VALDI

Valley Advanced Lung Diseases Institute

# PULMONARY HYPERTENSION

# 2023

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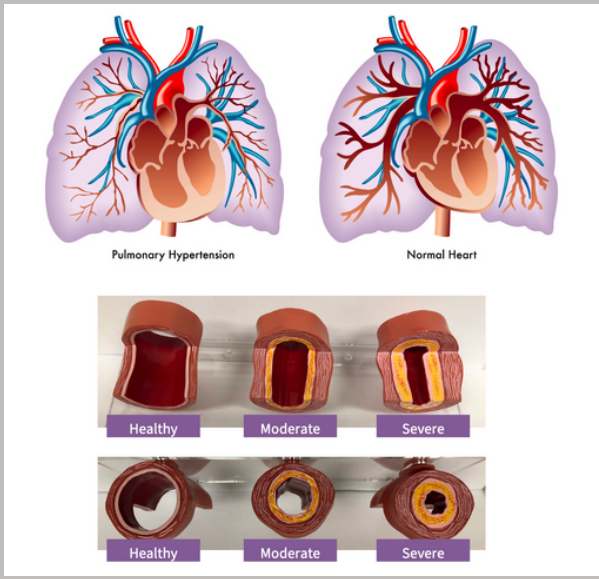
# WHAT IS PULMONARY HYPERTENSION (PH)?

Pulmonary Hypertension (PH), or high blood pressure in the lungs, occurs due to the progressive narrowing of small blood vessels in the lungs which causes the right side of the heart to work harder. Over time, the right side of the heart will become enlarged and weaker, pumping blood less efficiently into or within the lungs and throughout the body. It is a complex and uncommon health condition, that can have serious health consequences, including premature death, if left undiagnosed and/or untreated.




Rare diseases in general practice, such as pulmonary hypertension, are often referred to as the zebra among the horses because “when you hear hoofbeats, you don’t expect to see a zebra”.

# SYMPTOMS OF PH

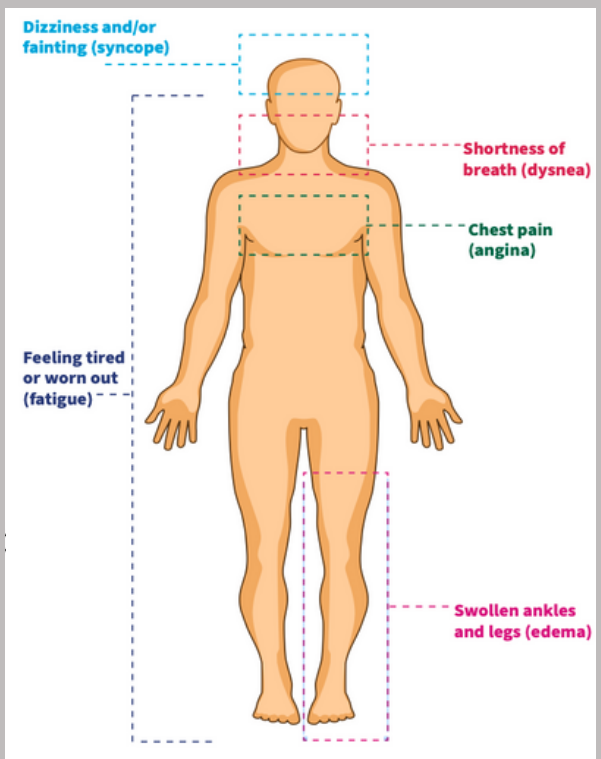
**Syncope**
Dizziness, fainting, or a sudden temporary loss of consciousness caused by a fall in blood pressure.

**Dysnea**
Shortness of breath; difficult or labored breathing.

**Angina**
Severe pain in the chest, often also spreading to the shoulders, arms, and neck.

**Fatigue**
Feeling overtired, with low energy and a strong desire to sleep that interferes with normal daily activities.

**Edema**
Puffiness or swelling caused by fluid in your body’s tissues, often occurring in the feet, ankles and legs.



# TYPES OF PH

**Group I:**

Pulmonary Arterial Hypertension (PAH)
Progressive narrowing of small blood vessels in the lung

1. Unknown Cause (Idiopathic)
2. Familial (genetic)
3. Associated with HIV
4. Connective tissue disease, such as Scleroderma, Rheumatoid arthritis, Lupus, etc.
5. Congenital heart diseases (Heart abnormalities some people are born with such as “holes” in the heart)
6. Chronic liver disease
7. Drugs or toxins, such as street drugs (methamphetamine,
8. cocaine) or certain diet medication (Fenphen and similar pills)
9. A rare entity Pulmonary Veno-Occlusive Disease (PVOD)

**Group II:** PH due to “back-pressure” from left sided heart disease

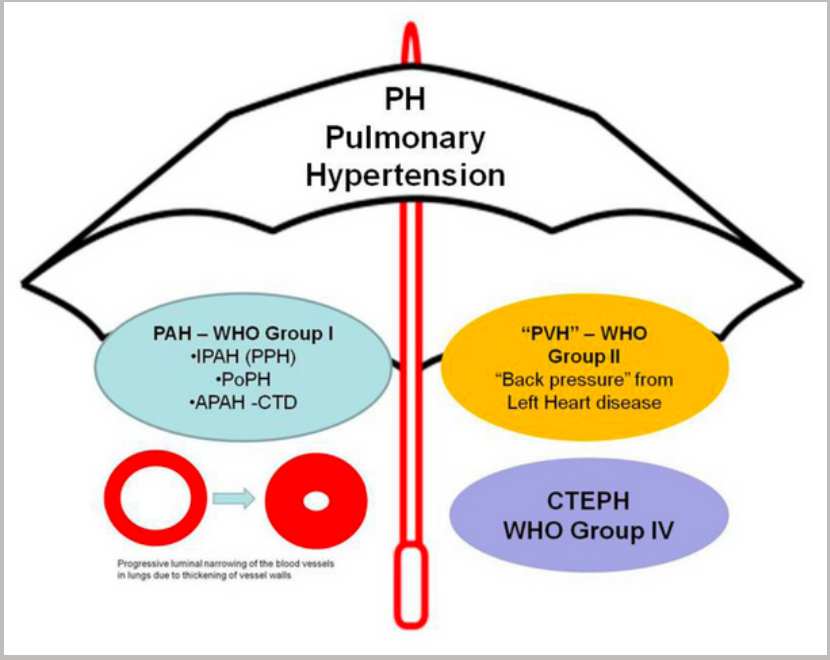
**Group III:** PH due to chronic lung disease such as Pulmonary fibrosis,

**Group IV:**
COPD, sleep apnea and others
PH due to chronic build up of blood clots in the lungs: the most common form of pulmonary hypertension is Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

**Group V:** Mixed bag of rare diseases

# CAUSES OF PH

Many causes of pulmonary hypertension have been identified. PH can affect a person of any age, race, and ethnic background. It is more common in women than men.



# CAUSES OF PH

**GROUP I: PAH**

- Idiopathic Pulmonary Arterial Hypertension (IPAH)

Cannot be linked to other causes and typically occurs in individuals who were otherwise healthy before development of the condition.

- Familial Pulmonary Hypertension

A diagnosis given to patients with idiopathic PH who have siblings with the same diagnosis. About one in 20 patients with idiopathic PH will have one or more relatives with the disease.

- Connective Tissue Diseases (CTD)

A group of diseases in which the immune system becomes "overactive" leading to inflammation in different organs of the body including the lungs (i.e., lung blood vessels). Some types of collagen vascular disease include lupus, scleroderma, and rheumatoid arthritis.

- PH Related to Diet Pills and Stimulants

Use of certain diet pills, weight loss pills, appetite suppressants and stimulants have been associated with the development of PH. In addition, recreational drug abuse, such as methamphetamines and cocaine have been linked to the development of PH.

- Chronic Liver Disease

The mechanisms that lead to PH are more complex with liver disease, but it is well known that a small percentage of patients with cirrhosis will develop PH.

- Pulmonary Veno-Occlusive Disease (PVOD)

This is a rare variant of pulmonary arterial hypertension (PAH) where the small veins/ venules in the lungs are also affected by smooth muscle proliferation resulting in blockage. This is a dangerous variety and traditional PAH drugs may not work.

**GROUP II:**

- **PH due to Left-Sided Heart Disease**

Secondary PH, due to disease in the left side of the heart, typically occurs in patients who have impaired contractility or impaired relaxation of the left heart muscle (also called diastolic dysfunction). Older patients and especially those with a history of coronary artery disease, systemic hypertension, diabetes, and sleep apnea are at a higher risk of developing a "stiff" left heart muscle that leads to impaired relaxation and elevation in left heart pressures. Increased pressure in the left side of the heart will, in turn, back up into the lung blood vessels ("traffic jam" like phenomenon), leading to PH.

**GROUP III:**

- **Chronic Lung Disease**

People who have chronically inflamed or "damaged" lungs from conditions such as emphysema or lung fibrosis (scarring) may be at a higher risk of developing PH.

- **Sleep Apnea and/or Low Oxygen Levels**

Sleep apnea is a condition in which there is narrowing or complete blockage of the airway during sleep. Patients with significant sleep apnea or who experience low oxygen levels at night carry a higher risk of developing PH.

**GROUP IV:**

- **Chronic Thromboembolic Pulmonary Hypertension (CTEPH)**

Patients who have had blood clots in their veins such as deep vein thrombosis (DVT) and/or pulmonary embolism (PE) can infrequently develop PH in due course over a period of months to years as a result of "small clots" clogging up the small lung blood vessels.

**GROUP V:**

- **Miscellaneous**

A miscellaneous group of rare diseases that can result in PH due to unknown mechanisms.

# SEVERITY ASSESSMENT
## – BY FUNCTIONAL CLASS

The severity of the condition is often assessed by a combination of many factors. Functional status" of a patient is often determined by the following scale.

### WHO-NYHA FUNCTIONAL CLASSES

| | |
|---|---|
| CLASS I | No symptoms with ordinary physical activity. |
| CLASS II | Some symptoms with ordinary activity and slight limitation of physical activity. |
| CLASS III | Symptoms with less than ordinary activity and increased limitation of physical activity. |
| CLASS IV | Symptoms with any activity, possibly even while at rest. |

# EVALUATION

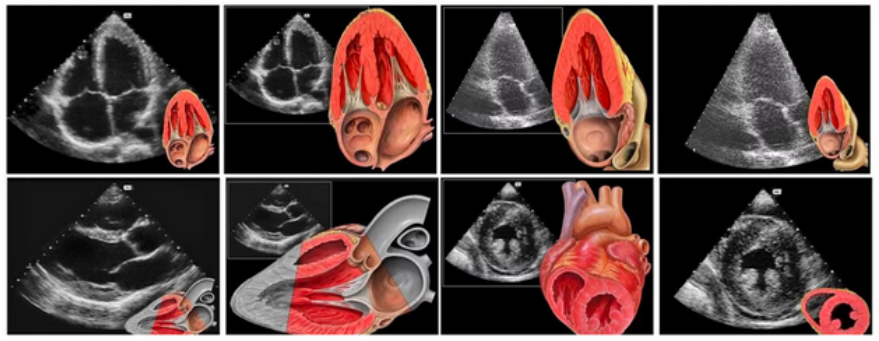
Given the complexity of the disease state and interactions, many different tests may be required to achieve an accurate diagnosis.

The tests may broadly include:

- Laboratory Testing
- Imaging: X-rays, CT Scan and VQ Scans, Cardiac MRI
- Special echocardiograms (ECG) referred to as “PH Protocol”
- Pulmonary function testing including a six-minute walk test.

## TRANSTHORACIC ECHOCARDIOGRAM (TTE)

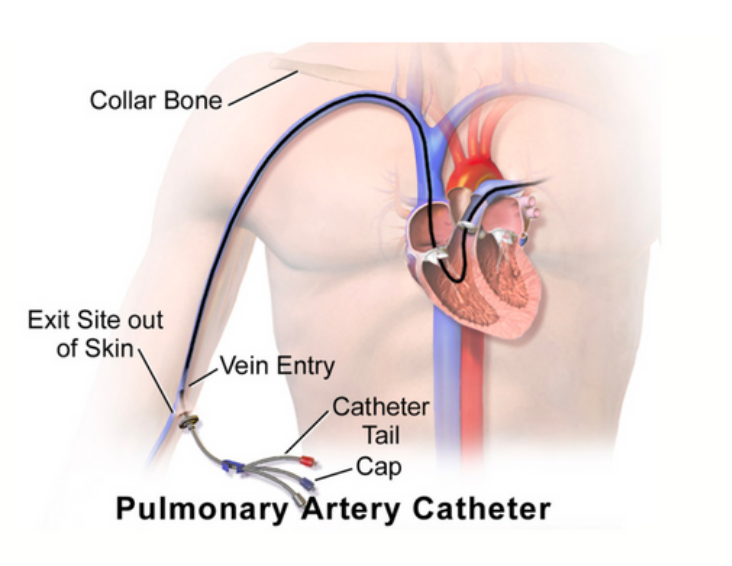
A non-invasive procedure which uses high frequency sound waves (ultrasound) to create a moving picture of your heart through the chest wall. This allows for real-time evaluation of how the heart is working.



## RIGHT HEART CATHETERIZATION

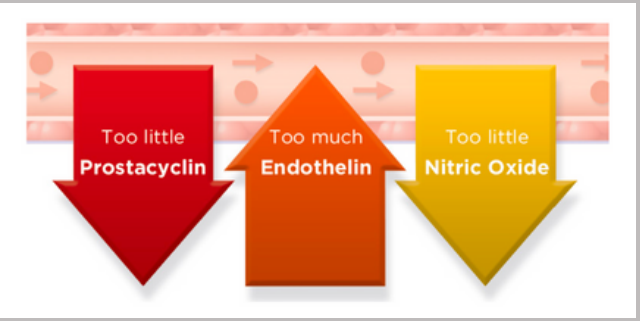
An invasive test that involves a tiny puncture of the skin and into a vein to directly measure the pressures in your heart and lungs. This is a painless procedure that is easily done in about half a day at the hospital.

This is the most important test that confirms a definitive diagnosis and type.



# TREATMENT OF PH

PH is a chronic condition that is incurable. It is difficult to diagnose. Fortunately, newer therapies have emerged over the last two decades that have dramatically influenced the management of this challenging condition. With modern therapeutic options, patients feel better and live longer.




Three main pathways have been well described in the mechanism of this condition. Treatment consists of influencing these pathways towards a favorable response of "opening up" the small blood vessels in the lungs. They are often referred to as "vasodilators" i.e., chemicals that open blood vessels. Prostacyclin, endothelin, and nitric oxide are three substances that are present in the body. If their levels become unbalanced, the blood vessels may narrow, which can lead to PH.

## VASODILATORS

**I. Nitric Oxide Pathway**

**a. Phosphodiesterase inhibitors:** Sildenafil (Revatio) - three times per day and Tadalafil (Adcirca) - once a day — This class of medication works through the nitric oxide pathway and enriches nitric oxide in the blood vessel resulting in the opening up of small blood vessels in the lungs.

**b. Riociguat:** (Adempas) - three times per day — This drug also works through the nitric oxide pathway and "stimulates" its production, resulting in the opening up of small blood vessels of the lungs.

**II. Endothelin Pathway**

**a. Endothelin antagonists:** Macitentan (Opsumit) - once per day, Ambrisentan (Letairis - once a day) and Bosentan (Tracleer) - twice a day. This class of medication works through inhibiting the "endothelin" in the blood vessels resulting in improved flow of blood through the blood vessels in the lungs.

**III. Prostacyclin Pathway**

a. **Prostacyclin analogues** are compounds that directly replace or replenish the body's own "prostacyclin" and open up blood vessels. This medication can be administered via several routes:

i. Oral formulation as a pill - three times per day

ii. Inhaled route via a nebulizer apparatus (see Figures 1 & 2) four times per day. New, alternative inhalers will become available in the near future.

iii. Continuous intravenous infusion through a long term IV line and a special delivery pump (see Figure 3). These modalities need special training and education to use efficiently.

iv. Subcutaneous route (under the skin) - continuous infusion via a special pump. One option resembles a cell phone (see figure 4) and the other is a smaller more discreet version (see fig 5)

# TREATMENT OF PH

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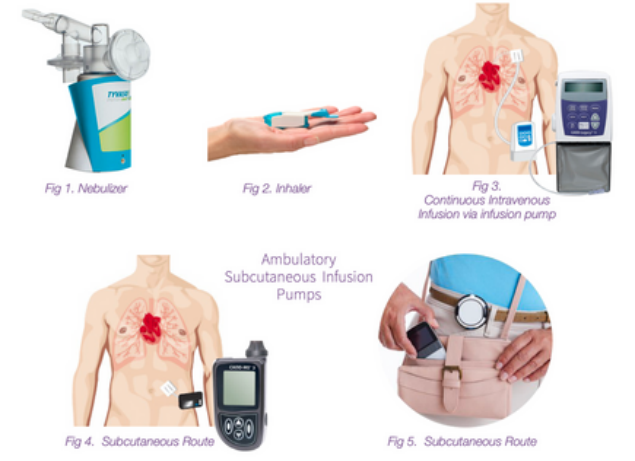


The continuous injectable form of medication delivery is considered to be the strongest mode of intervention and often is the preferred choice in patients deemed to have very severe disease.

b. Another option is Selexipag (Uptravi), a prostacyclin "stimulator" tablet that works by stimulating the body's own prostacyclin production. It is taken twice daily.

**IV. Calcium Channel Blockers**

a. This "old" medication may help in a small proportion of patients who reacted quickly and favorably to nitric oxide gas during right heart catheterization. It does not work and/or may be harmful in patients who did not show this response.

## SUPPORTIVE THERAPIES

- Oxygen – Inhaled by patients via a nasal cannula or face mask.
- Diuretics – Rids excess fluid that puts pressure on the heart. Excess fluid management is a key aspect in the optimization of this condition.
  This can be achieved by:
  1. Salt restriction via dietary intake
  2. Diuretic medication that rids excess salt from the body
- Anticoagulants – Blood-thinning agents.
- Digoxin – Assists the pumping of the heart.

Several new medications are on the horizon. Therefore, there are many choices of therapies for patients currently being studied.

## LUNG TRANSPLANTATION

Lung transplantation might be appropriate for some patients with very advanced disease despite maximum therapy. Given the complexity of the diagnosis and treatment modalities, it is very important that patients are evaluated at a pulmonary hypertension center with trained physicians who can diagnose and treat PH with the full range of treatment options available.

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