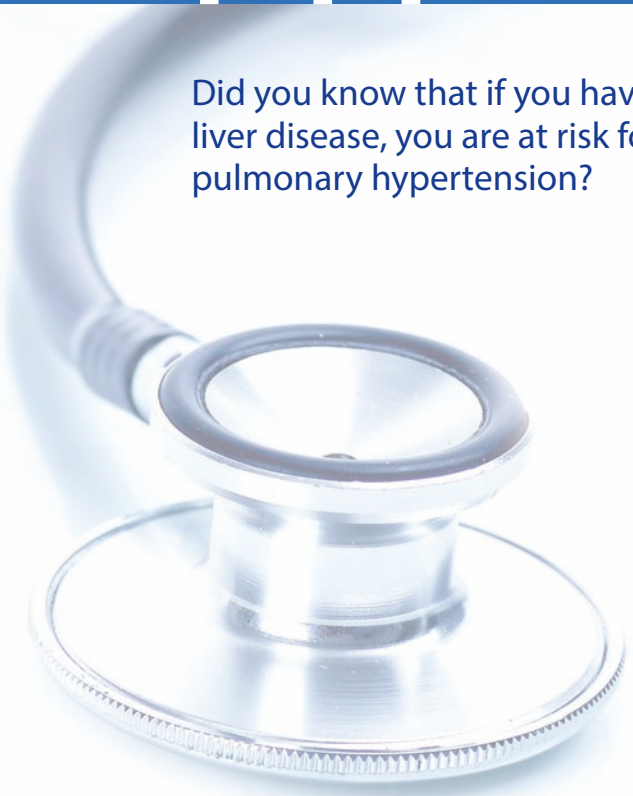
Liver Disease & PH Pulmonary Hypertension

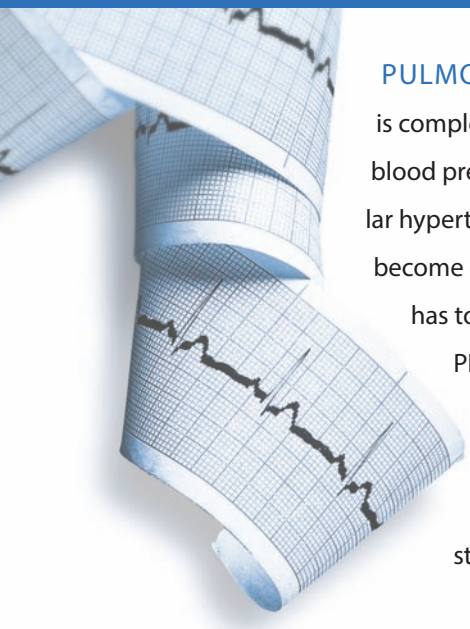
Did you know that if you have liver disease, you are at risk for pulmonary hypertension?



PHA Pulmonary Hypertension Association
Empowered by hope

www.PHAssociation.org

About Pulmonary Hypertension



PULMONARY HYPERTENSION, OR PH, is complex and often misunderstood. PH means high blood pressure in the lungs. PH is different from regular hypertension. In PH, the blood vessels in the lungs become damaged and/or narrowed and the heart has to work harder to pump blood through them. PH can be caused by many different problems such as heart failure, diseases that damage the lung or multiple hardened blood clots, to name a few. It is important to understand that not all PH is the same.

PH affects people of all ages and ethnic backgrounds. The most common symptoms are shortness of breath with physical activity, fatigue, lightheadedness and sometimes fainting. Because these symptoms can be caused by any number of other medical problems, diagnosis is often delayed. Identifying a case of PH can be difficult and may require a specialist. Once the type of PH is diagnosed, however, treatment can begin immediately.

One form of PH is called pulmonary arterial hypertension (PAH). PAH is a complex, progressive type of PH where the high blood pressure in the lungs occurs because tiny blood vessels that carry blood through the lungs (pulmonary arteries) are narrowed, thickened and stiff. As PAH advances, the heart may lose its ability to pump enough blood through the lungs to meet the needs of the body.

There are several types of PAH. Idiopathic PAH (IPAH) means that the patient develops PAH without any other obvious medical problem leading to high blood pressures in the lung. Heritable PAH (HPAH) comes from abnormal genes that cause PAH. Heritable PAH may be passed on to some members of your family. PAH can be associated with other medical conditions such as connective tissue diseases (scleroderma and

lupus for example), chronic liver disease, congenital heart disease, or HIV infection. Finally PAH can be associated with past or present drug use, such as methamphetamines or certain diet pills. It is not known exactly how these medical problems or drugs cause PAH.

PAH is a serious condition, and without treatment, symptoms can only become worse, leading to heart failure and even death. Proper diagnosis and therapy from a doctor who understands PAH is essential. Every patient is different. The choice of treatment is based on how sick a patient is and the risks and benefits of any particular therapy. Regardless of risk, is it important that patients and their healthcare providers engage in frequent follow-ups with ongoing discussions about the management of their condition. Current guidelines suggest that changes in therapy should be considered for patients not reaching their treatment goals.

While no cure has yet been found for PAH, increased research has resulted in treatments that allow patients to live longer, fuller lives with far less interference from the disease. Even more promising research is being conducted every day that is not only advancing our understanding of the PAH disease but also potentially identifying new treatment options for patients in the future.

Liver Disease-Associated PH or Portopulmonary Hypertension

What is liver disease?

To understand liver disease, you must first understand what the liver does. The liver is the largest glandular organ in the body, and it has many jobs. It provides a substance that breaks down fats, produces several important compounds, stores certain vitamins, makes specific amino acids, converts glucose to glycogen, and makes sure there are certain levels of glucose in the blood. Most importantly for this discussion, however, the liver filters the blood and removes harmful substances from it.

Because it has so many jobs to do, the liver is an extremely important organ in keeping the body healthy. Therefore, if the liver becomes damaged or diseased, it creates problems throughout the body. Liver disease can take the form of cirrhosis (damage and scarring of the liver tissues that results in blocked blood flow and impaired liver function), or obstruction of blood flow to the liver without cirrhosis.

How does liver disease relate to pulmonary hypertension?

Liver disease can cause what is known as "portal hypertension," meaning increased blood pressure in the veins that enter the liver. This increased pressure causes blood to bypass the liver. As a result, the blood is not subject to the liver's work, which includes the removal or detoxification of chemicals and poisons in the body. The blood vessels of the lungs are then exposed to possible toxic substances, and this can damage the small arteries of the lungs, causing pulmonary arterial hypertension (PAH).

What is PoPH?

Portopulmonary hypertension, or PoPH, is a type of PAH that occurs as a result of advanced liver disease. This disease has the same characteristic symptoms as those found in cases of PAH that are not associated with liver disease. Those characteristic symptoms of PoPH include blood clots and other changes in the blood vessels of the lungs. Symptoms the patient may notice are similar to those associated with classic PH, including shortness of breath and limited ability to tolerate exercise.

Portopulmonary hypertension is different from hepatopulmonary syndrome (a type of liver disease-associated abnormality of the pulmonary vessels) in which small additional vessels in the lung form and cause to dramatically lower oxygen levels.

Why does PoPH develop?

The reason that PoPH develops is unclear, but research has given us some clues. It is known that patients with PoPH have a deficiency of prostacyclin (a substance that causes the blood vessels to relax), and an excess of endothelin I (an inflammatory mediator that causes the blood vessels to constrict, and also causes the inner and middle layers of the arteries of the lungs to grow). In addi-

tion, it appears that women and those with autoimmune-related cirrhosis may be predisposed to PoPH. Most patients diagnosed with PoPH are adults; few are children.

What makes PoPH so serious?

First, PoPH is a complication of liver disease, which is in itself very serious. Second, PoPH is a serious risk factor if a patient is being considered for a liver transplant. The risk of complications and death increase in a transplant patient with moderate or severe PoPH.

How is PoPH diagnosed?

A specialist can diagnose PoPH by identifying portal hypertension (high pressure in the veins of the liver), in conjunction with the usual signs of PAH. Patients who are being screened to be liver transplant candidates are given an echocardiogram as part of established practice guidelines. If the echocardiogram shows that the pressure in the right side of the heart is abnormally high, that patient will need to have another test, known as a right-heart catheterization, to rule out PoPH. Any patient with chronic liver disease and shortness of breath (even if he or she is not considering a transplant) should discuss with a specialist the possibility of having echocardiography to be screened for PH.

How is PoPH treated?

Treatment of patients with PoPH is an area that is still being studied. Because patients with PoPH have not been included in many of the regular PAH drug studies, our knowledge is limited in terms of which drugs are most beneficial in caring for PoPH patients. However, there is hope that existing PH treatments may be helpful. Small studies done in the U.S. with epoprostenol have been encouraging. In both Europe and the U.S., improvement in PoPH patients has also been observed in small drug studies with bosentan, ambrisentan or sildenafil.

Can patients with PoPH be candidates for a liver transplant?

There is not yet an easy answer to this question, again because studies are so limited. The outcome for patients with PoPH when liver transplant is attempted continues to be unpredictable. If the pressure is high in the lungs during transplant, mortality during and after surgery is more likely.

However, limited but encouraging data suggests that patients who respond to 24-hour continuous intravenous epoprostenol, treprostinil, oral bosentan or sildenafil and who then undergo liver transplantation have excellent survival and in some cases complete resolution of PoPH. In all cases, the sooner a patient is tested, the sooner problems like PoPH can be ruled out or addressed, generally leading to a better outcome for the patient.

PHA Resources

The Pulmonary Hypertension Association (PHA) was founded by and for PH patients. The organization has led the way in bringing pulmonary hypertension into the national and international consciousness. PHA is constantly increasing its services to the medical community through educational programming, membership sections for medical professionals, and much more:

Website:

PHA's website is a comprehensive source of information for patients, caregivers and medical professionals. Please visit us at www.PHAssociation.org.

Find a Doctor:

The "Find a Doctor" section of PHA's website allows patients and referring physicians to search for PH-treating physicians by state at: www.PHAssociation.org/Patients/FindADoctor. While PHA does not endorse any of these physicians, PHA strongly recommends that all PH patients see a PH specialist who will be able to provide them with the best PH care.

Pulmonary Hypertension: A Patient's Survival Guide:

This extraordinary 300+ page book was written by a patient and is medically reviewed and updated annually. It presents the illness in a very human and readable way, covering a wealth of topics like the mechanics of PH, the latest treatments, patient care and lifestyle issues. PHA members receive a discount on this resource. The *Survival Guide* is available for purchase as a paperback and an e-book at: www.PHAssociation.org/SurvivalGuide.

Online information about PH:

For information on PH diagnosis, symptoms, treatments and more, visit www.PHAssociation.org/Patients/AboutPH.

Support Groups:

From the first support group started in 1990 around a kitchen table in Florida, PHA grew to 45 groups in 2001 and to more than 245 in 2013. In many places, patients have the opportunity to meet, learn from and find common understanding with others in similar circumstances. Find a support group in your area at www.PHAssociation.org/LocalSupportGroups.

About the Pulmonary Hypertension Association

The mission of the Pulmonary Hypertension Association is to find ways to prevent and cure pulmonary hypertension, and to provide hope for the pulmonary hypertension community through support, education, research, advocacy and awareness. PHA's members form a community that is fighting back against this terrible illness.

PHA fulfills its mission through:

- Funding for research
- Quarterly medical journal *Advances in Pulmonary Hypertension*
- *PHA Online University* offering free CME credits and the latest information on pulmonary hypertension (www.PHAOnlineUniv.org)
- Professional membership sections:
  - PH Clinicians and Researchers (PHCR)—for physicians and doctorate-level researchers
  - PH Professional Network—for nurses and allied health professionals
- Educational conferences and materials for medical professionals and patients
- A wealth of information in the *Survival Guide*
- PH patient support groups
- Quarterly newsletter *Pathlight*
- Advocacy and awareness campaigns
- Toll-free Patient-to-Patient Support Line (1-800-748-7274)
- PHA website with PH discussion boards, email groups and online support chats (www.PHAssociation.org/ConnectOnline)

More Information on Liver Disease

American Liver Foundation: www.liverfoundation.org

International Liver Transplantation Society: www.ilts.org

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

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This publication was supported by Contract Number 200-2007-M-22234 from the Centers for Disease Control and Prevention. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention, the Department of Health and Human Services or the U.S. government.

This publication was produced through an unrestricted educational grant from Actelion Pharmaceuticals US, Inc., Gilead Sciences, Inc. and Pfizer, Inc.