Pulmonary Hypertension: Causes, Symptoms and Treatment

Pulmonary Hypertension is defined as a mean pulmonary artery pressure (mPAP) ? **25 mmHg at rest** (per older definitions) or **>20 mmHg** based on newer guidelines confirmed by **right heart catheterization** .

- **Normal mPAP** : 10–20 mmHg
- **PH Threshold** : >20 mmHg (at rest)
- **PH with clinical significance** : Often with **pulmonary vascular resistance (PVR) ? 3 Wood units**

  High-Yield : Right heart catheterization is the **gold standard** for diagnosis.

Pathophysiology

PH results from **increased pulmonary vascular resistance (PVR)** or **elevated left heart pressures** , leading to **right ventricular strain and failure** over time.

Key Mechanisms:

1. **Vasoconstriction**
2. **Vascular remodeling** – due to endothelial dysfunction, proliferation, and fibrosis
3. **Thrombosis in situ**
4. **Inflammation**

Histological Features:

- Intimal fibrosis
- Medial hypertrophy
- Plexiform lesions in advanced disease
- Thrombotic arteriopathy

  High-Yield Mnemonic : " **V-R-I-T** "
  V asoconstriction, **R** emodeling, **I** nflammation, **T** hrombosis

Classification (WHO Groups)

Group	Cause
Group 1	Pulmonary Arterial Hypertension (PAH): idiopathic, heritable, drugs (e.g., fenfluramine), connective tissue disease
Group 2	Left heart disease (e.g., LV dysfunction, mitral valve disease)

Group	Cause
Group 3	Lung diseases/hypoxia (e.g., COPD, ILD, sleep apnea)
Group 4	Chronic thromboembolic pulmonary hypertension (CTEPH)
Group 5	Multifactorial or unclear causes (e.g., sarcoidosis, metabolic disorders)

New York Heart Association (NYHA)/WHO Functional Classification

Class	Symptoms
I	No limitation; ordinary physical activity does not cause symptoms
II	Slight limitation; comfortable at rest; ordinary activity causes symptoms
III	Marked limitation; less-than-ordinary activity causes symptoms
IV	Inability to perform any activity without symptoms; signs of right heart failure present

Clinical Features

Symptoms:

- **Exertional dyspnea** (most common)
- Fatigue
- Chest pain (angina)
- **Syncope**
- Non-productive cough
- Hemoptysis (rare)
- Palpitations

Physical Examination:

- **Loud P2** (accentuated pulmonary component of S2)
- Right ventricular heave
- Jugular venous distension (JVD)
- Right-sided S3 gallop
- **Tricuspid regurgitation murmur**
- Hepatomegaly
- Peripheral edema
- Cyanosis (advanced disease)

Diagnosis

Gold Standard:

- **Right Heart Catheterization** – confirms mPAP >20 mmHg

Supporting Investigations:

Test	Findings
Echocardiography with Doppler	RV hypertrophy/dilatation, elevated PAP
CT Chest	Enlarged pulmonary arteries
Chest X-ray	Prominent pulmonary arteries, RV enlargement
ECG	Right axis deviation, right atrial enlargement, RBBB
ABG	Respiratory alkalosis (low PaCO?) due to hyperventilation
V/Q Scan	Used to detect CTEPH
Pulmonary Function Test (PFT)	Rule out obstructive/restrictive diseases
MRI	RV structure/function analysis
Laboratory	ANA, HIV serology to assess for secondary causes

Treatment

General Measures:

- Oxygen therapy (especially if hypoxemic)
- Diuretics for volume overload
- Salt restriction
- Vaccination (influenza, pneumococcal)
- Anticoagulation (especially in CTEPH)

Targeted Therapies for PAH (Group 1):

Drug Class	Examples	Indication
Calcium Channel Blockers	Amlodipine, Nifedipine	Only if vasoreactivity testing is positive
Endothelin Receptor Antagonists	Bosentan, Ambrisentan	WHO Class II or III
PDE-5 Inhibitors	Sildenafil, Tadalafil	WHO Class II or III
Prostacyclin Analogs	Epoprostenol (IV), Treprostinil	Severe cases, Class III-IV
Soluble Guanylate Cyclase Stimulators	Riociguat	PAH and CTEPH
Inhaled Nitric Oxide (iNO)	ICU use for refractory hypoxemia	Reduces PVR

High-Yield : **Epoprostenol** (continuous IV infusion) is the only treatment shown to **improve survival** in advanced PAH.

Treatment by WHO Group:

- **Group 1 (PAH)** – Targeted therapies + supportive care
- **Group 2 (Left heart disease)** – Treat underlying cardiac condition
- **Group 3 (Lung disease)** – Oxygen therapy, treat primary lung disorder
- **Group 4 (CTEPH)** – **Anticoagulation** , **pulmonary thromboendarterectomy** , **riociguat**
- **Group 5** – Treat underlying multifactorial cause

Surgical Options:

- **Atrial septostomy** (palliative)
- **Lung transplantation**
- **Heart-lung transplantation** in selected cases

Prognosis

Prognosis depends on:

- Underlying cause
- Response to treatment
- Functional class
- RV function (most important determinant of survival)

Formula to Remember

mPAP = LAP + (PVR × CO)

- LAP = Left Atrial Pressure
- CO = Cardiac Output
- PVR = Pulmonary Vascular Resistance

Clinical Pearls:

- Women (ages 20–40) are more commonly affected in idiopathic PAH.
- Exercise intolerance is often the earliest symptom.
- Always assess for connective tissue disease, HIV, and chronic thromboembolic disease.
- In patients with COPD and PH, **oxygen therapy** improves survival.
- Use **V/Q scan** over CT angiography to evaluate CTEPH.