Pulmonary hypertension is defined as a pulmonary artery mean pressure (PAPm) of 25mmHg or greater and may be precapillary or postcapillary in etiology.

Laboratory investigations:
- A collagen vascular screen, including antinuclear antibodies, rheumatoid factor, and erythrocyte sedimentation rate, is often helpful in detecting autoimmune disease, although some patients with IPAH/PPH will have a low titer positive antinuclear antibody test.
- Liver function tests (aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase) may be elevated in patients with right ventricular failure and passive hepatic congestion but may also be associated with underlying liver disease. Liver disease with portal hypertension has been associated with the development of pulmonary hypertension.
- Thyroid function tests may be abnormal in patients with IPAH/PPH and should be excluded with thyroid function testing.
- HIV testing and hepatitis serologic studies should be considered in patients at risk.
- Routine laboratory studies such as the complete blood cell count, complete metabolic panel, prothrombin time, and partial thromboplastin time are recommended during the initial evaluation and as indicated to monitor the patient's long-term clinical status.

Echocardiography:
- Doppler echocardiography is useful in estimating the severity of pulmonary hypertension and detecting left-sided heart disease.
- Bubble contrast echocardiography may detect a right-to-left shunt, but exclusion of a left-to-right intracardiac shunt may require cardiac catheterization with an oximetry series.

Radiological investigation:
- Chest radiography may reveal enlargement of the central pulmonary vessels and evidence of right ventricular enlargement.
- Evidence of parenchymal lung disease may be apparent.
- When pulmonary hypertension is suspected, pulmonary function testing and high-resolution computed tomography (HRCT) of the chest may be indicated.
- Ventilation-perfusion lung scanning should be performed in an attempt to exclude chronic-recurrent pulmonary thromboembolic disease, which is among the most preventable and treatable causes of pulmonary hypertension.
- Although contrast medium-enhanced CT has been popularized recently for the diagnosis of acute pulmonary thromboembolic disease, there is limited experience with this technique in chronic thromboembolic disease.

Pulmonary function testing:
- Pulmonary function testing is indicated to detect underlying parenchymal lung disease.
- The diffusing capacity is often reduced in pulmonary vascular disease, consistent with impaired gas exchange.
- Oximetry testing of patients at rest, with exertion, and nocturnally, is useful in detecting hypoxemia and the need for supplemental oxygen.

Right heart catheterization:
- Right-sided heart catheterization remains an important part of the evaluation. Left-sided heart dysfunction and intracardiac shunts can be excluded, the degree of pulmonary hypertension can be accurately quantified, and the cardiac output can be measured. PVR can then be calculated.
- Acute pulmonary vasoactivity can be assessed using a short-acting agent such as prostacyclin (epoprostenol), inhaled nitric oxide, or intravenous adenosine.
- The European Society of Cardiology consensus definition of a positive acute vasodilator response in an IPAH/PPH patient is a fall of PAPm of at least 10 mmHg to less than or equal to 40 mm Hg, with an increased or unchanged cardiac output.

The primary goal of acute vasodilator testing in patients with IPAH/PPH is to identify patients who may be effectively treated with oral calcium channel blockers.

1. Warfarin, Oxygen, Diuretics, Digoxin, and Vaccination:
   - Improved survival has been achieved with oral anticoagulation in IPAH/PPH. The target International Normalized Ratio in these patients is 1.5 to 2.5.
   - Anticoagulation of patients with PAH occurring in association with other underlying processes is controversial.

2. Calcium Channel Blockers:
   - Patients with IPAH/PPH who respond to vasodilators and calcium channel blockers generally have improved survival. Unfortunately, this lends support to the relatively small proportion of patients, comprising fewer than 20% of IPAH/PPH patients and even fewer patients with other causes of PAH.

3. Prostanoids:
   - Epoprostenol, iloprost, treprostinil, and beraprost.

4. Endothelin Receptor Antagonists:
   - Endothelin-1 is a vas constrictor and a smooth muscle mitogen that may contribute to the pathogenesis of PAH. Endothelin-1 expression, production, and concentration in plasma and lung tissue are elevated in patients with PAH, and these levels are correlated with disease severity.
   - Bosentan.

5. Phosphodiesterase Inhibitors:
   - Phosphodiesterase (PDE) inhibitors are enzymes that hydrolyze the cyclic nucleotides, cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP), and limit their intracellular signaling. Drugs that selectively inhibit cGMP-specific PDEs (or type 5, PDEs inhibitors) augment the pulmonary vascular response to endogenous or inhaled nitric oxide in models of pulmonary hypertension.
   - Iloprost.

6. Inhaled Nitric Oxide:
   - Inhaled nitric oxide has been shown to potentiate selective pulmonary vasodilator effects during brief treatment of adults with IPAH/PPH. It is a potent pulmonary vasodilator in newborns with pulmonary hypertension (PPHN), children with congenital heart disease, and patients with postoperative pulmonary hypertension, acute respiratory distress syndrome, or undergoing lung transplantation. It is of substantial benefit in PPHN, decreasing the need for support with extracorporeal membrane oxygenation (ECMO).

7. Lung transplantation:
   - Lung transplantation for PAH is generally reserved for patients whose condition is failing despite the best available medical therapy. The timing of transplantation in PAH is challenging. It is probably most useful in patients showing clear evidence of deterioration, such as decline in functional capacity and the development of right-sided heart failure, despite maximal medical therapy.

Pulmonary vascular disease in liver disease:
- Patients with chronic liver disease have an increased prevalence of pulmonary vascular disease. Two forms of pulmonary vascular disease can complicate chronic liver disease: the hepatopulmonary syndrome and portopulmonary hypertension. Both tend to occur in patients with chronic, late-stage liver disease, and death may increase the risk associated with liver transplantation.

Special situations in ICU:
- Initial therapy may be directed at an underlying cause or contributing factor, such as using continuous positive airway pressure (CPAP) and supplemental oxygen for PAH associated with obstructive sleep apnea.
- Following the identification and treatment of underlying associated disorders and contributing factors, specific therapy for PAH should be considered.
- IPAH/PPH carried a very poor prognosis (median survival approximately 2.8 years from the date of diagnosis) through the mid-1980s. Subsequently, a number of therapeutic options have been developed, and three have been approved by the U.S. Food and Drug Administration (FDA): epoprostenol, treprostinil, and bosentan.
   - Other agents that are being studied for PAH include sitaxsenten, ambrisentan, sildenafil, and inhaled iloprost.
   - Paul Young 09/01/09

Post-capillary causes include processes affecting the left side of the heart (e.g., left ventricular systolic or diastolic dysfunction, mitral stenosis or regurgitation, aortic valve disease) or, more rarely, the pulmonary veins (pulmonary veno-occlusive disease). Management of postcapillary pulmonary hypertension typically involves treating the underlying left-sided cardiac process. Medications used to treat precapillary pulmonary hypertension are often not only ineffective for postcapillary pulmonary hypertension but may, in fact, be harmful, potentially leading to the development of left-sided heart failure.