

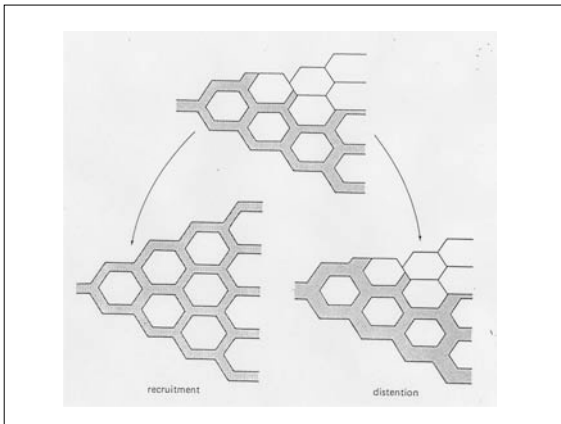
Pathophysiology II
Pulmonary Vascular Changes
in Heart Disease

- **Normal Circulatory Dynamics**
 Physiology
- **Pulmonary Hypertension**
 Definition
 Classification
 Pathology
 Pathophysiology
 Clinical Manifestations
 Diagnosis
 Treatment

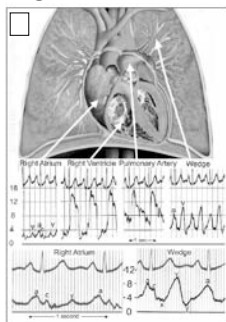
- Pulmonary Circulation**
- **Low resistance, high compliance vascular bed**
 - **Only organ to receive entire cardiac output (CO)**
 - **Changes in CO as well as pleural/alveolar pressure affect pulmonary blood flow**
 - **Different reactions compared to the systemic circulation**
 - **Normally in a state of mild vasodilation**

Exercise

- Pulmonary blood flow increases up to 4-5x BL
- Increased flow accommodated by both recruitment and vasodilation
- Net effect is a decrease in pulmonary vascular resistance (PVR)
- No further decrease in PVR once all vessels fully recruited and dilated



Normal Hemodynamic Measurements During Right Heart Catheterization



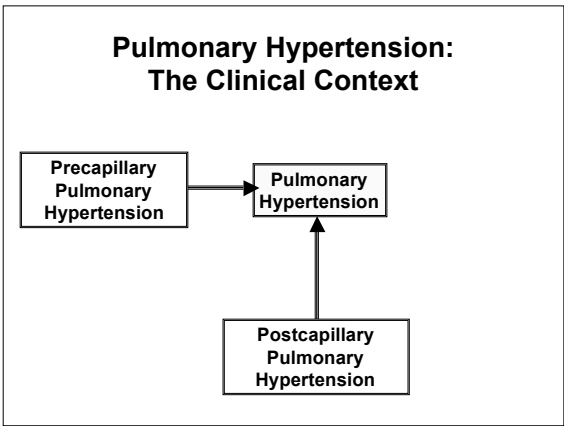
Oudiz RJ, Langleben D. *Advances in Pulmonary Hypertension* 2005;4(3):15-25

Normal Pulmonary Hemodynamics at Sea Level (Rest and Mild Exercise) and at Elevated Altitude (Rest)

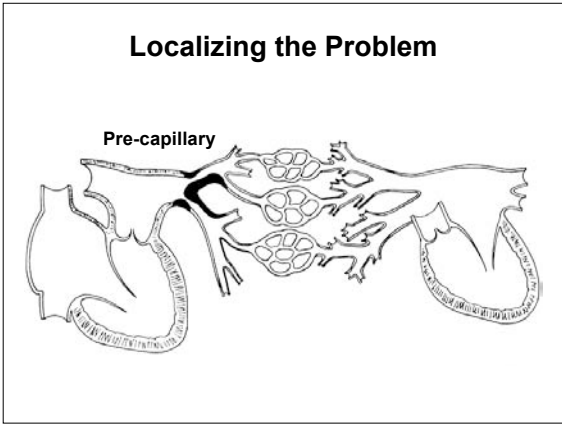
| | Sea level Rest | Sea level Mild Exercise | Altitude (~15,000 ft) Rest |
|--|----------------|-------------------------|----------------------------|
| Pulmonary arterial pressure, (mean) mmHg | 20/10(15) | 30/13(20) | 38/14(26) |
| Cardiac output, L/min | 6.0 | 12.0 | 6.0 |
| Left atrial pressure (mean), mmHg | 5.0 | 9.0 | 5.0 |
| Pulmonary vascular resistance, units | 1.7 | 0.9 | 3.3 |

Pulmonary Hypertension: Definition

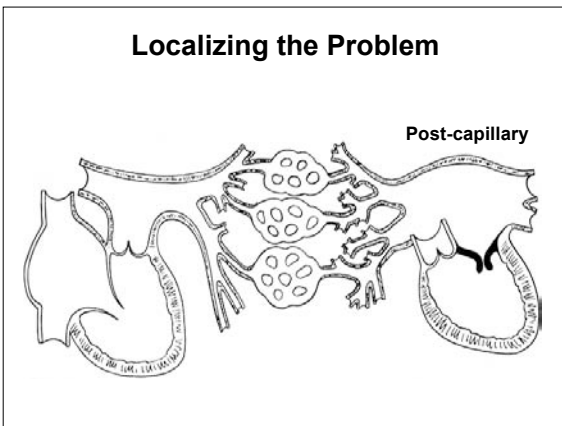
PAP mean \geq 25 mm Hg at rest or \geq 30 mmHg with exercise



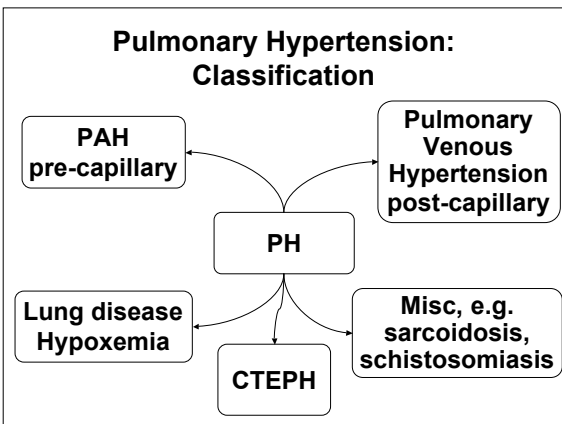
Localizing the Problem



Localizing the Problem



Pulmonary Hypertension: Classification

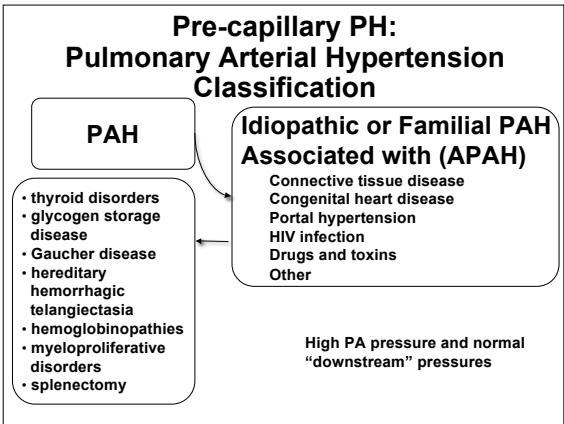


**Pre-capillary PH:
Pulmonary Arterial Hypertension
Definition**

- PAP mean ≥ 25 mmHg at rest or ≥ 30 mmHg with exercise

AND

- PCWP or LVEDP ≤ 15 mmHg
- PVRI ≥ 3 units $\cdot m^2$
- No left-sided heart disease

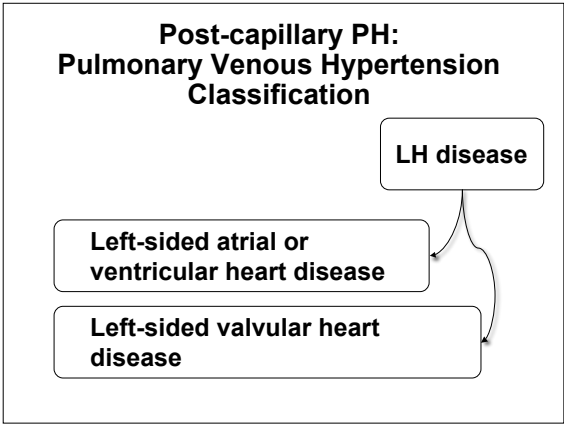


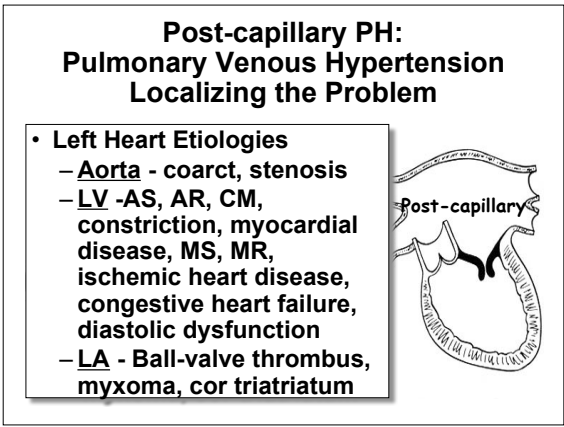
**Post-capillary PH:
Pulmonary Venous Hypertension
Definition**

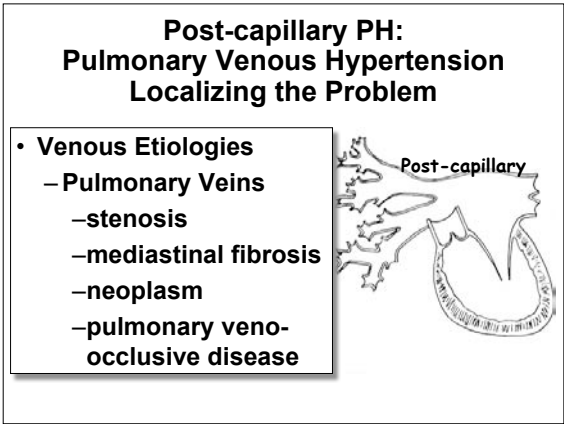
- PAP mean ≥ 25 mmHg at rest or ≥ 30 mmHg with exercise

AND

- PCWP or LVEDP >15 mmHg







Pulmonary Venous Hypertension Physiology

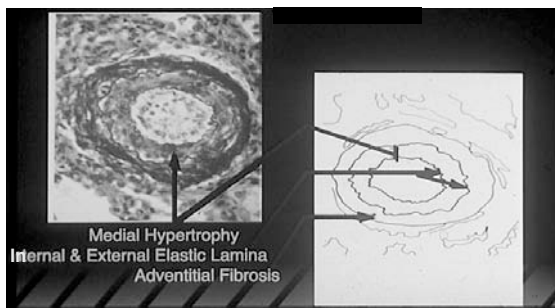
Pulmonary arterial → Lung → Pulmonary venous

| | | | |
|----------|-------------------------|--|----------------------|
| Normal | PAP mean 15 mmHg | → No obstruction → | PCWP mean 5 mmHg |
| PVPH | PAP mean 35 mmHg | → No obstruction → | PCWP mean 25 mmHg |
| Mixed PH | PAP mean 45-100 mmHg | → Pulmonary arteriolar obstruction → | PCWP mean 25 mmHg |

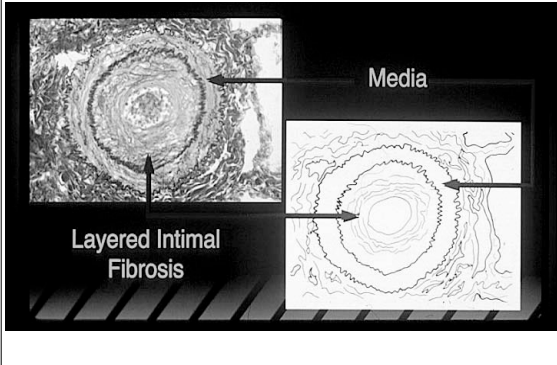
Mixed (Pulmonary Venous and Pulmonary Arterial Hypertension): Definition

- PAP mean ≥ 25 mmHg at rest or ≥ 30 mmHg with exercise
- PCWP or LVEDP > 15 mmHg
- PVRI ≥ 3 units $\cdot M^2$
- Increased Transpulmonary Gradient Across Pulmonary Vascular Bed

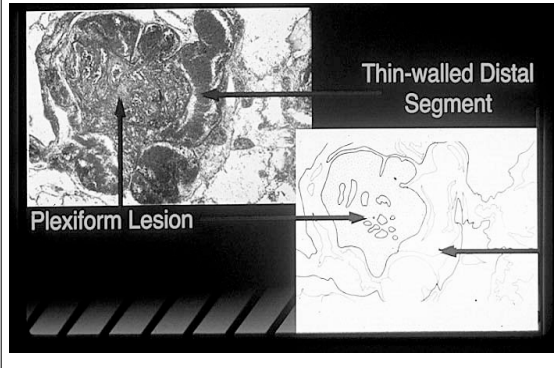
PH: Medial Hypertrophy



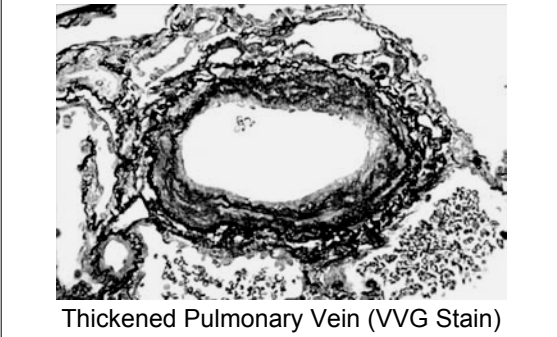
PH: Intimal Fibrosis



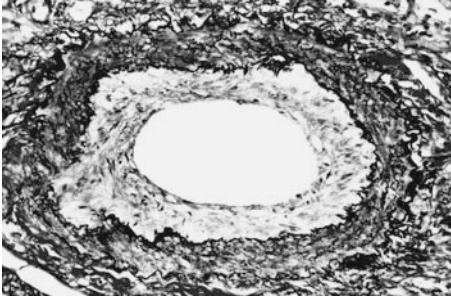
PAH: Plexiform Lesions



Pulmonary Venous Hypertension
Microscopic Features

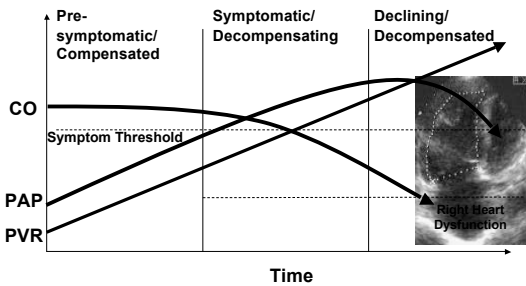


Pulmonary Venous Hypertension Microscopic Features



Thickened Muscular Pulm Art (VVG Stain)

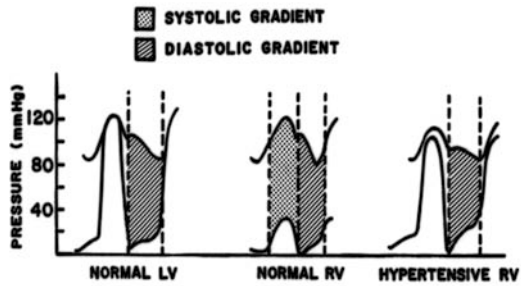
Pathophysiology: Hemodynamic Progression of PH



Right Ventricular Dysfunction in Pulmonary Hypertension

Right ventricular failure is a
consequence of chronic ischemia
on a hypertrophied pressure
overloaded ventricle

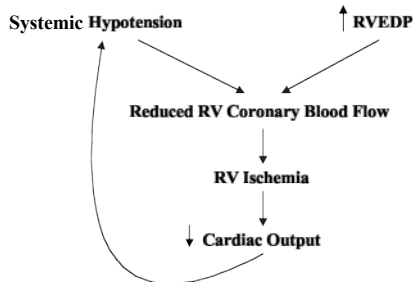
Coronary Driving Pressure Gradient and the Effect of Pulmonary Hypertension



Effects of pulmonary hypertension on RV myocardial perfusion

- Myocardial perfusion goes from being both systolic and diastolic to mostly diastolic
- The RV hypertrophies, but coronary blood supply remains unchanged
- RV work is dramatically increased without a compensatory increase in coronary blood flow
- Tachycardia makes everything worse

PH: Progressive Right Heart Failure



**Pulmonary Arterial Hypertension:
Clinical Manifestations - Symptoms**

- Dyspnea on Exertion/Rest
- Fatigue
- Chest Discomfort/Pain
- Cough
- Syncope/Presyncope
- Hemoptysis
- Edema
- Hoarseness

PAH: Clinical Manifestations

- Dyspnea
 - Reduced O2 diffusion
 - Ventilation-perfusion mismatching
 - Low O2 transport
- Angina
 - RV ischemia
 - Left main coronary compression
- Syncope
 - Hypotension due to systemic vasodilation and fixed pulmonary resistance
 - Arrhythmia
- Edema, hepatic congestion, ascites
 - RV failure

Pulmonary Venous PH: Symptoms

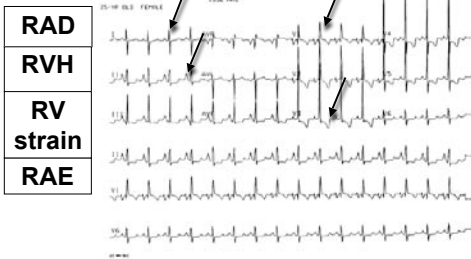
- Angina
- Syncope
- Congestive heart failure
- Dyspnea
- Hemoptysis
- Hoarseness
- Edema
- Ascites
- Paroxysmal nocturnal dyspnea
- Orthopnea
- Central and peripheral cyanosis



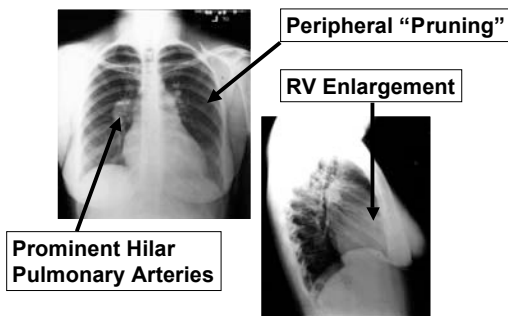
Diagnosis of PH: Procedures

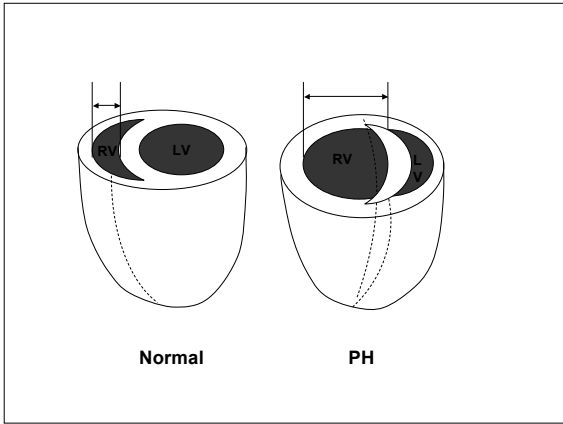
- Electrocardiogram
- Chest radiography
- Echocardiogram
- Ventilation perfusion scan (V/Q scan)
- Serologic studies, HIV
- Pulmonary function tests (PFT)
- Sleep study (if indicated)
- Right-heart catheterization (with acute vasodilator testing if PAH)

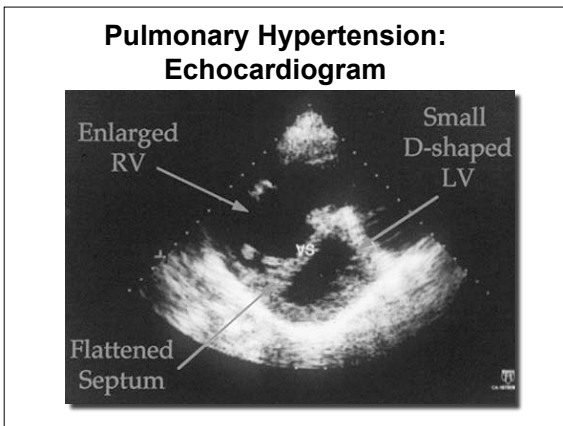
PAH: Screening - ECG



PAH: Screening - CXR



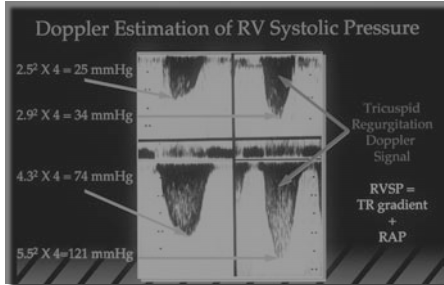




**Echocardiogram
Estimate of RVSP**

- $4V^2 = \text{Pressure Gradient } (\Delta P)$
(Modified Bernoulli Equation)
- $\text{RVSP} - \text{RAP mean} = \Delta P$
- $\text{RVSP} = \text{RAP mean} + \Delta P$

Echocardiogram



PH: Congestive Heart Failure - CXR hilar fullness and haziness



Diagnosis of PH: ECHO May Suggest an Underlying Etiology

- LV diastolic dysfunction
 - MS or MR
 - LV systolic dysfunction
- } Post-capillary pulmonary venous hypertension
- Congenital heart disease, e.g. ASD, VSD, PDA

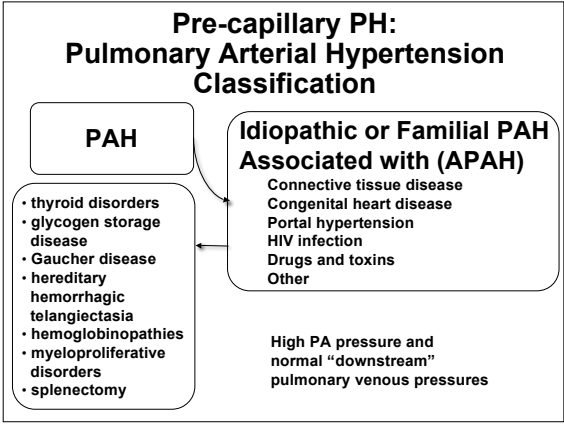
Cardiac Catheterization

- To exclude congenital heart disease
- To measure PCWP or LVEDP
- To establish severity and prognosis
- Acute vasodilator drug testing

Cardiac catheterization should be performed in patients with suspected pulmonary hypertension

Diagnosis of Pulmonary Hypertension

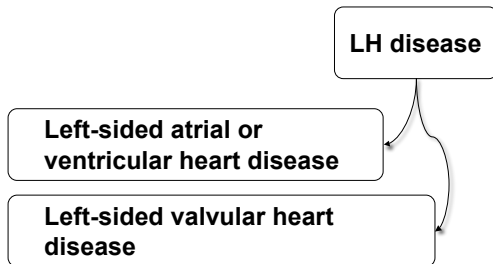
- High index of suspicion
- Thorough and complete evaluation



**Treatment: Pre-capillary PH -
Pulmonary Arterial Hypertension**

- Treat associated conditions, e.g. thyroid disease
- Early surgery to repair congenital heart disease, e.g. VSD, PDA
 - However, if no longer “operable” due to progressive pulmonary vascular obstructive disease, “corrective” surgery is contra-indicated
 - Medical PAH Therapy
 - Lung or Heart-Lung Transplantation

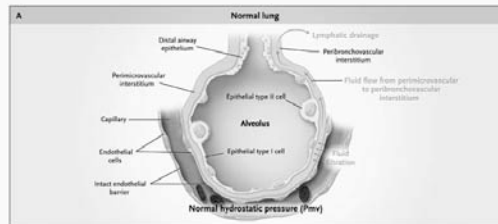
**Post-capillary PH:
Pulmonary Venous Hypertension
Classification**



Acute Pulmonary Edema

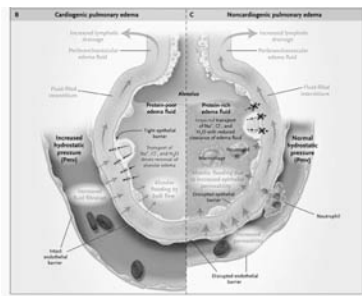
- Cardiogenic Pulmonary Edema
- Noncardiogenic Pulmonary Edema

Physiology of Microvascular Fluid Exchange in the Lung



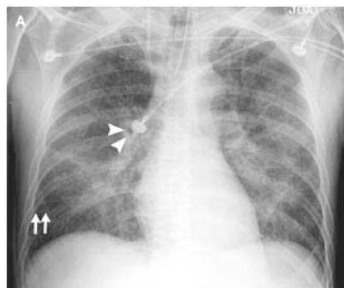
Ware L and Matthay M. N Engl J Med 2005;353:2788-2796

Physiology of Microvascular Fluid Exchange in the Lung



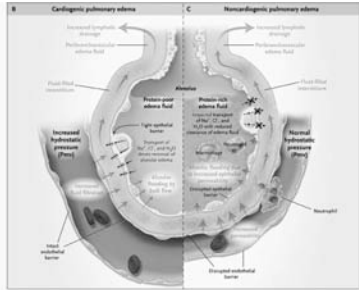
Ware L and Matthay M. N Engl J Med 2005;353:2788-2796

Representative Chest Radiograph from Patient with Cardiogenic Pulmonary Edema



Ware L and Matthay M. N Engl J Med 2005;353:2788-2796

Physiology of Microvascular Fluid Exchange in the Lung



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Representative Chest Radiograph from Patient with Noncardiogenic Pulmonary Edema



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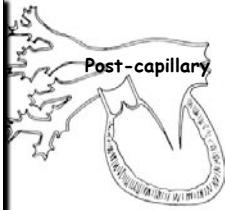
Treatment: Post-capillary PH - Pulmonary Venous Hypertension

- Surgery to eliminate left-sided cardiac obstruction
- Heart transplantation for left ventricular failure
- Additional medical and/or surgical treatment as needed
 - Specific re: left heart or pulmonary venous hypertension etiology
 - PAH treatment

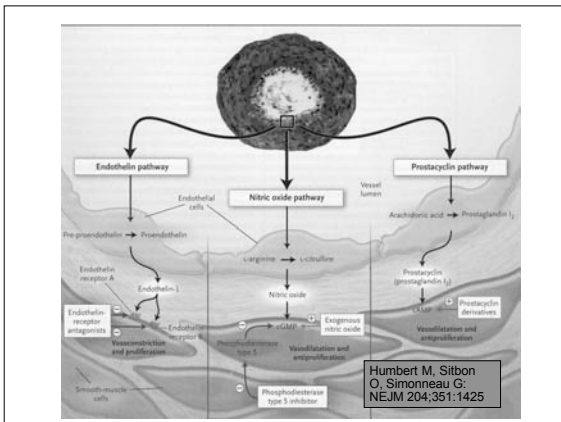
Pulmonary Venous Hypertension

Chronic Heart Failure Treatment

- Sodium restriction
- Afterload reduction, e.g. ACE inhibitors
- Inotropic support, e.g. digitalis
- Diuretics
- Beta-blockers
- Identification and treatment of underlying cause(s)

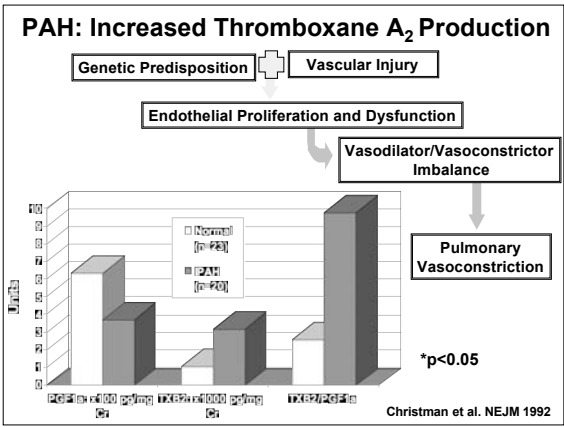


Targeted Pulmonary Arterial Hypertension Medical Treatment



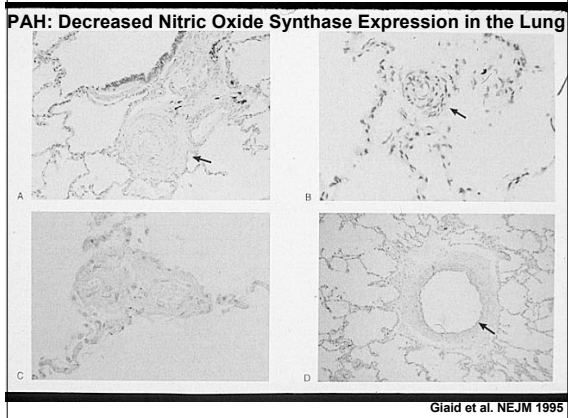
PAH: Decreased Expression of Prostacyclin Synthase in the Lung

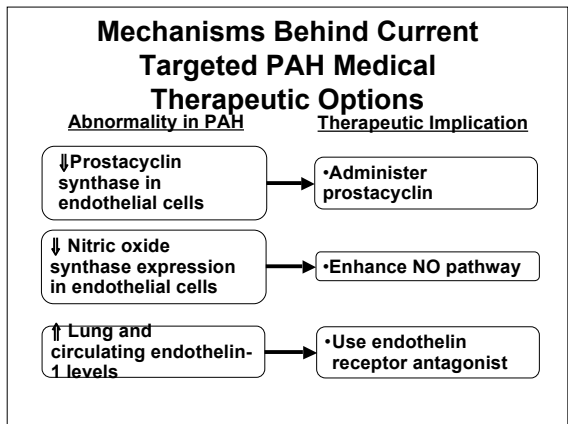
Tuder et al. AJRCCM 1999



PAH: Increased Expression of Endothelin in the Lung

Glaud A et al. NEJM 1993





Experience and Reason

“In Medicine one must pay attention not to plausible theorizing but to experience and reason together . . . I agree that theorizing is to be approved, provided that it is based on facts, and systematically makes its deductions from what is observed . . . But conclusions drawn from unaided reason can hardly be serviceable; only those drawn from observed fact.”

Hippocrates (460-377 BC): *Precepts*
