Pulmonary Artery HTN Diagnosis

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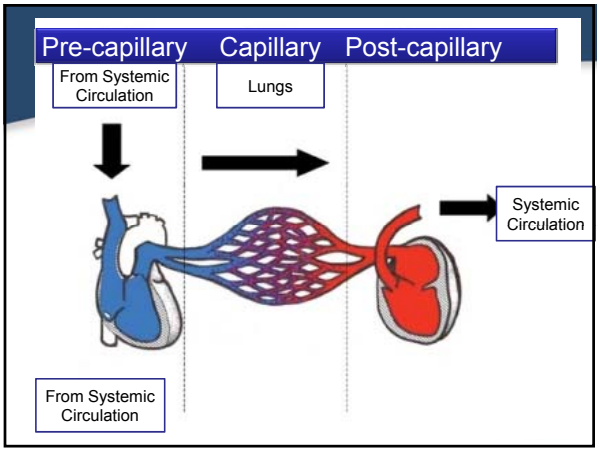
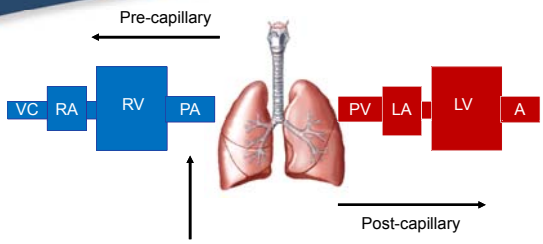
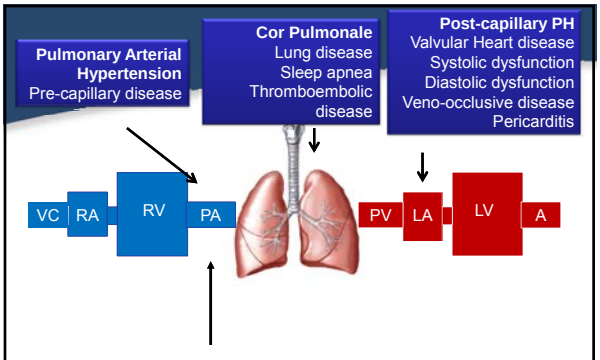
PULMONARY PHYSIOLOGY





Pulmonary Hypertension = abnormally high pressure in the pulmonary arteries



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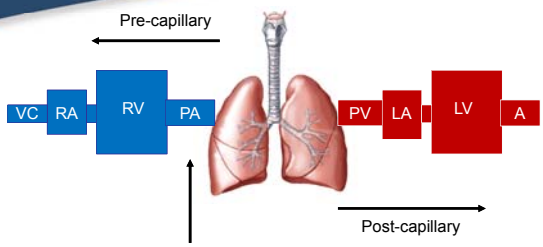


Pulmonary Arterial Hypertension = abnormally high pressure confined to the pre-capillary vessels

EPIDEMIOLOGY & PATHOPHYSIOLOGY

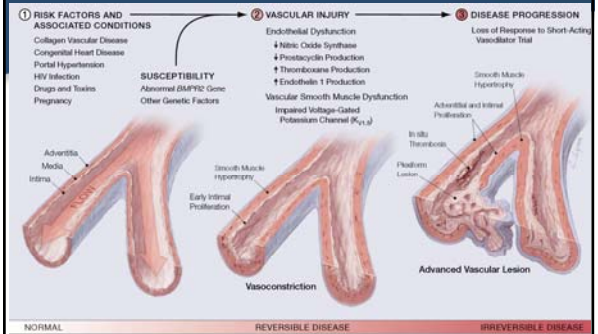
Clinical Classification of Pulmonary Hypertension 2008 Dana Point

- Pulmonary Artery Hypertension
- PH with L heart disease
- PH associated with lung diseases and/or hypoxia
- Chronic Thromboembolic PH (CTEPH)
- Multifactorial / Misc.

Publication pending

Risk Factor + Susceptibility → Vascular Injury → Disease Progression

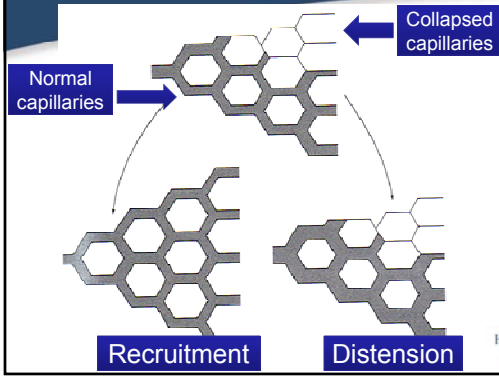
Pathogenesis



JAMA

Gaine, S. JAMA 2000;284:3160-3168.

Pulmonary Capillaries



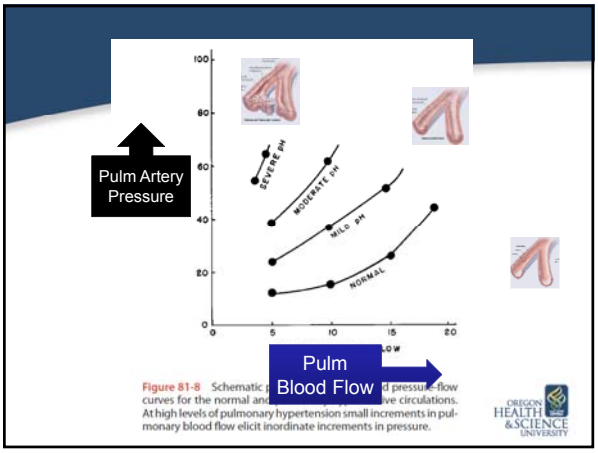
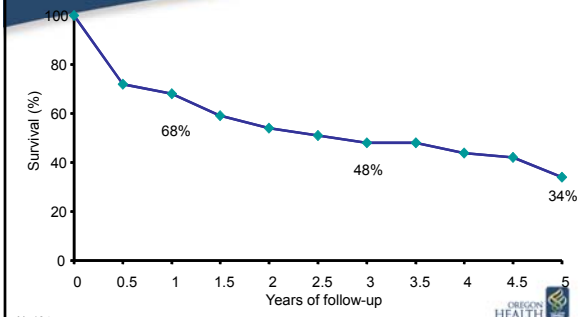


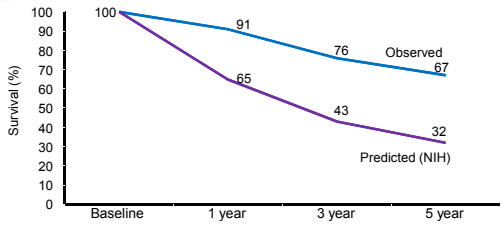
Figure 81-8 Schematic p d pressure-flow curves for the normal and ive circulations. At high levels of pulmonary hypertension small increments in pulmonary blood flow elicit inordinate increments in pressure.

Idiopathic PAH (iPAH)
Rapid Progression and Poor Survival



N=194.
D'Alonzo GE et al. *Ann Intern Med* .1991;115:343-349.

Survival in Current Era: Comparison with NIH Historical Controls



Thennapan T, et al. *Chest*. 2007;132(4 suppl):487S.

Prevalence of PAH: French National Registry

- Consecutive adult patients
  - ≥18 years of age
  - 17 French specialty centers
- B/W Oct 2002 - Oct 2003
- Prevalence of PAH: 15.0 cases/million
  - Prevalence of iPAH: 5.9 cases/million

Humbert M et al. *Am J Respir Crit Care Med*. 2006;173:1023-1030.

Prevalence of PAH: French National Registry

- Time interval b/w symptom onset and diagnosis: 27 months
- Mean age ~ 50yrs
- Twice as many women as men

Humbert M et al. *Am J Respir Crit Care Med*. 2006;173:1023-1030.

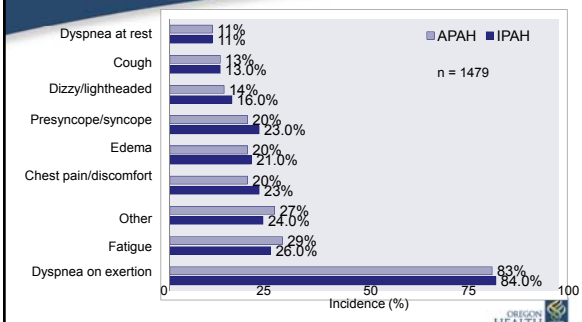
REVEAL: Database Characteristics

- 50-center US database
- Median time from initial symptoms to RHC
  - 14 months
- Median time from to first visit to pulmonary hypertension clinic
  - **15 months**
- Average body mass index
  - 28.9 + 18.4 kg/m2

	IPAH (n = 685)	APAH (n = 760)
Female-to-male ratio	3.42:1	4.43:1
Mean age at diagnosis (years)	45-54	45-54

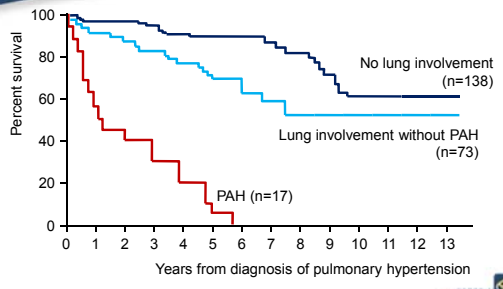
Badesh DB, et al. *Chest*. 2007;132(4 suppl):473S.

REVEAL: Symptoms at Diagnosis



Elliott EG, et al. *Chest*. 2007;132(4 suppl):631S.

PAH Associated With Scleroderma



Koh ET et al. *Br J Rheumatol.* 1996;35:989-993

PAH Associated With Connective Tissue Diseases (CTD)

- Prevalence: 10-15%
  - 33% Systemic sclerosis
  - 50% CREST
  - Overestimate: lack of RHC confirmation
- Systemic sclerosis: 75% of PAH associated with CTD
- Rapidly progressive PAH disease course
  - 1-year survival: 45% to 69%

Coghlan JG et al. *Lupus.* 2006;15:138-142. Mukerjee D et al. *Ann Rheum Dis.* 2003;62:1088-1093. Kawut SM et al. *Chest.* 2003;123:344-350. Braunwald E, Zipes BP, Lippy P, eds. Heart Disease. 2 vols. 6th ed. Philadelphia, PA: WB Saunders CO;2001:170,173, 372, 499, 1908, 1912, 1918-1921.

PAH Associated with Congenital Heart Disease (CHD)

- ~1.8 M Americans have congenital heart defect
  - 6 cases/1000 in general population
- 1.6–12.5 cases/million of PAH associated with CHD in adults
- Eisenmenger syndrome more common with large defects
  - Almost all cases of truncus arteriosus
  - 50% with large VSD
  - 10% with large ASD

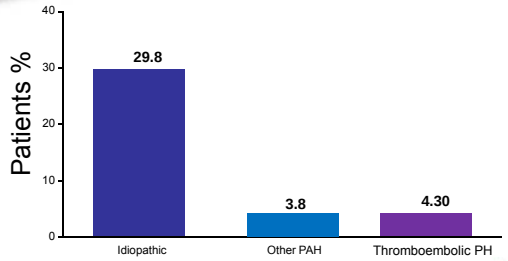
Marelli AJ et al. *Circulation.* 2007;115:163-172. Galiè N et al. *Drugs.* 2008;68:1049-1066. The Task Force on Diagnosis and Treatment of Pulmonary Arterial Hypertension of the European Society of Cardiology. *Eur Heart J.* 2004;25:2243-2278.

PAH Associated with HIV

- PAH occurs in 1 in 200 patients with HIV infection
  - PAH a significant mortality factor when present
  - With improved outcomes due to highly active antiretroviral therapy (HAART)
  - Near complete normalization of pressures with vasodilator therapy

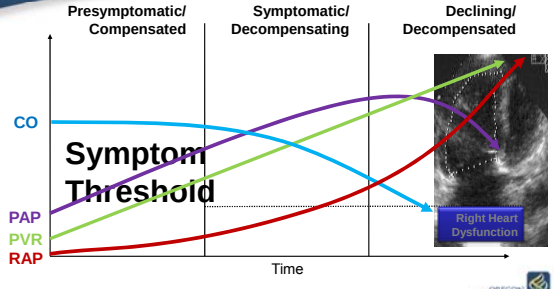
Opravil M et al. *Am J Respir Crit Care Med.* 1997;155:990-995. Speich R et al. *Chest.* 1991;100:1268-1271. Nunes H et al. *Am J Respir Crit Care Med.* 2003;167:1433 -1439.

Methamphetamine Use as a Risk Factor for PAH*



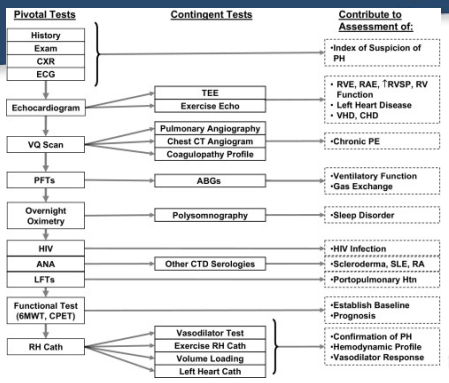
*Retrospective analysis at single PH center of adults with PH. Chin KM et al. *Chest.* 2006;130:1657-1663

PAH Progression

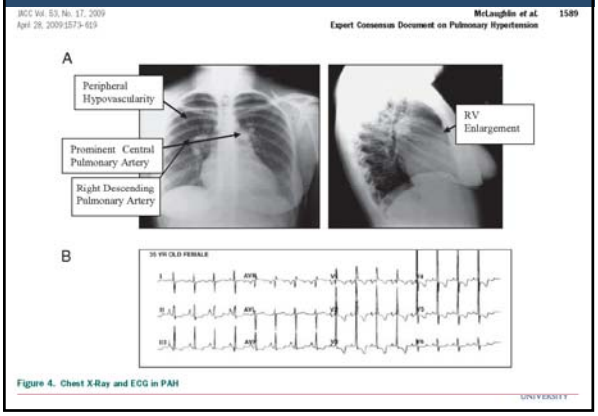


CO=cardiac output; PAP=pulmonary arterial pressure; PVR=pulmonary vascular resistance; RAP=right atrial pressure.

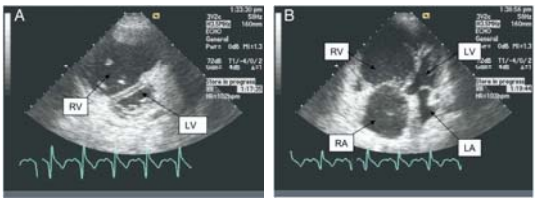
Diagnostic Approach to PAH



JACC Vol. 54, No. 1, Suppl S, 2009 Proceedings of the 4th World Symposium on PH



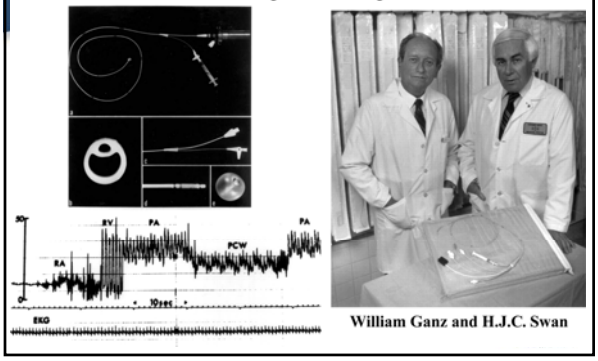
Echocardiography



Severity of Pulmonary Hypertension

Degree of Disease	Mean Pulmonary Artery Pressure (mm Hg) Cath	Systolic Pulmonary Artery Pressure (mm Hg) Echo
Mild	25-50	**40-60**
Moderate	41-55	**60-80**
Severe	>55	**>80**

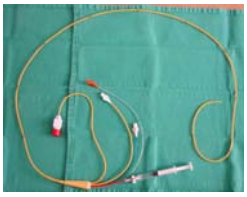
The Pulmonary Artery Catheter



William Ganz and H.J.C. Swan

Right Heart Catheterization

- Required to
  - Confirm diagnosis
  - Calculate PVR
  - Guide therapy for PAH
- Exclude other etiologies for PH
  - Intracardiac or extracardiac shunts
  - Left-heart disease

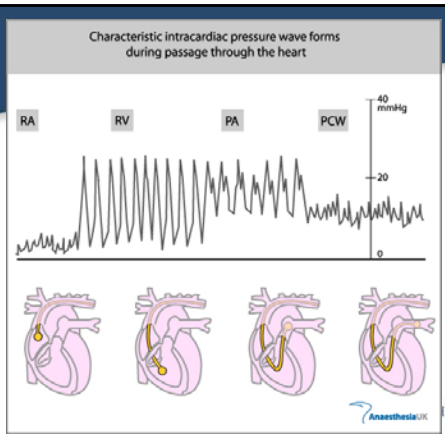


McGoon M. *Chest.* 2004;126:14S-34S.

Right Heart Catheterization

- Measure degree of right-heart dysfunction
  - Right atrial pressure
  - Cardiac output
- Vasodilator testing

McGoon M. *Chest.* 2004;126:14S-34S.



Normal Pulmonary Hemodynamic Values

Normal Pulmonary Hemodynamic Values	
Cardiac Output (liters/min)	4-6
Right atrial pressure (mmHg)	2-8
Pulmonary artery pressure (mm Hg)	
Systolic	16-24
Diastolic	5-12
Mean	9-16
Pulmonary wedge pressure (mm Hg)	5-12
Pulmonary vascular resistance (dynes/sec/cm^{-5})	80-160

Definition of PAH by Right Heart Catheterization

Increased mean pulmonary arterial pressure (mPAP)	≥25 mm Hg at rest, or ≥30 mm Hg during exercise
Normal pulmonary capillary wedge pressure (PCWP)	≤15 mm Hg
Increased pulmonary vascular resistance (PVR)	>3 woods units

Rubin LJ. *Chest.* 1993;104:236-250.

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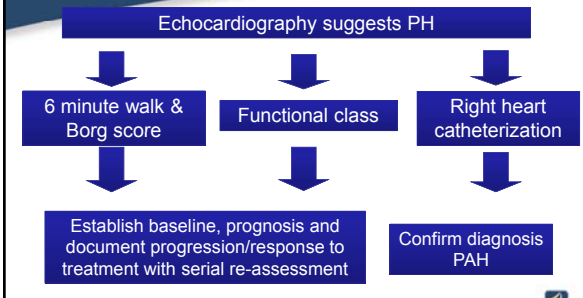
PAH Diagnostic Workup



McGoon M. *Chest.* 2004;126:14S-34S.

Case Presentation: History

- 52 year old male
  - 7 month h/o ***progressively worsening dyspnea***
- Walking slowly causes immediate severe dyspnea & dizziness **(WHO III)**
- Symptoms subside at rest

Case Presentation: History

- **2 *syncopal episodes***, both while walking at a brisk pace
- No cough, chest pain, or wheezing
- No other significant medical history
- Takes no medications

Clinical Problem 1

- Physical exam
  - Temp 37C
  - BP 105/60,
  - Pulse 102 at rest and 120 after walking,
  - RR 20/min
  - BMI 32 kg/m^2.
  - Jugular venous distention +
  - Lungs: Clear to auscultation with no wheezes or crackles

Clinical Problem 1

- Physical exam
  - ***Fixed splitting of the S2***
  - ***Increased pulmonic component***
  - Grade 1-2/6 ***holosystolic murmur at left sternal border near the fourth rib that increases with inspiration***
  - Lower extremity edema, No cyanosis or clubbing

Clinical Problem 1

- Diagnostic Data
  - CBC ***(polycythemia vera can lead to PAH)*** and resting ABG are normal
  - ***ECG rightward QRS axis and large R waves in V1***
  - Spirometry & plethysmography are normal
  - Chest radiograph shows no infiltrates or masses

Clinical Problem 1

- Which of the following is the best next step in the evaluation of this patient?

A. Bronchoscopy and trans-bronchial lung biopsy
   - Interstitial Lung Disease

B. Methacholine challenge test
   - Asthma

C. Right-heart catheterization & pulmonary angiography
   - Pulmonary Hypertension

D. Trans-thoracic echocardiography
   - Pulmonary Hypertension

Clinical Problem 1

- ANSWER: D
  - Transthoracic echocardiography
- In patients with suspected pulmonary HTN
  - TTE can suggest the presence of pulm HTN
  - Evaluate for cardiac causes of elevated pulm artery pressure

Goals of Management of PAH

- Improve survival
- Prevent worsening
- Improve hemodynamics
- Maintain or improve functional class
- Improve exercise capacity
- Improve daily functioning and quality of life

Considerations for Selecting Initial Therapy for PAH

- Severity of symptoms
- Physical examination (right-heart failure?)
- Rate of progression
- Echocardiogram (RV size and function)
- Right heart catheterization
  - Mean PA pressure and cardiac index

Considerations for Selecting Initial Therapy for PAH

- ***6-minute walk distance***
- BNP/NT-pro-BNP
- Capability of patient to handle parenteral therapy

Considerations for Selecting Initial Therapy for PAH

- Parenteral therapy is first choice in very advanced patients
- Other issues
  - Drug-drug interactions
  - Adverse events
  - Comorbid conditions (eg, diabetes)
  - Route of administration
  - Dosing intervals
  - Cost

Cost Analysis

- Approximate annual cost
  - Sildenafil $12 761
  - Bosentan $55 890
  - Ambrisentan $56 736
  - Iloprost $92 146
- Based on a 70-kg patient at the lower end of the dosing spectrum
  - Epoprostenol $33 153
  - Treprostinil $97 615

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Questions

PAH Determinants of Risk

Lower Risk	Determinants of Risk	Higher Risk
No	Clinical evidence of RV failure	Yes
Gradual	Progression	Rapid
II, III	WHO class	IV
Longer (>400 m)	6MW distance	Shorter (<300 m)
Minimally elevated	BNP	Very elevated
Minimal RV dysfunction	Echocardiographic findings	Pericardial effusion, significant RV dysfunction
Normal/near normal RAP and CI	Hemodynamics	High RAP, low CI

McLaughlin VV, McGoon MD. *Circulation*. 2006;114:1417-1431.