PH&

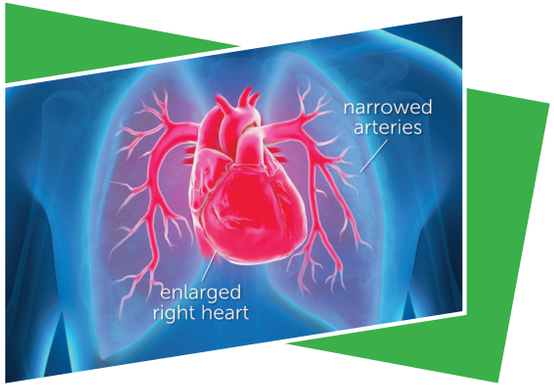
Pulmonary Hypertension
& LIVER DISEASE

PHA
Pulmonary Hypertension Association
Empowered by hope

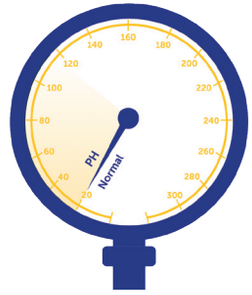
ABOUT PULMONARY HYPERTENSION

Pulmonary hypertension (PH) is a complex and often misunderstood disease. The term PH simply means high blood pressure in the arteries of the lungs. In regular hypertension — also known as high blood pressure or systemic hypertension, which you can check with a blood pressure cuff — the pressure in the arteries of the entire body is higher than it should be. In PH, the blood vessels specifically in the lungs are affected. They can become stiff and narrow, and the right side of the heart must work harder to pump blood through them. There are five groups of PH based on different causes.

Each form of PH is different, so it is important for newly diagnosed patients to find a PH specialist who can accurately pinpoint what is causing their PH. They then can develop a treatment plan for that specific type as soon as possible after a confirmed diagnosis. Every individual with PH is different, and new research with the potential to improve the outlook for people living with this disease is conducted on a continual basis. Once in the care of a PH-treating health care team and on appropriate therapy, individuals with PH can live for many years.



PH, or high blood pressure in the lungs, frequently results from a narrowing of the small blood vessels in the lungs, which leads to a larger right side of the heart.



LIVER DISEASE-ASSOCIATED PH — PORTOPULMONARY HYPERTENSION

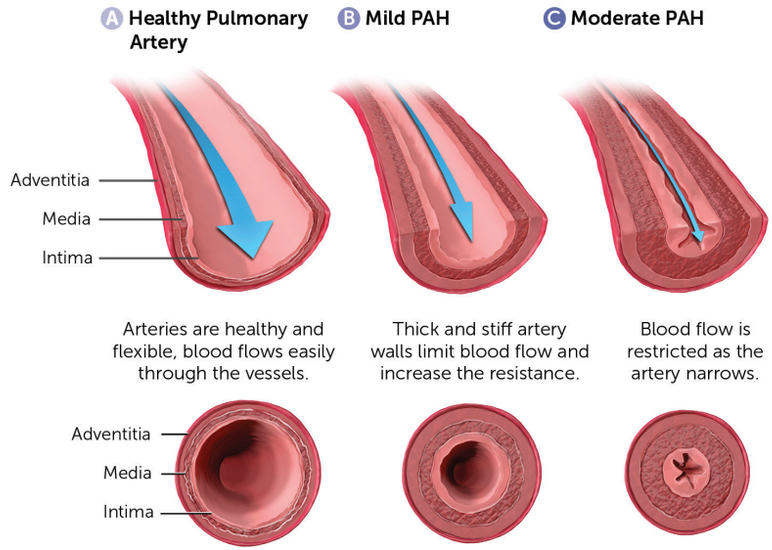
The liver is the largest solid organ in the body, and it has many jobs that are crucial for survival. It produces a substance called bile that breaks down fats for digestion, stores vitamins, makes proteins that are necessary for blood clotting and other functions, and ensures there are stable levels of glucose (sugar) in the blood. Most importantly for this discussion, however, the liver filters the blood and removes harmful substances from it.

If the liver becomes damaged or diseased, it can create problems throughout the rest of the body. Damage to the liver over time can lead to a condition called cirrhosis, which refers to scarring of the liver tissue. This blocks how much blood flows through the liver and impairs its function.

Cirrhosis is the most common cause of portal hypertension, which is increased blood pressure in the portal veins that transport blood from the intestines to the liver. This increased pressure causes blood to bypass the liver. As a result, the blood is not filtered by the liver and chemicals and toxins are not removed from the blood. The blood vessels of the lungs are then exposed to potentially toxic substances that may damage the small arteries of the lungs and cause World Health Organization Group 1 PH (pulmonary arterial hypertension, or PAH).

Portopulmonary hypertension (PoPH) is a type of PAH that occurs as a result of portal hypertension and advanced liver disease. Patients with PoPH experience similar symptoms as patients with other forms of PAH that are not associated with liver disease. These symptoms can include shortness of breath with activity, increased fatigue, swelling of the ankles, legs or abdomen, chest discomfort or pain, and light-headedness and fainting.

PoPH is different from hepatopulmonary syndrome, another type of liver disease-associated abnormality of the pulmonary vessels. In contrast to PoPH, hepatopulmonary syndrome is characterized by widening of the pulmonary blood vessels and low oxygen levels in the blood.



The reason that PoPH develops is unclear, but research has given us some clues. Patients with PoPH have a deficiency of prostacyclin (a substance that causes the blood vessels to relax),[1] and an excess of endothelin 1 (a substance that causes the blood vessels to constrict and the vessel walls to thicken).[2] In addition, it appears that women and those with autoimmune-related cirrhosis may be at increased risk of developing PoPH.[3] Most patients diagnosed with PoPH are adults.

DIAGNOSING POPH

A specialist can diagnose PoPH by identifying high blood pressure in the liver in conjunction with the usual signs of PAH.

A specialist can diagnose PoPH by identifying high blood pressure in the liver in conjunction with the usual signs of PAH. Individuals with PoPH also may be identified when they undergo tests to determine if they are candidates for a liver transplant. All patients who are being evaluated for a liver transplant undergo an echocardiogram (ultrasound of the heart) to screen for PoPH as part of expert recommendations.[4] If the echocardiogram estimates that the pressure in the right side of the heart is higher than normal, that patient must have another test known as a right heart catheterization to test for PoPH. Any patient with chronic liver disease and shortness of breath, even if they are not considering a transplant, should discuss the possibility of having an echocardiogram with a specialist to screen for PH.

[1] Tuder RM, et al. Am J Resp Crit Care Med. 1999;159(6):1925-32.
[2] Benjaminov FS, et al. Gut. 2003;52(9):1355-62.
[3] Kawut SM, et al. Hepatology. 2008;48(1):196-203.
[4] Murray KF, et al. Hepatology. 2005;41(6):1407-32.

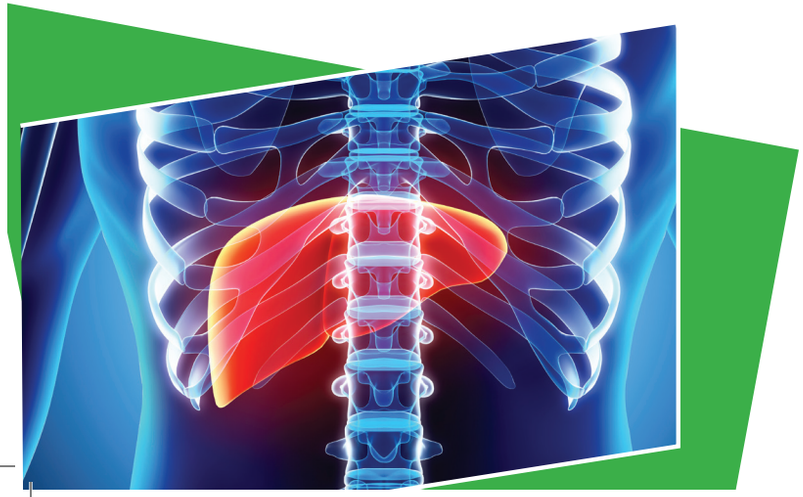
TREATMENT OPTIONS FOR POPH

Treatment options for patients with PoPH are still being studied. Because individuals with PoPH have been excluded from most of the PH-specific drug clinical trials, PAH treatment recommendations for PoPH must be taken from other PAH studies. However, there is hope that existing PH-specific treatments may be helpful. Small studies have described improvement in PoPH with drugs such as epoprostenol, treprostinil, bosentan, ambrisentan, macitentan and sildenafil.[5]

The outcome for persons with PoPH when a liver transplant is attempted continues to be unpredictable. The risk of complications and death from liver transplants increases with higher pressures in the pulmonary arteries.[6] For this reason, it is important to lower the pressure in the pulmonary arteries with PH-specific treatments before liver transplantation. If the pressure is high in the lungs during transplant, mortality during and after surgery is more likely.

However, limited but encouraging data suggest that carefully selected patients who respond to PH-specific therapy can undergo liver transplantation with excellent survival rates and in some cases improvement or complete resolution of PoPH.[7] In all cases, the sooner a patient is tested, the sooner problems like PoPH can be ruled out or addressed.

[5] Krowka MJ, et al. Transplantation. 2016;100(7):1440-52.
[6] Krowka MJ, et al. Liver Transplant. 2000;6(4):443-50.
[7] Savale L, et al. Hepatology. 2017;65(5):1683-92.



ABOUT THE PULMONARY HYPERTENSION ASSOCIATION

PHA's mission is to extend and improve the lives of those affected by PH. PHA's vision is a world without PH, empowered by hope.

The Pulmonary Hypertension Association (PHA) is a community of individuals with PH, caregivers, families, medical professionals and researchers who work together to empower people battling the disease, while supporting research toward improved treatments. PHA was the first organization in the world dedicated to providing comprehensive PH patient and caregiver support, medical education, research and services that improve patients' quality of life.

PHA facilitates more than 200 active support groups around the country and serves as a model for more than 85 international PH organizations. In addition to in-person support, PHA offers a telephone support line, an email mentorship program, educational patient programs and a variety of print and online publications. Every two years, PHA hosts its International PH Conference and Scientific Sessions, which brings together nearly 1,500 individuals with PH, caregivers and medical professionals to share information on the latest research, treatments and lifestyle coping tips.

PHA also has provided more than $8 million for PH research and offers continuing education programs for medical professionals through the *PHA Online University* and an in-person CME program.

PHA would like to thank the following member of the PH medical community for his work in the writing, review and development of this brochure:

Hilary DuBrock, M.D., M.M.Sc., Mayo Clinic, Rochester, Minn.

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