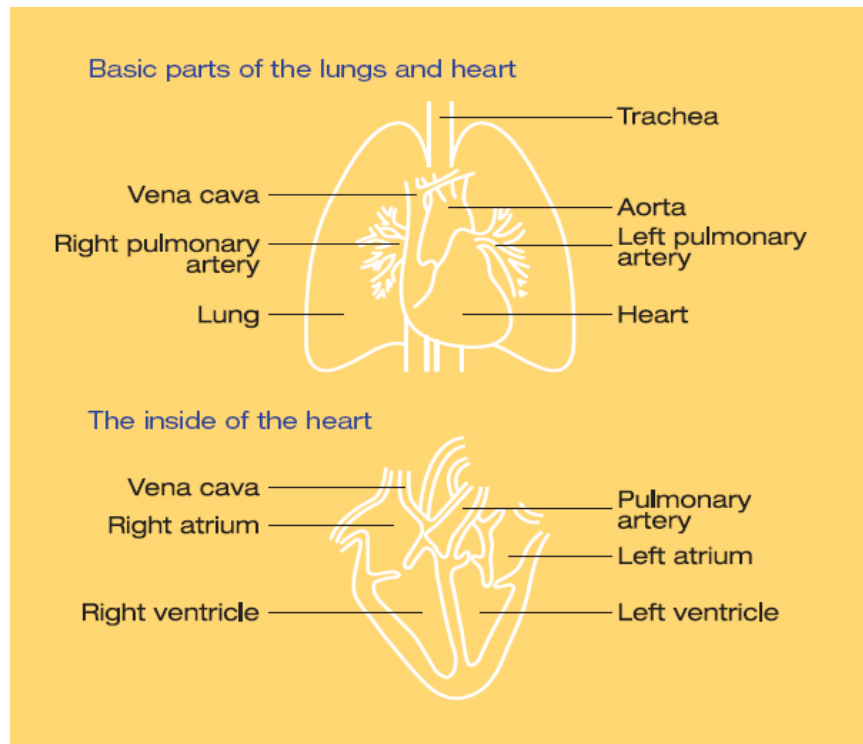


PULMONARY HYPERTENSION-INFORMATION FOR PATIENTS AND PUBLIC

An introduction to Pulmonary Hypertension (PH)

Pulmonary hypertension (PH) is a rare lung disorder in which the blood pressure in the pulmonary artery rises far above normal levels. At the same time as the pressure rises, the walls of the blood vessels (pulmonary arteries) become thicker. PH can occur with or without an identifiable or known cause.

The pulmonary arteries are the blood vessels carrying “oxygen-poor” blood from the right ventricle, one of the pumping chambers of the heart, to the lungs. Once oxygenated (that is, blood which is now *richer* in oxygen) in the little air sacks of the lungs, the blood is carried back to the left side of the heart by the pulmonary veins. The oxygenated blood is then pumped to the rest of the body by the left ventricle (through the aorta, the largest blood vessel in the body). This blood is carried to the body by the systemic arteries where the muscles and organs use the oxygen. Once the oxygen has been extracted the blood is carried back to the right side of the heart by the systemic veins (these are called the inferior and superior vena cava). This cycle then repeats itself.



During periods of exercise, such as walking, the muscles require larger amounts of oxygen to provide them with extra energy. Therefore the body adapts to this increased oxygen demand by increasing the heart rate which increases the amount of blood flowing through the lungs. For this to happen the pulmonary arteries have to be able to open wider. In other words the vessels have to be flexible.

In patients with PH the vessel walls are thicker and therefore the vessels become less flexible. This makes it harder for the right ventricle to pump more blood through the lungs. The right ventricle is a muscle and like any other muscle in the body, if it is worked harder it becomes bigger. However if the heart has to work harder than usual over a long period of time (months and often years) without a rest, it begins to work much less effectively.

When the right ventricle contracts it pressurizes the blood within its chamber. The pressure forces the blood through the pulmonary arteries, in turn increasing the pressure within them. After the right ventricle has contracted, it relaxes causing the pressure in the pulmonary arteries to decrease. In other words the pressure in the pulmonary arteries increases when it contracts and decreases when it relaxes. In a healthy person the pressure increases to about 20 mmHg (millimeters of mercury) and decreases to as low as about 5 mmHg.

Often when doctors talk about the pressure in the pulmonary arteries they talk about a single figure. This figure is what is known as the mean (average) pulmonary artery pressure (this is often abbreviated to mPAP) and is a number between the highest and lowest pressures. In the healthy person the mean is about 14 mmHg. The diagnosis of PH may be considered when the mean pulmonary artery pressure rises above 25 mmHg whilst the patient is resting or 30mmHg on exercise.

Although in the majority of cases we do not know the exact cause of PH, we do know that it occurs often in people with other specific diseases. For instance we know that people with a condition called “systemic sclerosis” may have a life time risk of developing PH of 10-20% which is higher than the normal risk. PH can also be said to occur in association with portal hypertension (liver problems), HIV infection and most commonly in patients with congenital heart disease. PH can also be genetically inherited, although this is very rare.

Facts about Pulmonary Hypertension:

What is pulmonary hypertension?

Pulmonary hypertension is a medical term describing conditions in which blood pressure is abnormally high within the blood vessels of the lungs. It is generally unrelated to the more common type of hypertension (high blood pressure) which affects only arteries in the body outside of the lung.

What can cause pulmonary hypertension?

Many conditions can cause pulmonary hypertension including lung diseases (eg, emphysema, sleep apnea), poor performance of the heart or heart valves, congenital heart disease, obstruction of the pulmonary vessels by blood clots, auto immune diseases(e.g., scleroderma, lupus), use of certain drugs (e.g. Fen-Phen), or infection with the human immunodeficiency virus (HIV). When no cause can be found, pulmonary hypertension is termed "primary."

Why is pulmonary hypertension harmful?

Pulmonary hypertension interferes with the body's ability to take up oxygen from the air into the bloodstream. Over time, high pressures in the pulmonary vessels put a strain on the right-sided chambers of the heart and cause them to fail. The result of these two processes is that an individual's activity is progressively limited by the ability of the heart and lungs to deliver adequate amounts of oxygen to exercising muscles. Ultimately, the heart enlarges, becomes more susceptible to abnormal rhythms, and may ultimately become unable to pump adequately.

What symptoms can pulmonary hypertension cause?

The most common complaint by people with pulmonary hypertension is that they become short of breath with exertion. The onset of symptoms is usually slow and gradual, and patients frequently attribute these sensations to being "out of shape." Other symptoms can include a chronic cough (sometimes productive of blood), hoarseness, fatigue, chest pain, lightheadedness, lethargy, and fainting with exertion. If pulmonary hypertension progresses to cause heart failure, swelling of the legs may be apparent, and congestion of the liver may produce abdominal pain and nausea.

What is the treatment for pulmonary hypertension?

The optimal treatment of pulmonary hypertension requires proper identification and maximal treatment of its underlying cause. In patients with primary pulmonary hypertension, additional testing is required to determine if treatment with pills (e.g. Calcium channel blockers, Sildenafil or endothelin receptor antagonists) can be effective in lowering pulmonary pressures. If pills are not effective treatment, prostacyclins can be administered intravenously (epoprostenol /Flolan), subcutaneously (treprostinil /Remodulin) or inhaled (Iloprost). Combination of these drugs may be used in certain situations where single drug is not effective. Lung transplantation may ultimately be required.

Tests needed to diagnose pulmonary hypertension.

The following are typical approaches used by PH specialists, but the diagnostic procedure will vary from doctor to doctor.

Physical exam. A routine checkup seldom discovers PH, so it often goes undiagnosed. Because the symptoms of PH are common to many diseases, personal and family medical histories are important. Your doctor will use a stethoscope to listen for unusual heart sounds. Your doctor will also feel for a right ventricular or parasternal lift, for an enlarged (or even throbbing) liver, and for fluid in your abdomen (ascites). Your ankles and lower legs will be checked for swelling (edema), and the jugular vein in your neck examined for swelling. The doctor will probably look at your fingers, because a long period of low concentrations of oxygen in the blood sometimes causes nail beds to take on a bluish tint (cyanosis) or fingers to form a small bulge at the end (clubbing).

Electrocardiogram (ECG). This is one of the first tests done on a potential PH patient. Electrodes are stuck to your skin and a recording is made of the electrical impulses of your heart.

Blood tests are done to find any underlying cause of pulmonary hypertension and look for effect of pulmonary hypertension on the body.

Chest x-rays is done to look for the size of the heart, pulmonary vessels and lung condition as a whole.

Doppler Echocardiogram. This procedure is painless and is often used both to make a preliminary diagnosis and to later monitor a patient's condition. Doppler-echocardiography can also show that a patient has congenital heart disease, which may have caused the patient's PH.

Here's what to expect: a technician will put some sticky-backed electrodes (patches) on your skin. You lie on your side in a darkened room while the technician uses bouncing sound waves (sonar, or ultrasound) to make a moving image of your heart (the machine works a lot like a fisherman's depth and fish finder, and is the same machine that obstetricians use to take pictures of a fetus developing in a mother's uterus). A chilly "transducer" (it looks like a microphone attached to a cable) is pressed against your chest, along with some clear jelly to enhance the transducer's ability to pick up sound waves. The microphone first sends the sound waves into your body and then picks up their echoes when they hit internal surfaces like a heart valve.

Because some PH patients may have an elevated PAP only while exercising, many experts do exercise echos while their patient is exercising, usually on a semi-erect or supine bicycle. When an exercise echo is done immediately after the patient stops exercising, the results are less accurate.

As far as is known, it does not harm the body to have these high-frequency sound waves pass through it. No x-rays or needles are involved in this procedure. This is why the procedure is called "noninvasive."

An echo can reveal whether the right ventricle is contracting well or poorly. Cardiac output can be estimated from an echo, although the measurement is not always accurate.

After the test, mathematical calculations usually allow an expert to estimate your systolic pulmonary artery pressure (PAP). To calculate your mean PAP you need to know your diastolic PAP as well, which is only with a cardiac catheterization (see below).

Computed tomography (CT or CAT scans) uses a computer hooked up to an x-ray machine that rapidly rotates around you taking pictures from many angles. The computer translates these images into detailed, 3-D "slices" of your body, revealing much that can't be seen by an ordinary x-ray. CT scans are getting better and better as a diagnostic tool, and can detect blood clots in the large arteries of your lungs, yield information about your heart, and diagnose lung disease. CT scans can sometimes find other causes for your symptoms, such as pulmonary fibrosis or emphysema (these diseases can lead to PH). A CT scan may reveal blood clot (chronic thromboembolic) problems (although a negative scan doesn't completely rule out such clots), blocked pulmonary veins (venooclusive disease), tumors, inflamed vessels, or mediastinal fibrosis. Some PH specialists are now using ultra fast CT scans (called electron-beam tomography or EBT) in addition to echocardiograms, to monitor changes in the size of a patient's right atrium and right ventricle. These scanners take their pictures faster than conventional CT scanners and thus can better "freeze" the heart in motion.

Magnetic resonance imaging (MRI) scans for PH have also improved. Like CT scans, they are noninvasive (nothing goes inside your body). Magnetic fields and radio waves produce pictures of your heart and arteries; no radiation is involved and the procedure is not thought to involve any risk. It's painless, but expensive. The pictures look sort of like x-rays, but can often show some tissues x-rays miss.

An MRI might be ordered to look for large blood clots (although it can't totally rule them out), problems with the structure of pulmonary arteries, the size and shape of the right ventricle, the thickness of the wall of the right ventricle (which correlates, in an MRI, with mean PAP) and other relevant things. Your mean PAP can be estimated from information obtained with an MRI.

Nuclear scan (ventilation / perfusion scan or V/Q scan). This is done to take a look at the plumbing in your lungs and see if the trouble could lie in the large or the small vessels.

The Q of V/Q: a radioactive isotope is injected into a peripheral vein, and your chest is then scanned for radioactivity. It is usually done on an outpatient basis. The isotope's movement in the pulmonary arteries is tracked from outside your body by special cameras (sort of like Geiger counters). Your doctor looks for areas where blood flow is blocked or reduced by clots. If none are found, it means the problem is probably in the small vessels. If significant blockages (clots) are found in the larger arteries, this can be good news, because chronic thromboembolic disease can often be cured by surgery. Therefore, these clots should be looked for in all PH patients. If your V/Q scan is normal, you can usually (not always) rule out chronic thromboembolic disease.

Pulmonary function tests. These tests measure how much air your lungs can hold, how much air moves in and out of them, and their ability to exchange oxygen and carbon dioxide. They may be done to assess the severity of your PH and glean clues as to its cause.

In one test, you breathe in until it hurts, then expel that breath as fast and thoroughly as you can. This reveals your lung volume. The lungs of many persons with PH process a slightly smaller volume of air, probably because the PH makes them stiffer. (If the volume found is less than 70 percent of normal, something other than PH may be causing the reduction in volume.)

In another test, you breathe in and out as deep and fast as you can. It can be quite stressful, especially when the technician is yelling at you to try harder.

Pulmonary function tests can also tell if there is a blockage in the trachea, a nerve problem, or a muscular weakness that contributes to breathing difficulties, and whether you hyperventilate (blow off too much carbon dioxide, making you lightheaded).

Carbon monoxide diffusing capacity test (DLCO). A DLCO estimates how well oxygen is transferred from your lungs' air sacs into your blood. Because it's hard to measure this movement using oxygen itself, carbon monoxide (CO) is substituted. You breathe in a little CO, hold your breath for 10 seconds, and then exhale into a CO detector. If no CO is detected, it means it was well absorbed by your lungs (and that oxygen would be well absorbed, too). If CO is still found in the air you breathe out, then it wasn't transferred well from the lungs' air sacs into the blood vessels surrounding them. Patients with IPAH, familial PH, or PH due to chronic thromboembolism often do not exchange quite as much oxygen as they should. However, many lung diseases other than PH can also cause a poor diffusing capacity. A normal test strongly suggests that a patient's PH is not caused by pulmonary fibrosis, emphysema, etc.

If you have limited systemic sclerosis or scleroderma (see Chapter 3), the higher your PAP, the lower you can expect your DLCO to be. Your doctor will probably want to repeat a DLCO test once or twice a year to see if your pulmonary vessels are becoming more damaged.

Exercise tolerance tests. Your doctor might ask you to walk on a treadmill or give you a 6-minute walk test to find your exercise tolerance level. A healthy person should be able to walk at least 500 meters in 6 minutes; someone with moderate PH might manage only 300-400 meters. Children might be asked to ride a stationary bicycle. Your weight, physical conditioning (or lack thereof), lack of effort, and PH may all affect how well you do on the tests.

Cardiopulmonary exercise testing (CPET). CPET is used to tell your specialist how sick you are, and also to see what effects treatments have had upon your condition. In a CPET, you breathe into a mouthpiece (maybe while riding a stationary bicycle or walking on a treadmill) while an ECG is being done. Although not painful, it's not a glamorous procedure. If you are feeling tired the day you take exercise tests, you may find them exhausting in more than one sense, and may want to arrange for somebody to drive you home afterwards.

Polysomnogram. This is a combination of tests done if sleep apnea is suspected. (Sleep apnea is when you episodically stop breathing at night.) The tests monitor brain wave activity (with an electroencephalogram or EEG), the amount of oxygen in your blood (with a pulse oximeter), and the movement of air in and out a nostril as you breathe, and the up and down movement of your chest wall.

Right-heart catheterization. This is still one of the most accurate and useful tests for PH, and the only test that directly measures the pressure inside the pulmonary arteries. It should be done in all patients at least once, to get a definitive diagnosis (unless there is some special safety reason for not doing so). If your doctor has good reason to suspect PH, but PH didn't show up on a resting or exercise echo, then a right-heart catheterization might be called for. Because of the accuracy of this test, some doctors use it not only to diagnose, but also to monitor their PH patients. When combined

with the injection of contrast dye (pulmonary angiography) it can tell whether chronic thromboembolic disease is causing your PH.

A right-heart catheterization, vasodilator study, and maybe an angiogram are usually done while you are awake, because the docs need your cooperation in taking deep breaths and such. Children and some adults might be sedated to make them less anxious. You have to spend a long time lying on a hard table (thus earning the appellation “patient”) but most find the procedures more uncomfortable than painful.

Cardiac cath is also a way of finding congenital defects in the heart, such as a hole between heart chambers or the large arteries that isn’t supposed to be there. (Unfortunately, a cardiac cath does not detect every type of congenital heart disease.)

For a **pulmonary angiogram**, sometimes done at the same time as the cardiac cath, x-ray dye is injected through the catheter and then an x-ray is taken of the pulmonary arteries to see whether the vascular tree has been “pruned” or blocked by blood clots. This is the very best way to define the anatomy of such clots. (If a lung scan or CT scan has excluded clots in the lungs as a cause, an angiogram is often not necessary.)

Left-heart catheterization. Similar to a right-heart cath, but with the catheter inserted via an artery rather than a vein, this test allows measurements of pressures on the left side of the heart, and is also done to take pictures of the heart and the coronary arteries (a coronary angiogram). In PH patients it is usually done to exclude the possibility that abnormal pressures in the left heart are causing, or contributing to, the elevation of a patient’s PAP.

Heart catheterizations are usually safe if done by a physician with experience working on PH patients. But there are risks involved. Although most complications are minor, and most hospitals are well equipped to deal with them, there is still a tiny risk of infection (less than one in a thousand), and of various uncommon problems (including heart attack, stroke, bleeding, or even death).

Vasodilator study (acute vasodilator challenge). If you have PH, you’d much rather take a pill (such as a calcium channel blocker, or CCB) than undergo more complicated therapy. Therefore, while the catheter is still in place, doctors can evaluate your response to drugs that relax your pulmonary arteries. Sometimes, some doctors will skip this step on certain types of patients who are unlikely to respond well and/or are unlikely to tolerate CCBs: those who have connective tissue disease, advanced Class IV symptoms, significant right ventricular failure, or who are rapidly deteriorating.

Doctors can’t agree on what constitutes “vasoreactivity” or a good (“acute”) response. In the past, it has been somewhere in the neighborhood of a 15-30 percent decline in PVR. But recently, Dr. Olivier Sitbon in (Université Paris-Sud, Clamart, France) showed that for a patient to have a really good response, their mean PAP should fall to at least 40 mm Hg or even lower while being given the vasodilator.

Maybe 10 to 15 percent of IPAH patients have a good response to a vasodilator. Even fewer patients with secondary PH have a good response. But among children, 30 to 35 percent are vasoreactive.

Not surprisingly, the lucky few are called “responders.” Why do they respond? It is thought that in the early stages of PH, the structural changes to pulmonary arteries are likely to be less, and you are more likely to respond well. If you have really severe PH, the damage to your small pulmonary arteries probably goes well beyond the muscle layer of the vessels, which relaxes in response to vasodilators. The vessel wall becomes stiff and less able to relax.

Responders are usually sent home with CCB pills. After being sent home, responders are carefully monitored. Over time (weeks, months) the dose is usually gradually increased if the patient can tolerate it.

Lung biopsies are only done now in special circumstances, because they yield too little information for the risk involved.

New tests for PH in the future? If you’ve read this far, you’re probably thinking that better ways are needed to diagnose PH and determine the disease’s likely course in different patients. You are right. We need a test that is easy, that can be done in a standard way at any treatment center with reproducible results, that correlates well with survival, that doesn’t hurt much, and that doesn’t cost a lot. That’s wishing for a lot, and is probably more than any one test could ever do given all the types of PH. But improvements over the present diagnostic system are both needed and possible.

Drug therapy for pulmonary hypertension

Secondary hypertension is described in detail in drug therapy section.