still be performed.⁶

A chest x-ray (also known as a chest radiograph) takes an image of the inside of the body, which can show heart enlargements that are a result of PAH. A normal chest x-ray can rule out moderate to severe PAH, but it cannot detect mild versions of the disease.⁶

A transthoracic Doppler-echocardiography (TTE) is another test that can help diagnose PAH. A TTE uses ultrasound waves to create an image of the heart and measure the flow of blood through it. This test can detect the abnormal heart ventricles and pulmonary high blood pressure that are typical of PAH.⁶

A right heart catheterization is an invasive procedure that involves guiding a catheter (a long thin hollow tube) through the chambers of the heart and into the large blood vessels of the lungs. The procedure is also known as pulmonary artery catheterization or Swan-Ganz catheterization. Left in place in a pulmonary (lung) artery, the catheter measures pressures in the heart and large blood vessels and checks how well the heart is working. A right heart catheterization is not for diagnosis alone: it can be done following initiation of treatment or after several years to assess the progress of the disease.⁹

After PAH is diagnosed, there are several ways to identify how far the disease has progressed. Tests can be done to check the function of the lungs and, if required, images of the lungs can also be taken. A doctor may choose to test how well the lungs handle the exchange of the many gases in our air, including oxygen, carbon dioxide, and carbon monoxide. In addition, a high-resolution CT (computerized tomography) scan of the lungs may be done to get a better understanding of the extent to which the disease has affected them.⁸

While the tests described above are used to see if and how the heart and lungs have been affected by PAH, there are also tests that measure how this disease affects someone's ability to function day-to-day.⁸ For example, the six-minute walk test is a simple way to evaluate a PAH patient's ability to perform physical activity. In the test, patients walk for six minutes on a predetermined circuit marked by two cones and the distance they have walked



in this time, their level of shortness of breath and their level of fatigue are noted.¹⁰ Another test involving exercise is called cardiopulmonary exercise testing, or CPET, which measures how much oxygen the lungs receive during exercise.⁶

Doctors will also check whether or not a patient has one or more PAH risk factors and may perform blood tests to confirm the presence of associated conditions, such as connective tissue disease or HIV.⁶ Some blood tests can help confirm the presence of PAH by measuring levels of a special protein released by the brain when there are changes in blood pressure.¹¹

PAH classifications as used by doctors are based on two similar classification systems: one from the World Health Organization (WHO) and the other from the New York Heart Association (NYHA). There are four functional classes of PAH based on the severity of the disease:⁶

Class I: Patients with pulmonary hypertension who do not experience limitations on their ability to perform everyday physical activity. Ordinary physical activity does not cause excessive shortness of breath, fatigue, chest pain, or near fainting.⁶

Class II: Patients with pulmonary hypertension who have slight limitations on their ability to perform everyday physical activity. These patients are comfortable at rest, but ordinary physical activity causes some shortness of breath, fatigue, chest pain, or near fainting.⁶

Class III: Patients with pulmonary hypertension who experience significant limitations on their ability to perform everyday physical activity. These patients are comfortable at rest, but even small amounts of physical activity cause unusual dyspnea (shortness of breath), fatigue, chest pain, or near fainting.⁶

Class IV: Patients with pulmonary hypertension who are unable to perform any physical activity without experiencing symptoms and who show signs of right heart failure even while resting. Shortness of breath and/or fatigue may be present at rest, and discomfort is increased by any physical activity.⁶

Treatment for someone with PAH will be based in part on the class of their disease.

How is pulmonary arterial hypertension treated?

There is currently no cure for pulmonary arterial hypertension.² However, research on PAH has progressed significantly over the past decade and has shed more light on how it affects the body and how to improve the quality of life of people with this disease.⁹ A doctor will choose a course of treatment for patients with PAH based on the progress of their disease, medications that they are already taking, and the presence of any other conditions.⁸ Treatment success can vary from person to person.

Treatments for PAH include:

- **Medicines that prevent blood clots**

These medicines, called anticoagulants, are taken orally and make blood less able to clot in the vessels. This means that they may help prevent blockages in blood flow caused by clots, and help reduce the work load on the heart. However, anticoagulants will not always be recommended because they make stopping bleeding more difficult.⁶

- **Medicines that help the heart**

These medicines, such as digoxin, can help the heart function better, which allows it to compensate for the extra amount of work it has to do as the arteries in the lungs of someone with PAH narrow.⁶

- **Medicines that reduce swelling**

These medicines include diuretics, which get rid of swelling caused by the excess fluid buildup that occurs in some people with PAH. Because this excess fluid can increase pressure in the heart, the fluid release caused by diuretics can also help the heart work better.⁶

- **Oxygen therapy**

People with PAH may be given extra oxygen if they find breathing very difficult and they are not receiving enough oxygen while at rest.⁶

- **Medicines that help relax the arteries**

Medications called vasodilators help relax the narrowed or constricted arteries of people with PAH, creating more space for blood to flow through and reducing the workload on the heart.⁶

Calcium-channel blockers, or CCBs, are one type of vasodilator sometimes used to treat people with PAH. However, CCB use is limited because research has shown that very few PAH patients actually benefit from them. A doctor will determine if CCBs are the best treatment option.⁶

There are also newer drug therapies that are specific to PAH, such as a group of drugs called endothelin receptor antagonists which include drugs named bosentan, sitaxsentan and ambrisentan, a drug named sildenafil from a group called PDE-5 inhibitors, and a group of drugs called prostacyclin analogues, which includes the drugs epoprostenol and treprostinil. These therapies work on the arteries to relax them or prevent them from narrowing so that the heart doesn't have to work as hard to pump blood through the body.⁸

Drugs from the endothelin receptor antagonist group work by blocking the effect of a molecule in the body called endothelin-1 (ET-1) that can cause arteries to close up.⁸ Bosentan, sitaxsentan, and ambrisentan are all taken orally in tablet form.¹² In Canada, bosentan is available to people with primary PAH who are WHO functional class III or IV or who also have scleroderma, congenital heart disease, or HIV and have not responded to other treatments.¹² Sitaxsentan and ambrisentan are available to people with primary PAH, or who have PAH secondary to connective tissue disease, with WHO functional class III and have not responded to other treatments. It can also be used in patients with WHO functional class II who have not responded to other treatments.¹³

These drugs can potentially increase liver enzymes, so they may not be the best treatment choice for people with liver problems. It is recommended that patients on endothelin receptor antagonists get liver function tests monthly.¹² Common side effects from bosentan include headache, fluid retention, and anemia; from sitaxsentan, headache, fluid retention, nasal congestion and nausea; and from ambrisentan, fluid retention, headache, nasal congestion, palpitations and constipation.¹²

Sildenafil and tadalafil block the effect of an enzyme in the body called phosphodiesterase type 5 (PDE-5). By blocking PDE-5, these products allow the increase of a molecule called cyclic guanosine monophosphate (cGMP), which maintains relaxation of the arteries and helps prevent cells within them from overgrowing.⁶ Both PDE-5 inhibitors are taken orally in tablet form.^{15, 18} In Canada, sildenafil is available to people with PAH who are WHO functional class II or III or who also have connective tissue diseases and have not responded to other treatments.^{15, 18} In addition, tadalafil can be used in people with PAH who also have congenital heart disease or secondary to anorexigen use. Sildenafil and tadalafil are not recommended for people who are taking medications that contain nitrates such as certain heart medication.¹⁵ The most common side effects for sildenafil are headache, dizziness, flushing (becoming markedly red in the face or other areas of the skin), and upset

stomach or digestion (dyspepsia).¹⁵ For tadalafil the most common side effects are: headache, muscle pain, pharyngitis, flushing, respiratory tract infection, dyspepsia.¹⁸

Epoprostenol and treprostinil are drugs modeled on a natural molecule in the body called prostacyclin that relaxes arteries, prevents blood clots, and can prevent arteries from thickening due to cell growth.⁶ In Canada, epoprostenol is available as a long-term intravenous treatment for people with primary PAH, as well as PAH patients who have scleroderma, are NYHA functional class III and IV, and have not responded to other treatments.¹⁶ The most common side effects of epoprostenol include jaw pain, flushing, and headache.¹⁶ In Canada, treprostinil is available as a long-term subcutaneous (beneath the skin) or intravenous treatment for people with PAH who are NYHA functional class III and IV and have not responded to other treatments.¹⁷ The most common side effects of treprostinil include pain or reaction at the injection site, rash, edema, vasodilation, nausea, and jaw pain.⁸

Living with pulmonary arterial hypertension⁶

Having PAH does not have to limit enjoyment of life, but some lifestyle adjustments are necessary to prevent the disease from becoming worse.

Here are some strategies for coping with PAH:

- **Seek immediate medical attention when fighting infections.** People with PAH are less able to fight off infections, especially in the lungs, and there is an increased risk of death should they get sick with the flu or pneumonia. It is also recommended that people with PAH receive certain vaccines that can protect them from respiratory infections—such vaccination should be discussed with a doctor.
- **Avoid becoming pregnant.** A sad, but unfortunate truth is that pregnancy and delivery of a baby could worsen the severity of PAH for women or even lead to death. It is recommended that women of childbearing age use contraception to avoid becoming pregnant. The kind of contraception used should be discussed with a doctor.
- **Be aware of drug interactions.** It's also important to keep in mind how PAH treatments might interact with other drugs, such as those that could interfere with oral anticoagulants or increase the chance of internal bleeding. People with PAH should discuss any potential interactions with their doctor before taking supplements or medications, even if they are natural supplements or over-the-counter medications.
- **Get support.** It can take time to come to terms with the diagnosis of a serious disease. People with PAH may feel frustrated that they cannot do all the things they could previously, especially when it comes to exercise. Some PAH patients may even feel anxious or depressed as a result of the new limitations imposed on their life. One way to cope with these feelings is to find a support group of people who understand what it is like to be affected by PAH and can provide suggestions on how to deal with the disease. Some people also find that it is helpful to speak with a psychiatrist or psychologist. The bottom line is that taking care of emotional health is no less important than maintaining good physical health in the battle against PAH.
- **When flying, consider using an oxygen mask.** People with PAH can be affected by flying and travelling to places at high altitudes where the thinner air can make it more difficult for the body to receive the oxygen it requires. Using an oxygen mask is one way PAH patients can still enjoy travelling while protecting their health.

Empowering patients and caregivers

As discussed in the previous section, some patients with PAH may suffer anxiety or depression, especially when they are first diagnosed. There are ways to overcome these difficult feelings by being properly informed about the condition, joining a support group, or talking to a psychiatrist or psychologist. Treatment for PAH shouldn't only be physical; a patient's emotional needs are just as important.

Caregivers, friends, and family members can play an important role in providing emotional support to someone with PAH.

The first step is to learn everything you can about PAH, which will make it easier to talk about the disease with your loved one. Knowing the obstacles and challenges involved in PAH will also allow you to better understand what your loved one is going through and give you the tools to better help him or her adjust to life with this condition. Sites like this one and the resources provided below will help you get information on how PAH affects the body, progresses, and how they can be treated.

It is also important to keep communicating with a loved one affected by PAH. Ask about symptoms, and whether there have been any improvements or additional problems, such as treatment-related side effects. You may even want to offer to accompany your loved one to doctors' appointments and support group meetings.

Creating a support network and a sense of community are essential for helping PAH patients cope successfully with their disease and enjoy happy, fulfilling lives.

Patient Resources

These websites are neither owned nor controlled by Pfizer. Pfizer is not responsible for the content or services on these sites.

Patient associations

ALBERTA

Alberta PH Support Group—email for more information:
Edmonton PAH Society—email for more information:

sproudfroot@phacanada.ca
lm.cox@telus.net

BRITISH COLUMBIA

British Columbia PH Society

<http://www.bcphs.org/>

MANITOBA

Manitoba PH Support Group

http://ca.geocities.com/mb_ph_group/

NEW BRUNSWICK

New Brunswick PH Society

<http://www.nbphs.org/>

ONTARIO

Pulmonary Hypertension Association of Canada—Toronto chapter

<http://www.phatoronto.ca/>

QUEBEC

Fondation HTAP Quebec

<http://www.htapquebec.ca/>

American:

Pulmonary Hypertension Association (PHA)

<http://www.phassociation.org>

Disease awareness site(s)

Living with PH	http://www.livingwithph.ca/
Know Your PH	http://www.knowyourph.org/
PH Central	http://www.phcentral.org/

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