

# Pulmonary Hypertension

Pulmonary hypertension (PH) is a progressive condition characterized by elevated pressure in the pulmonary arteries, leading to right heart strain and potential failure if untreated. This guide provides physician assistant (PA) students with a comprehensive framework to understand the pathophysiology, clinical presentation, diagnostic tests, etiologies, WHO classifications, echocardiogram pearls, right heart catheterization findings, treatment strategies, management of decompensated PH with volume overload, and cautions in acute decompensated PH, with case scenarios to apply the knowledge.

## Introduction and Pathophysiology

Pulmonary hypertension is defined as a mean pulmonary artery pressure (mPAP)  $\geq 20$  mmHg at rest, measured by right heart catheterization (RHC). It results from increased pulmonary vascular resistance (PVR) due to vascular remodeling, endothelial dysfunction, and vasoconstriction. The pathophysiology involves:

- Endothelial Dysfunction:
  - Imbalance of vasoactive mediators (e.g., decreased nitric oxide, increased endothelin-1) leads to vasoconstriction and proliferation of vascular smooth muscle.
- Vascular Remodeling:
  - Intimal hyperplasia, medial hypertrophy, and adventitial fibrosis narrow pulmonary arterioles, increasing PVR.
- Thrombosis and Inflammation:
  - In situ thrombosis and inflammatory cytokines contribute to vascular obstruction.
- Right Heart Strain:
  - Elevated pulmonary pressures overload the right ventricle (RV), causing hypertrophy, dilation, and eventual RV failure.
- PH leads to symptoms of dyspnea, fatigue, and right heart failure, with prognosis varying by etiology. Early diagnosis and classification are critical for targeted therapy.

## Clinical Presentation

### History:

- Symptoms:
  - Dyspnea on exertion (most common), fatigue, chest pain (angina-like due to RV ischemia), syncope (low cardiac output), peripheral edema (right heart failure).
- Risk Factors:
  - Connective tissue diseases (e.g., scleroderma), congenital heart disease (CHD), chronic lung diseases, history of pulmonary embolism (PE), family history of PH.
- Systemic Symptoms:
  - Weight gain (edema), cyanosis, palpitations, hoarseness (Ortner's syndrome due to left recurrent laryngeal nerve compression).

### Physical Exam:

- General: Cyanosis, clubbing (if underlying lung disease).
- Cardiac: Loud P2 (pulmonary valve closure), right ventricular heave, tricuspid regurgitation murmur, S3/S4 gallop.
- Pulmonary: Crackles (if left heart disease), wheezing (if COPD).
- Other: Jugular venous distension (JVD), hepatomegaly, ascites, peripheral edema (right heart failure signs).

## Diagnostic Tests and Studies

### Initial Labs:

- CBC: Polycythemia (chronic hypoxia), anemia (if underlying disease).
- BNP/NT-proBNP: Elevated in right heart failure.
- LFTs: Elevated in hepatic congestion (right heart failure).
- HIV, ANA, RF: Screen for HIV, connective tissue diseases (e.g., scleroderma, SLE).
- Thyroid Function: Hyperthyroidism can exacerbate PH.

### Imaging:

- Chest X-Ray: Enlarged pulmonary arteries, RV enlargement, pruning of peripheral vessels.
- CT Chest/CTPA: Assess for chronic thromboembolic disease (CTEPH), interstitial lung disease (ILD), or parenchymal abnormalities.

- Ventilation-Perfusion (V/Q) Scan: Preferred to rule out CTEPH (mismatch indicates chronic emboli).

### Echocardiogram (ECHO):

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- Findings: RV hypertrophy/dilation, tricuspid regurgitation (TR), elevated pulmonary artery systolic pressure (PASP), flattening of interventricular septum ("D-sign").
- Pearls for ECHO in Euvolemic Patients:
  - Ensure euvolemia (no volume overload) to avoid overestimating PASP due to elevated preload.
  - Use TR jet velocity to estimate PASP ( $\text{PASP} = 4 \times [\text{TR velocity}]^2 + \text{RAP}$ ); right atrial pressure (RAP) estimated by IVC size and collapsibility.
  - Assess RV function (e.g., TAPSE <16 mm indicates RV dysfunction; normal  $\geq 16$  mm).
  - Look for secondary causes (e.g., left heart disease with elevated left atrial pressure, shunts).
  - Avoid misinterpretation due to poor acoustic windows; consider agitated saline for shunt detection.

### Pulmonary Function Tests (PFTs):

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Assess for underlying lung disease (e.g., COPD, ILD); restrictive or obstructive patterns may suggest WHO Group 3 PH.

### Right Heart Catheterization (RHC):

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- Gold Standard:
- Confirms PH diagnosis ( $\text{mPAP} \geq 20$  mmHg), classifies etiology.
- Key Measurements:
  - **mPAP:** Mean pulmonary artery pressure;  $\geq 20$  mmHg confirms PH.
  - **Pulmonary Artery Wedge Pressure (PAWP):** Reflects left atrial pressure;  $\leq 15$  mmHg indicates pre-capillary PH (e.g., PAH);  $> 15$  mmHg suggests post-capillary PH (e.g., left heart disease).
  - **PVR:** Calculated as  $(\text{mPAP} - \text{PAWP}) / \text{Cardiac Output}$ ;  $> 3$  Wood units indicates pre-capillary PH.
  - **Cardiac Output (CO):** Low CO indicates RV failure; measured via thermodilution or Fick method.
- Vasoreactivity Testing:
  - Inhaled nitric oxide to assess response (positive if mPAP decreases  $> 10$  mmHg to  $< 40$  mmHg); predicts calcium channel blocker (CCB) response in PAH.

**Table: RHC Findings in Pulmonary Hypertension**

Parameter	Normal Value	PH Finding	Interpretation
mPAP	<20 mmHg	≥20 mmHg	Confirms PH diagnosis
PAWP	≤15 mmHg	≤15 mmHg: Pre-capillary PH	>15 mmHg: Post-capillary PH (e.g., left heart disease)
PVR	<3 Wood units	>3 Wood units	Indicates pre-capillary PH (e.g., PAH, CTEPH)
Cardiac Output	4-8 L/min	Decreased (<4 L/min)	Suggests RV failure

## Different Etiologies and WHO Classifications

### WHO Group 1: Pulmonary Arterial Hypertension (PAH):

- Causes:
  - **Idiopathic (IPAH):** No identifiable cause.
  - **Heritable:** BMPR2 mutations (70% of familial cases).
  - **Associated with:** Connective tissue diseases (e.g., scleroderma), HIV, portal hypertension, CHD, schistosomiasis.
  - **Drug/Toxin-Induced:** Appetite suppressants (e.g., fenfluramine), amphetamines.
- Pathophysiology:
  - Pre-capillary; vascular remodeling, increased PVR.

### WHO Group 2: PH Due to Left Heart Disease:

- Causes:
  - Systolic/diastolic HF (HFrEF, HFpEF).
  - Valvular heart disease (e.g., mitral stenosis, aortic regurgitation).
- Pathophysiology:
  - Post-capillary; elevated left atrial pressure increases pulmonary venous pressure.

### WHO Group 3: PH Due to Lung Diseases and/or Hypoxia:

- Causes:
  - COPD, ILD, obstructive sleep apnea (OSA), chronic high-altitude exposure.
- Pathophysiology:
  - Pre-capillary; hypoxia-induced vasoconstriction, parenchymal destruction.

## WHO Group 4: Chronic Thromboembolic Pulmonary Hypertension (CTEPH):

- Causes:
  - Chronic PE, non-resolving thrombi in pulmonary arteries.
- Pathophysiology:
  - Pre-capillary; mechanical obstruction, secondary vascular remodeling.

## WHO Group 5: PH with Unclear or Multifactorial Mechanisms:

- Causes:
  - Hematologic disorders (e.g., sickle cell disease, myeloproliferative disorders).
  - Systemic disorders (e.g., sarcoidosis, vasculitis).
  - Metabolic disorders (e.g., thyroid disease, Gaucher's disease).
  - Pathophysiology: Varies; often multifactorial.
- **Table:** WHO Classifications of Pulmonary Hypertension

WHO Group	Etiology	Causes	Pathophysiology
Group 1 (PAH)	Pulmonary Arterial Hypertension	Idiopathic, heritable, CTD, HIV, drugs	Pre-capillary, vascular remodeling
Group 2	Left Heart Disease	HFrEF, HFpEF, valvular disease	Post-capillary, elevated LA pressure
Group 3	Lung Diseases/Hypoxia	COPD, ILD, OSA, high altitude	Pre-capillary, hypoxia-induced
Group 4 (CTEPH)	Chronic Thromboembolic	Chronic PE, non-resolving thrombi	Pre-capillary, mechanical obstruction
Group 5	Multifactorial	Sickle cell, sarcoidosis, thyroid disease	Varies, often multifactorial

## Treatment of Decompensated PH with Volume Overload in the Hospital Setting

Decompensated PH with volume overload is a medical emergency, often presenting with worsening RV failure, systemic congestion, and low cardiac output. The goal is to reduce RV preload, improve RV function, and avoid further decompensation.

## Initial Stabilization:

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- Diuresis:
  - IV Loop Diuretics:
    - Furosemide 40-80 mg IV bolus, then 5-20 mg/h infusion (titrate to urine output >100 mL/h). Monitor for hypokalemia, renal function.
    - Add Thiazide: If resistant, metolazone 5-10 mg PO 30 minutes before furosemide dose.
  - Vasodilators (if BP permits):
    - Nitroprusside: 0.3-5 µg/kg/min IV (reduces afterload); monitor BP closely, avoid in severe RV failure with hypotension.
    - Nitroglycerin: 10-50 µg/min IV (reduces preload); contraindicated if SBP <90 mmHg.
  - Oxygen Therapy: Maintain SpO<sub>2</sub> >90% to reduce hypoxic vasoconstriction; avoid over-oxygenation in COPD (risk of CO<sub>2</sub> retention).
  - Inotropic Support:
    - Dobutamine: 2-10 µg/kg/min IV (improves RV contractility); start low, titrate to CO and BP.
    - Milrinone: 0.375-0.75 µg/kg/min IV (inodilator, reduces PVR); caution in hypotension.

## Advanced Therapies (if refractory):

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- Prostacyclin Analogues:
  - Epoprostenol 2-4 ng/kg/min IV (continuous infusion); for severe RV failure in PAH (Group 1).
- Mechanical Support:
  - Extracorporeal membrane oxygenation (ECMO) as a bridge to recovery or transplant in refractory cases.

## Monitoring:

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- Hemodynamics:
  - Central venous pressure (CVP), PAWP via Swan-Ganz catheter (if available); goal CVP <10 mmHg.
- Renal Function:
  - Daily BUN/Cr, electrolytes (hypokalemia risk with diuresis).
- RV Function:
  - Serial ECHO (TAPSE, RV strain); monitor for worsening RV dilation.
- Systemic Perfusion:
  - Lactate, urine output, mental status (low CO signs).

## Cautions in Acute Decompensated PH

Managing acute decompensated PH requires careful consideration to avoid exacerbating RV failure or systemic hypoperfusion. Key cautions include:

### Hypoxia:

Worsens PH by causing pulmonary vasoconstriction; maintain SpO<sub>2</sub> >90% with supplemental oxygen. Avoid permissive hypoxia strategies used in other conditions (e.g., ARDS).

### Preload Dependence of RV:

1. The RV is highly preload-dependent in PH; aggressive diuresis can reduce RV filling, leading to low cardiac output and hypotension.
2. Avoid over-diuresis; monitor CVP and urine output, titrate diuretics cautiously (e.g., reduce dose if CVP <8 mmHg or SBP drops).

### Intubation Risks:

1. Positive pressure ventilation increases intrathoracic pressure, reducing RV preload and worsening RV output.
2. Sedation during intubation can cause systemic vasodilation and hypotension, further compromising RV function.
3. Precaution:
4. Use non-invasive ventilation (e.g., BiPAP) if possible; if intubation required, use low tidal volumes (6 mL/kg), minimize PEEP, and support with inotropes (e.g., dobutamine) to maintain RV preload and BP.

### Systemic Hypotension:

1. Avoid vasodilators (e.g., nitroglycerin) if SBP <90 mmHg; RV perfusion is pressure-dependent, and hypotension can lead to RV ischemia.
2. Use inotropes (e.g., dobutamine, milrinone) to support RV function if hypotensive.

### Arrhythmias:

Atrial arrhythmias (e.g., AF) can significantly reduce RV filling; avoid negative inotropes (e.g., beta-blockers) acutely, as they may worsen RV failure.

## Fluid Overload:

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While diuresis is key, avoid rapid fluid shifts; monitor electrolytes (e.g., potassium, magnesium) to prevent arrhythmias.

## Vasopressors:

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Norepinephrine (5-20 µg/min IV) preferred over phenylephrine (less RV inotropic support); avoid vasopressors that increase PVR (e.g., high-dose dopamine).

## Treatments Depending on Etiology

### General Principles:

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Treat underlying cause (e.g., optimize HF, manage lung disease).

**Supportive care:** Oxygen for hypoxia (SpO<sub>2</sub> >90%), diuretics for RV failure, anticoagulation in select cases (e.g., CTEPH, IPAH).

Advanced therapies (e.g., vasodilators) primarily for WHO Group 1 (PAH).

### WHO Group 1: Pulmonary Arterial Hypertension (PAH):

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- Vasodilators:
  - Endothelin Receptor Antagonists (ERAs):
  - Bosentan 62.5 mg PO BID (titrate to 125 mg BID); monitor LFTs monthly.
  - Phosphodiesterase-5 Inhibitors (PDE5i):
  - Sildenafil 20 mg PO TID; improves exercise capacity.
- Prostacyclin Analogues:
  - Epoprostenol IV (continuous infusion, 2-40 ng/kg/min); treprostinil SC/IV/inhaled.
- Vasoreactivity Responders:
  - High-dose CCBs (e.g., amlodipine 20-30 mg PO daily) if positive vasoreactivity test.
- Supportive:
  - Diuretics (e.g., furosemide 40 mg PO daily for edema), oxygen, anticoagulation (if IPAH).



## WHO Group 2: PH Due to Left Heart Disease:

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- Optimize Left Heart Function:
  - HFrEF:
    - ACEi/ARB (e.g., lisinopril 10 mg PO daily), beta-blockers (e.g., carvedilol 6.25 mg PO BID), diuretics.
  - HFpEF:
    - Diuretics for volume overload, manage comorbidities (e.g., hypertension).
  - Valvular Disease:
    - Surgical repair/replacement (e.g., mitral valve repair for mitral stenosis).
- Avoid Vasodilators:
  - PAH-specific therapies (e.g., sildenafil) may worsen pulmonary edema.

## WHO Group 3: PH Due to Lung Diseases and/or Hypoxia:

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- Treat Underlying Lung Disease:
  - COPD:
    - Bronchodilators (e.g., albuterol), inhaled corticosteroids, oxygen.
  - ILD:
    - Immunosuppressants (e.g., prednisone for sarcoidosis), antifibrotics (e.g., nintedanib for IPF).
- Oxygen Therapy:
  - Maintain SpO<sub>2</sub> >90% to reduce hypoxic vasoconstriction.
- Avoid Vasodilators:
  - Limited benefit, may worsen V/Q mismatch.

## WHO Group 4: Chronic Thromboembolic Pulmonary Hypertension (CTEPH):

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- Pulmonary Endarterectomy (PEA):
  - Surgical removal of chronic thrombi; first-line for operable patients.
- Medical Therapy:
  - Riociguat (guanylate cyclase stimulator): 1-2.5 mg PO TID; monitor for hypotension.
- Anticoagulation: Lifelong warfarin (INR 2-3) or DOACs (e.g., apixaban).
- Supportive: Diuretics, oxygen as needed.

## WHO Group 5: PH with Unclear or Multifactorial Mechanisms:

- Treat Underlying Cause:
  - Sickle Cell: Hydroxyurea, transfusions.
  - Sarcoidosis: Corticosteroids (e.g., prednisone 20-40 mg PO daily).
- Supportive: Diuretics, oxygen, manage comorbidities.

**Table:** Treatment Approaches by WHO Group

WHO Group	Primary Treatment	Medications/ Interventions	Notes
Group 1 (PAH)	Vasodilators, supportive care	Bosentan, Sildenafil, Epoprostenol	CCBs if vasoreactive; monitor LFTs (ERAs)
Group 2	Optimize left heart function	ACEi, beta-blockers, diuretics	Avoid PAH-specific therapies
Group 3	Treat lung disease, oxygen	Bronchodilators, oxygen, antifibrotics	Avoid vasodilators (worsens V/Q mismatch)
Group 4 (CTEPH)	PEA, anticoagulation, riociguat	Warfarin, Riociguat	PEA for operable patients; lifelong anticoagulation
Group 5	Treat underlying cause	Corticosteroids, hydroxyurea	Tailored to specific etiology

### Key Pearls

**Pathophysiology:** PH involves vascular remodeling, increased PVR, leading to RV strain/failure.

**Presentation:** Dyspnea, fatigue, RV failure signs (edema, JVD); look for underlying causes.

**Diagnosis:** ECHO for initial assessment (RV strain, PASP); RHC confirms (mPAP  $\geq 20$  mmHg).

**WHO Classes:** Group 1 (PAH, pre-capillary), Group 2 (left heart, post-capillary), Group 3 (lung disease), Group 4 (CTEPH), Group 5 (multifactorial).

**ECHO Tips:** Ensure euvolemia, use TR jet for PASP, assess RV function (TAPSE), look for shunts.

**RHC:** mPAP  $\geq 20$  mmHg, PAWP  $\leq 15$  mmHg (pre-capillary), PVR  $> 3$  Wood units; vasoreactivity testing for PAH.

**Decompensated PH:** Diuresis (furosemide), inotropes (dobutamine), oxygen; avoid hypoxia, over-diuresis, and intubation risks.

**Treatment:** Vasodilators for Group 1, treat underlying cause for Groups 2-5, PEA for Group 4.

## References

**UpToDate:** "Pulmonary Hypertension: Diagnosis and Management" (2025). UpToDate PH

**ESC/ERS:** "Guidelines for the Diagnosis and Treatment of Pulmonary Hypertension" (2024). ESC Guidelines

**AHA:** "Management of Chronic Thromboembolic Pulmonary Hypertension" (2023). AHA CTEPH

**NEJM:** "Pulmonary Arterial Hypertension: Advances in Therapy" (2024). NEJM PAH

## Case Scenarios

### Case 1: A 45-Year-Old Female with Dyspnea

- **Presentation:** A 45-year-old female with scleroderma presents with progressive dyspnea and fatigue for 6 months. Exam shows JVD, RV heave, TR murmur, SpO<sub>2</sub> 94% on room air.
- **Labs/ECHO/RHC:** **BNP 500 pg/mL**, **ECHO:** PASP 60 mmHg, RV dilation, TAPSE 14 mm. RHC: mPAP 45 mmHg, PAWP 10 mmHg, PVR 8 Wood units, positive vasoreactivity test.
- **Diagnosis:** WHO Group 1 PH (PAH, Scleroderma-Associated) → Dyspnea, RV strain, pre-capillary PH.
- **Management:** Admit for PH management. Start amlodipine 20 mg PO daily (positive vasoreactivity). Add sildenafil 20 mg PO TID to improve exercise capacity. Diuretics (furosemide 40 mg PO daily) for RV failure. Monitor LFTs, BP. Refer to PH specialist for advanced therapies (e.g., bosentan). Discharge with follow-up.

### Case 2: A 70-Year-Old Male with Decompensated PH

- **Presentation:** A 70-year-old male with known IPAH (WHO Group 1) presents with worsening dyspnea, leg swelling, and fatigue. Exam shows T 37°C, BP 90/60 mmHg, HR 110 bpm, SpO<sub>2</sub> 88% on room air, JVD, RV heave, 2+ pitting edema.
- **Labs/ECHO:** BNP 1200 pg/mL, Cr 1.8 mg/dL (baseline 1.2), **ECHO:** PASP 80 mmHg, TAPSE 12 mm, RV dilation.
- **Diagnosis:** Decompensated PH with Volume Overload (IPAH) → Worsening RV failure, systemic congestion.

- Management: Admit to ICU. Start furosemide 80 mg IV bolus, then 10 mg/h infusion (target urine output >100 mL/h). Supplemental oxygen to maintain SpO<sub>2</sub> >90%. Dobutamine 2 µg/kg/min IV (titrate to CO and BP). Avoid intubation (use BiPAP if needed, low PEEP). Monitor CVP (goal <10 mmHg), renal function, lactate. Epoprostenol 2 ng/kg/min IV added for refractory RV failure. Consult PH specialist for escalation.

### Case 3: A 55-Year-Old Female with History of PE

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- Presentation: A 55-year-old female with a history of PE presents with dyspnea and chest pain for 3 months. Exam shows RV heave, loud P2, SpO<sub>2</sub> 93% on room air.
- Labs/ECHO/RHC: **V/Q scan shows mismatch, ECHO:** PASP 70 mmHg, RV hypertrophy. RHC: mPAP 50 mmHg, PAWP 12 mmHg, PVR 10 Wood units.
- Diagnosis: WHO Group 4 PH (CTEPH) → Dyspnea, RV strain, V/Q mismatch, pre-capillary PH.
- Management: Admit for CTEPH evaluation. Start riociguat 1 mg PO TID (titrate to 2.5 mg TID). Lifelong anticoagulation with apixaban 5 mg PO BID. Refer for pulmonary endarterectomy (operable candidate). Monitor BP (riociguat), INR (if on warfarin). Discharge with PH specialist follow-up.

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