Pulmonary Hypertension: Diagnosis and Management

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MGH/BIDMC/Harvard Pulmonary & Critical Care Medicine
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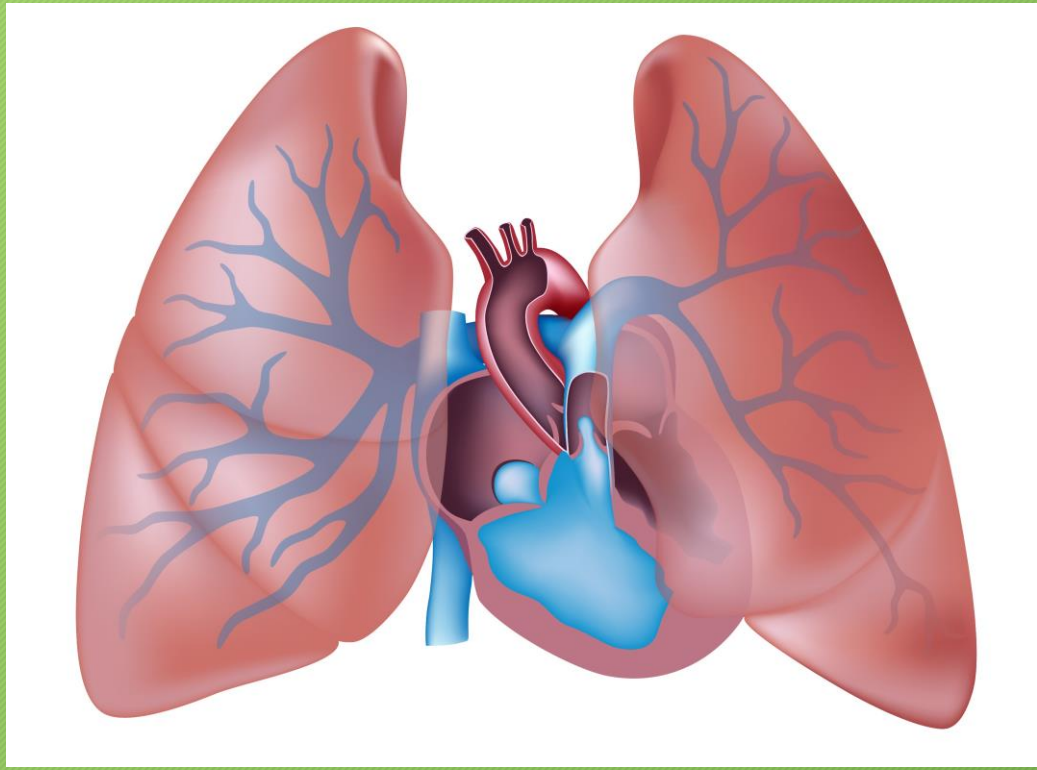
Today’s agenda



What is pulmonary hypertension (PH)?

What causes PH? How is this related to other lung diseases like pulmonary fibrosis?

How is PH identified and diagnosed?

What treatment options exist for PH?

Questions

What is pulmonary hypertension?

Pulmonary Hypertension

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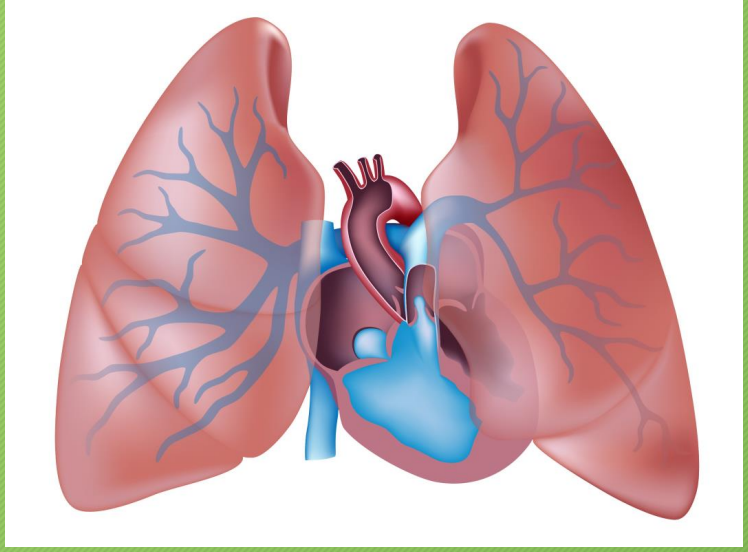
Elevation of blood pressure inside the lungs

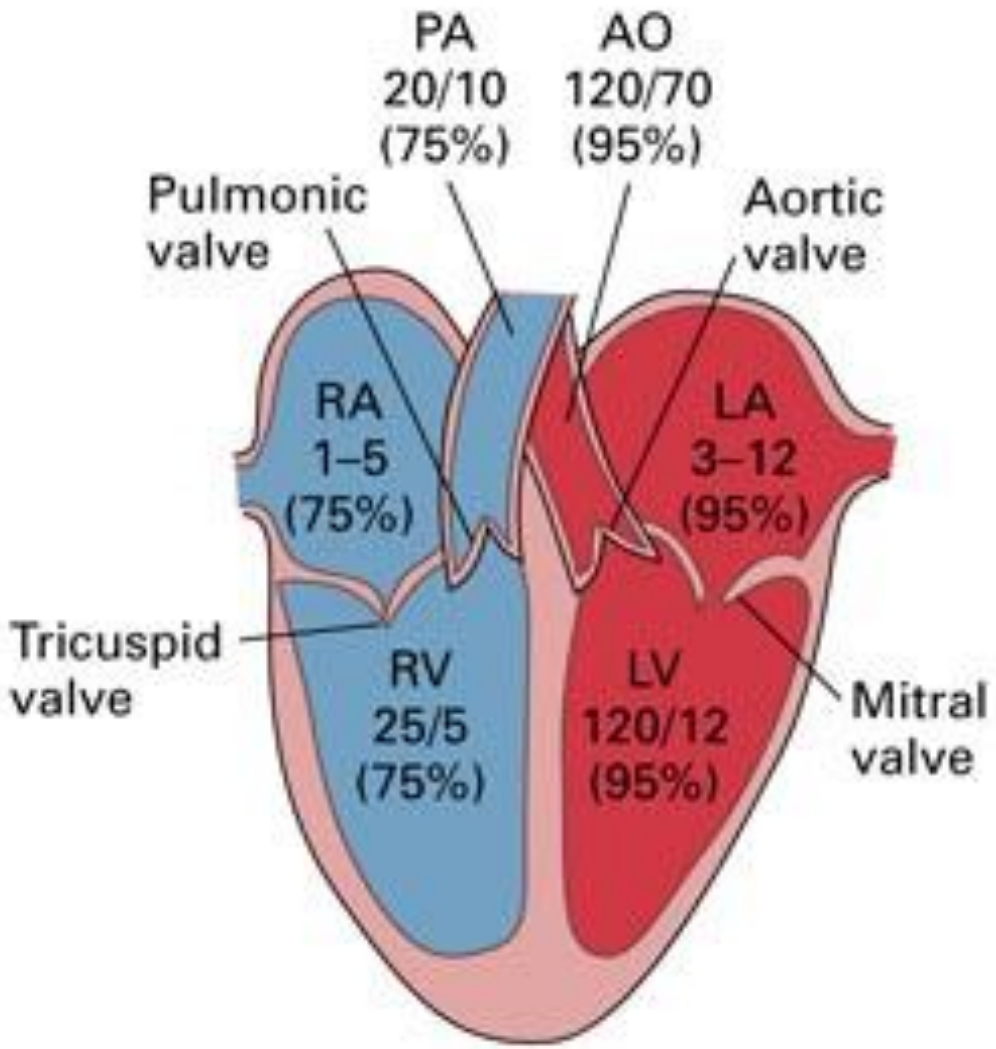
Pulmonary Hypertension

Strain on the right side of the heart

Shortness of breath and swelling

Right heart failure





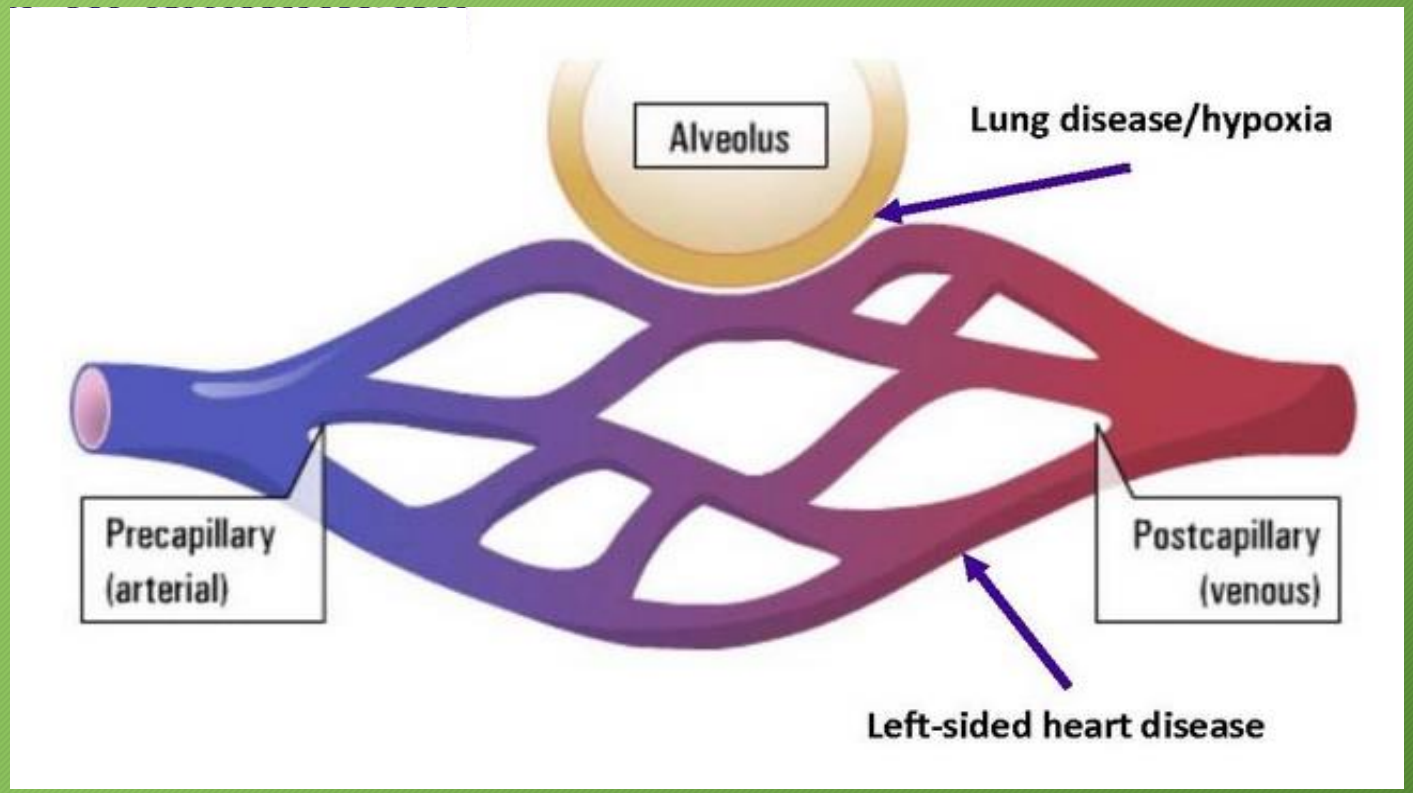
Legend:
AO = Aorta
PA = Pulmonary artery
RA = Right atrium
LA = Left atrium
RV = Right ventricle
LV = Left ventricle
% = O_2 content
Numbers = Normal cardiac pressures in mm Hg

What is pulmonary hypertension?

- Normal BP in the lungs (pulmonary artery (PA) pressure) = around 20/8 (mean 12)
- PH is defined as mean PA pressure greater than 20
- The pressure elevation can be caused by various abnormalities

What causes pulmonary hypertension?

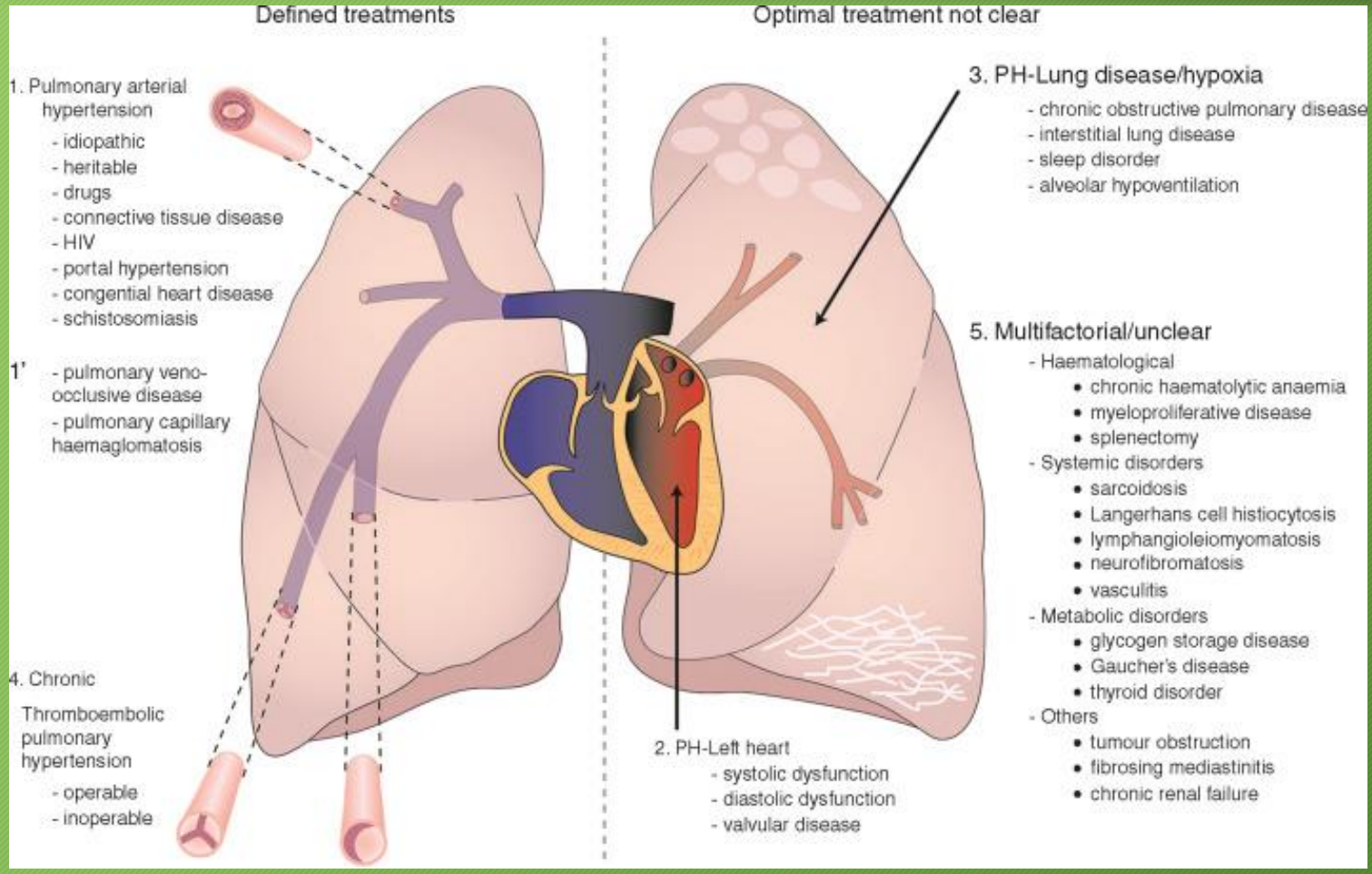
- The pressure elevation can be caused by various abnormalities



Classification of pulmonary hypertension

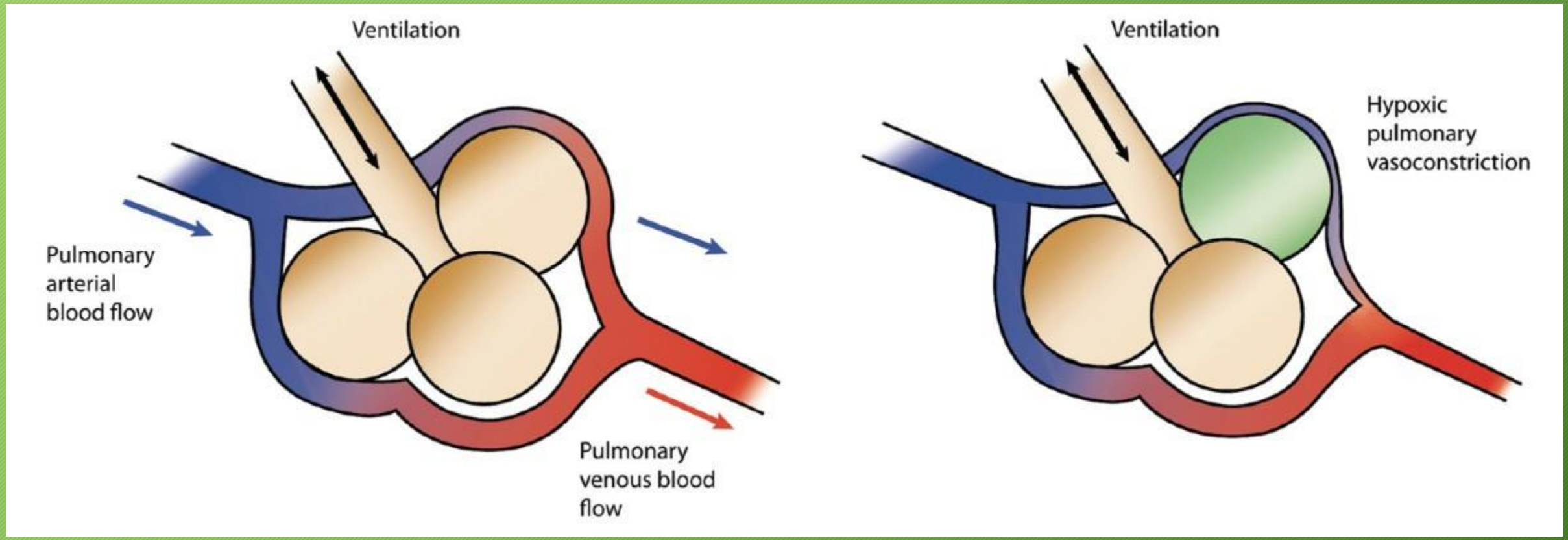
WHO group 1	Primary pulmonary vascular problem (caused by the blood vessels themselves)
WHO group 2	Caused by LEFT heart disease (elevation in the pulmonary venous pressures on the far side of the pulmonary capillaries)
WHO group 3	PH due to primary lung disease (like ILD)
WHO group 4	Chronic thromboembolic pulmonary hypertension
WHO group 5	Multifactorial or unclear mechanisms (for example - sickle cell disease, sarcoidosis, or metabolic disorders)

Classification of pulmonary hypertension



Kiely et al. BMJ 2013

Pulmonary hypertension due to lung disease



Abdo et al. Crit Care 2012

Pulmonary hypertension due to lung disease

Caused by:

- Hypoxic vasoconstriction
- Chronic decrease in pulmonary vasodilating signal (like nitric oxide)
- Chronic increase in pulmonary vasoconstricting signal (like endothelin)
- Vascular remodeling
- Vascular damage in parallel with lung tissue damage

Pulmonary hypertension due to lung disease

Patients with higher mean PA pressure have had had increased mortality in studies of patients with PH due to ILD

When should I suspect PH?

Most common presenting symptom in PH is dyspnea on exertion

- However, this is common in ILD

<u>Signs of PH due to ILD:</u>

- Shortness of breath or low oxygen levels not explained by degree of ILD
- Rapid decline in oxygen levels upon exercise
- Signs of right heart failure (chest pain on exertion, syncope, edema, bloating)
- Enlarged pulmonary artery on CT scan (typically with cut-off 3cm)
- Severely reduced DLCO, in particular out of proportion to other deficits on PFTs

How is PH diagnosed?

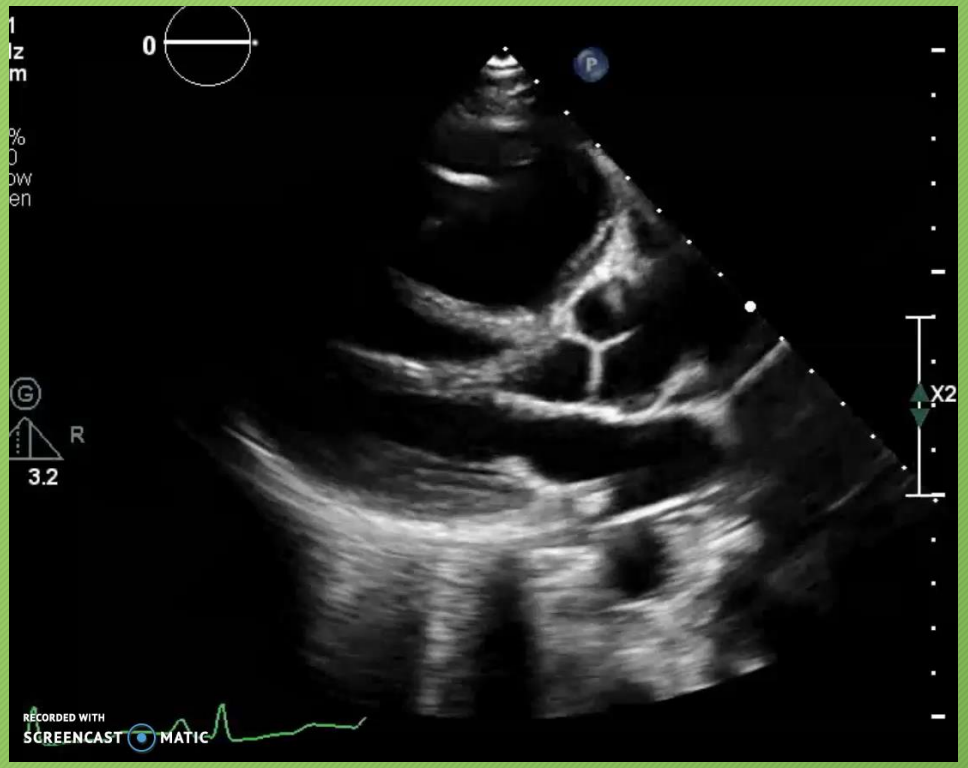
Initial screening test = echocardiogram (cardiac ultrasound)

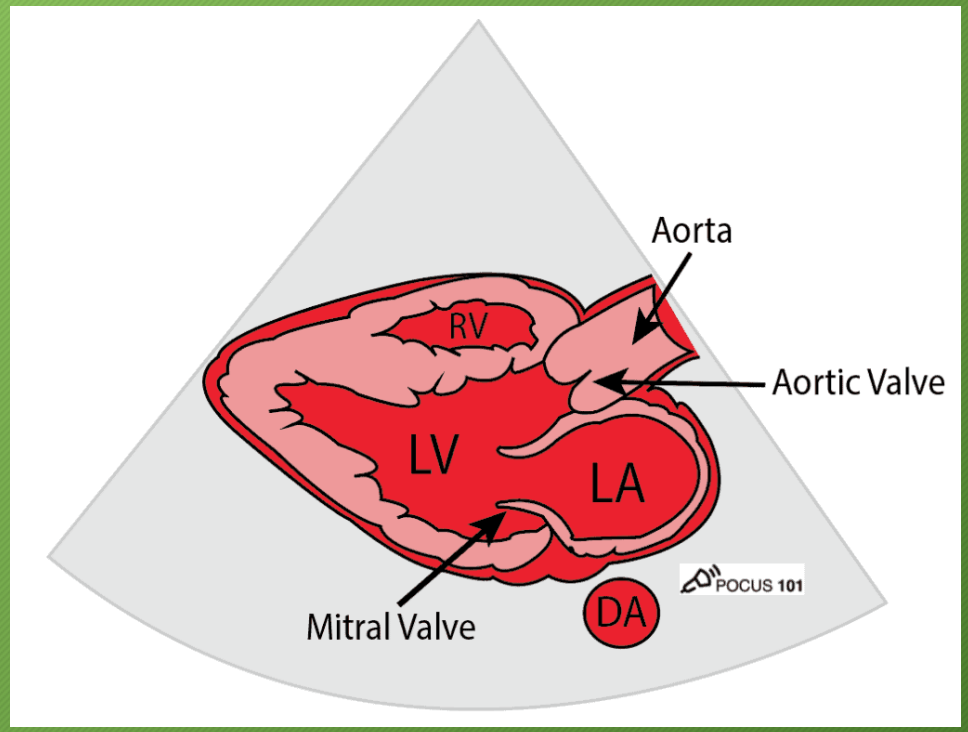
Confirmatory test = right heart catheterization

Echocardiography

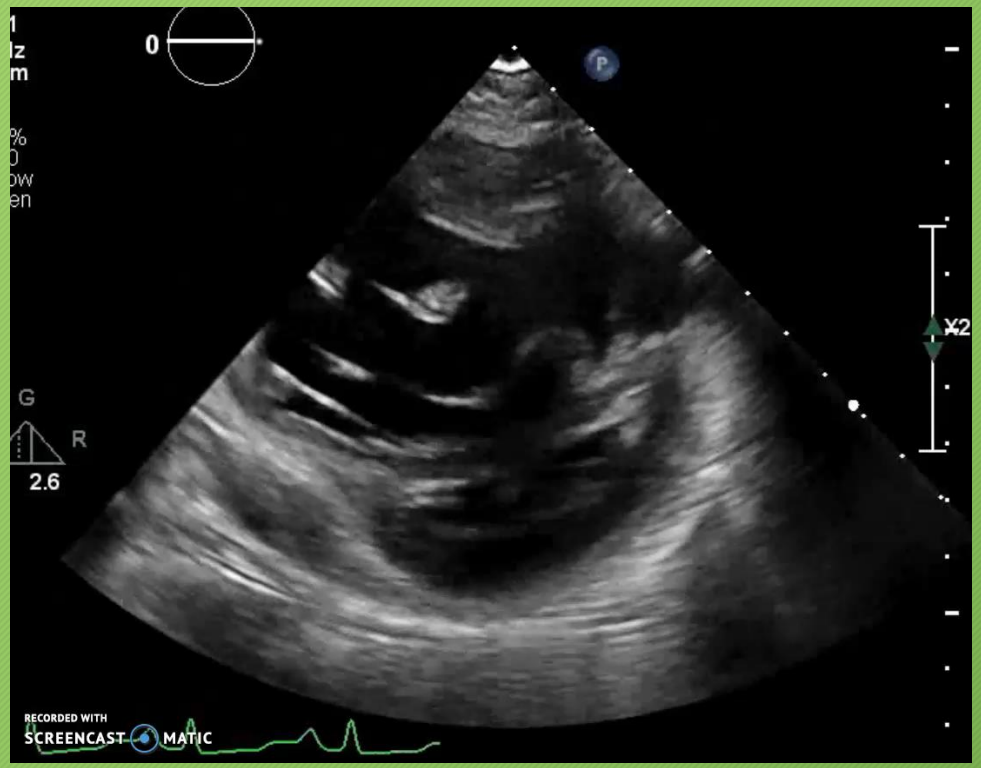
- A non-invasive ultrasound of the heart
- Allows for assessment of right heart function (how well the right ventricle squeezes and whether there is any sign of strain due to increased pressure)
- Also allows for an *estimation* of the pulmonary artery blood pressure

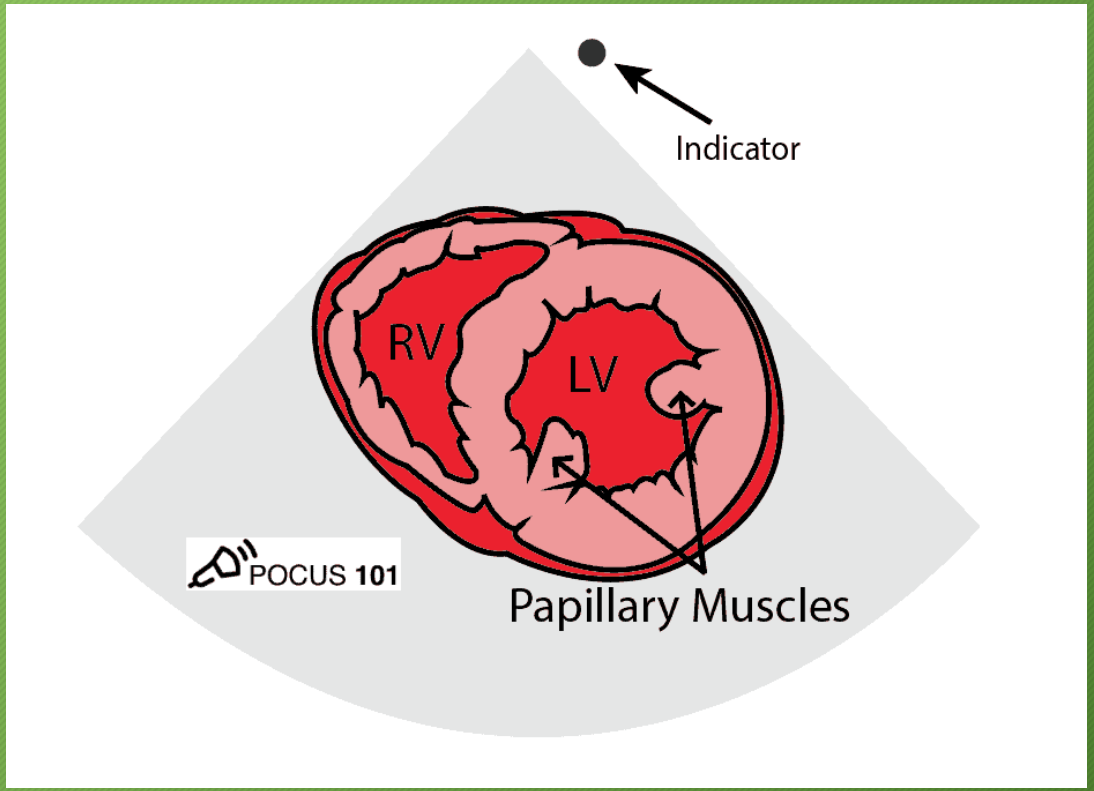
Echocardiography in PH





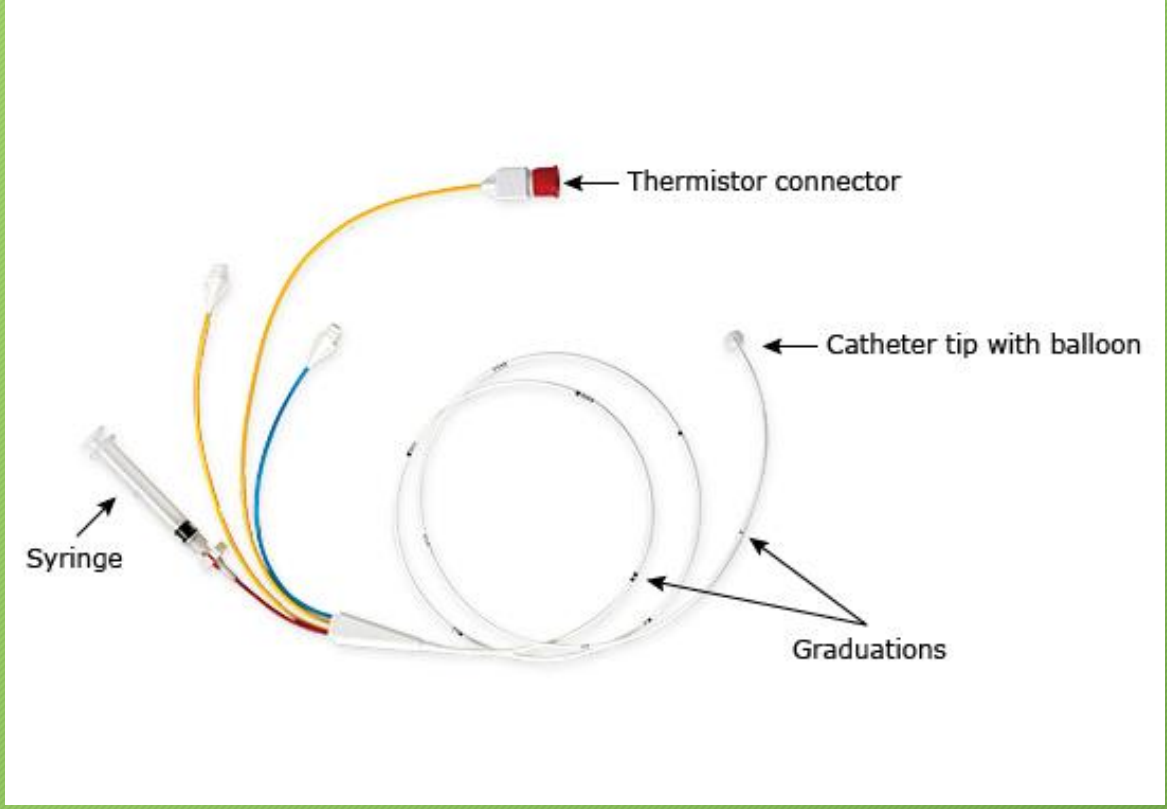
Echocardiography in PH

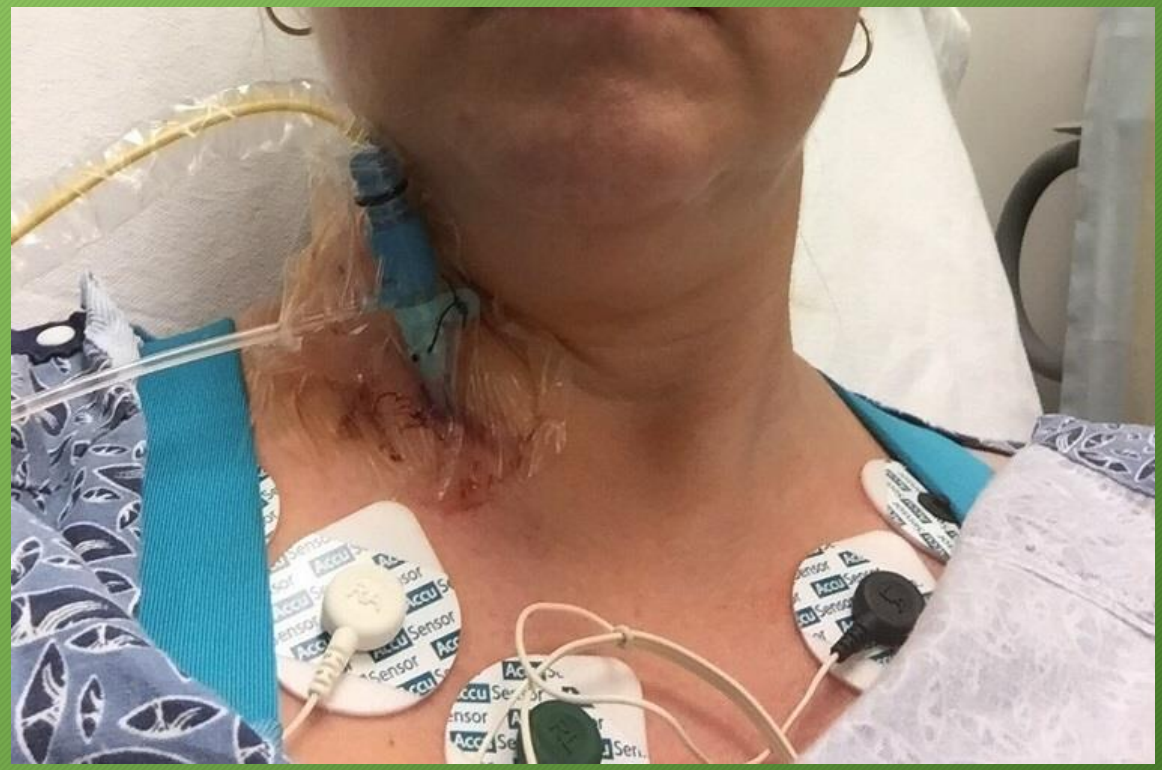




Right heart catheterization

- Invasive test to directly measure pulmonary artery pressures





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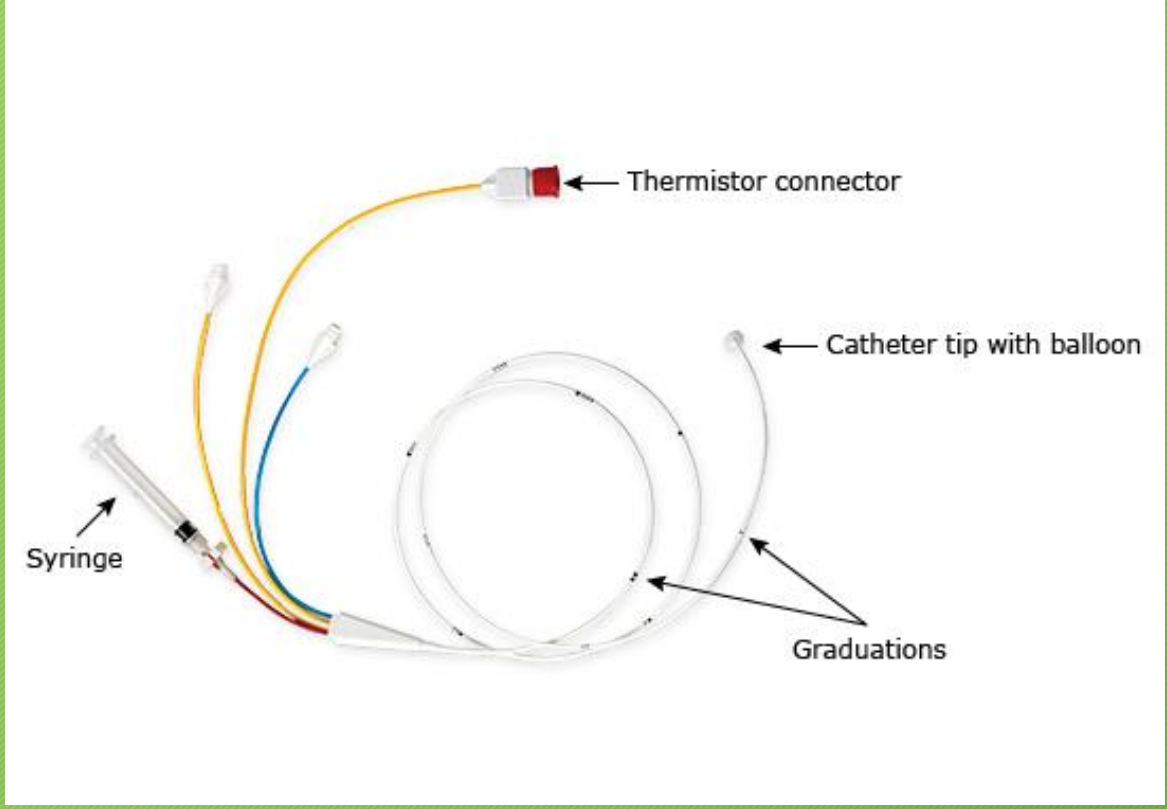

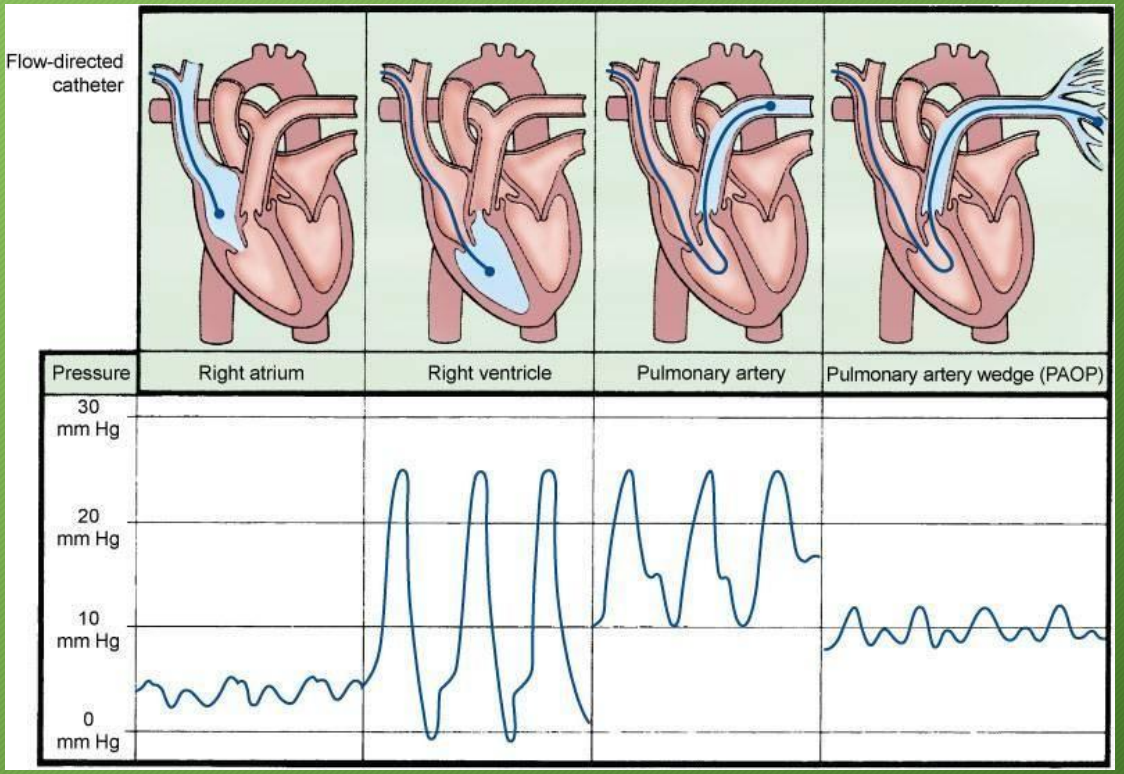

How is pulmonary hypertension treated?

Treatment of Pulmonary Hypertension

Don’t forget the basics!

- Exercise/rehab
- Vaccinations
- Smoking cessation
- Oxygen when needed
- Avoidance of pregnancy

Treatment of PAH

Pulmonary vasodilator therapy

- Phosphodiesterase-5 inhibitors (sildenafil, tadalafil)
- Guanylate cyclase stimulator (riociguat)
- Endothelin receptor antagonists (ambrisentan, macitentan)
- Prostanoids (IV epoprostenol (Veletri) or treprostinil (Remodulin), oral selexipag, inhaled treprostinil (Tyvaso))

These therapies have typically been reserved for severe or "out of proportion" cases of PH due to lung disease

Treatment of PH due to lung disease

- Treat the underlying condition and provide general supportive care

- Some pulmonary vasodilators have been associated with adverse effects in patients with PH due to ILD
  - Ambrisentan = worsening oxygenation, disease progression, increased hospitalization in patients with PH and IPF
  - Riociguat = phase II study in patients with PH due to idiopathic interstitial pneumonia stopped due to increased drug-related adverse events and mortality

Treatment of PH due to lung disease

- Treat the underlying condition and provide general supportive care

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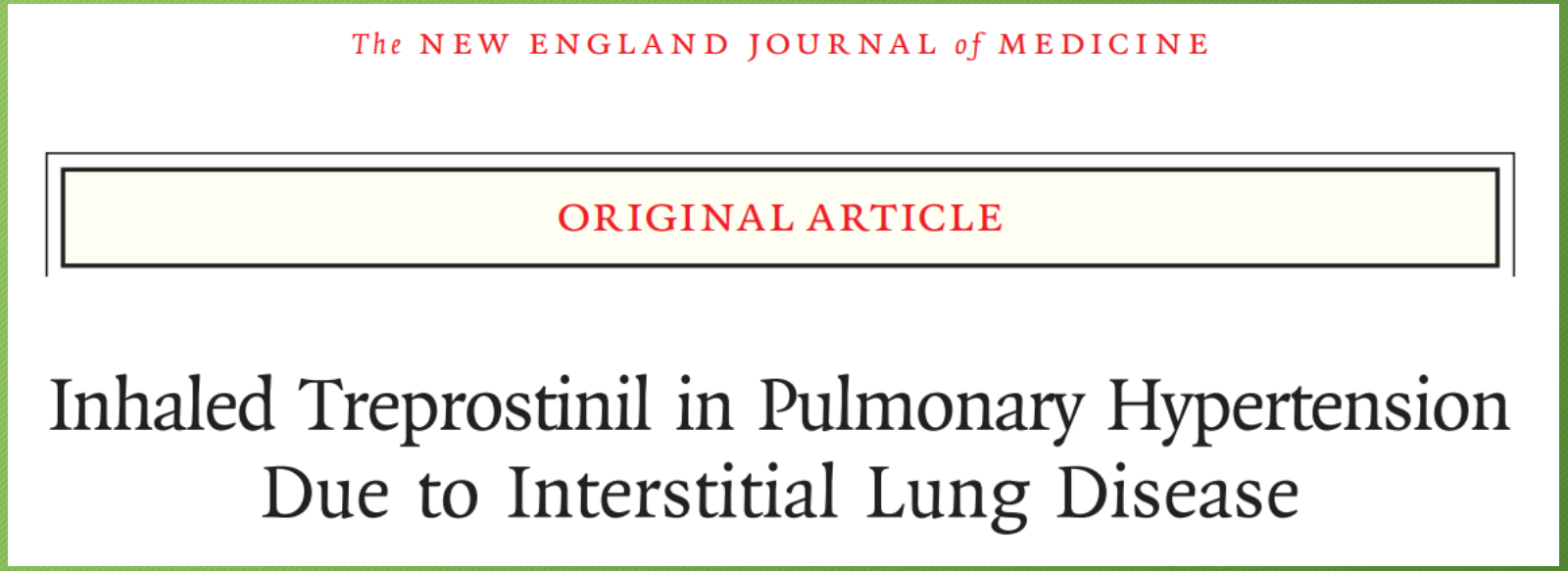


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Inhaled Treprostinil in Pulmonary Hypertension Due to Interstitial Lung Disease

Tyvaso (inhaled treprostinil)

- Inhaled delivery of prostanoid via ultrasonic, pulsed-delivery nebulizer
- Add distilled water and medication ampule
- Four times daily administration (takes 3-5 minutes per administration + assembly time)
- Started at 3 breaths four times a day, increased in increments of 1-3 breaths per administration up to max 12 breaths four times a day

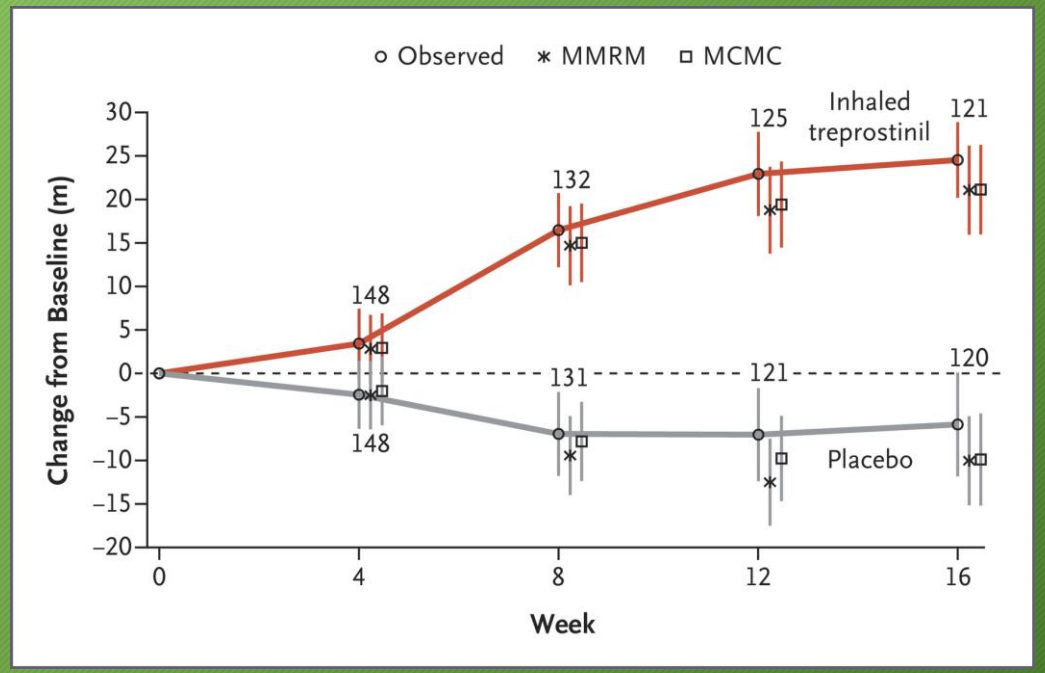
INCREASE trial (published Jan 2021)

- Inhaled delivery of treprostinil (Tyvaso)
- Multicenter, double-blind, randomized control trial of 326 patients with ILD-related PH
  - 18 years or older with diagnosis of ILD
  - Group 3 PH by right heart cath
  - Had to walk at least 100m on 6MWT
  - Patients on PH therapy not eligible
- Primary end point = change in 6-minute walk distance from baseline to week 16

Waxman et al. NEJM 2021

INCREASE trial (published Jan 2021)

- Small improvement in 6MWT distance (mean difference 31 meters) after 16 weeks of use
- Also, reduced NTproBNP and reduced number of patients with clinical deterioration during trial (22.7% vs 33.1%)
- Adverse effects included headache, cough, dyspnea, dizziness, nausea, fatigue, diarrhea, and throat irritation; no serious adverse events reported more frequently in treatment group vs placebo
- Now FDA approved for PH due to ILD



Waxman et al. NEJM 2021

Summary

- Pulmonary hypertension is an elevation of the blood pressure inside the lungs due to various causes
- Interstitial lung disease and other lung diseases can cause PH through hypoxic vasoconstriction, chronic changes in blood vessels, and damage to lung tissue/blood vessels
- PH due to lung disease can be difficult to identify due to chronic dyspnea in ILD alone, but can cause dyspnea out of proportion or signs of right heart failure (swelling, bloating, weight gain)
- PH is diagnosed by echocardiography and right heart catheterization
- Treatment of PH due to lung disease/ILD has been limited by lack of efficacy and possible harm, but newer data suggest a role for inhaled pulmonary vasodilator therapy (inhaled treprostinil)

Questions?

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