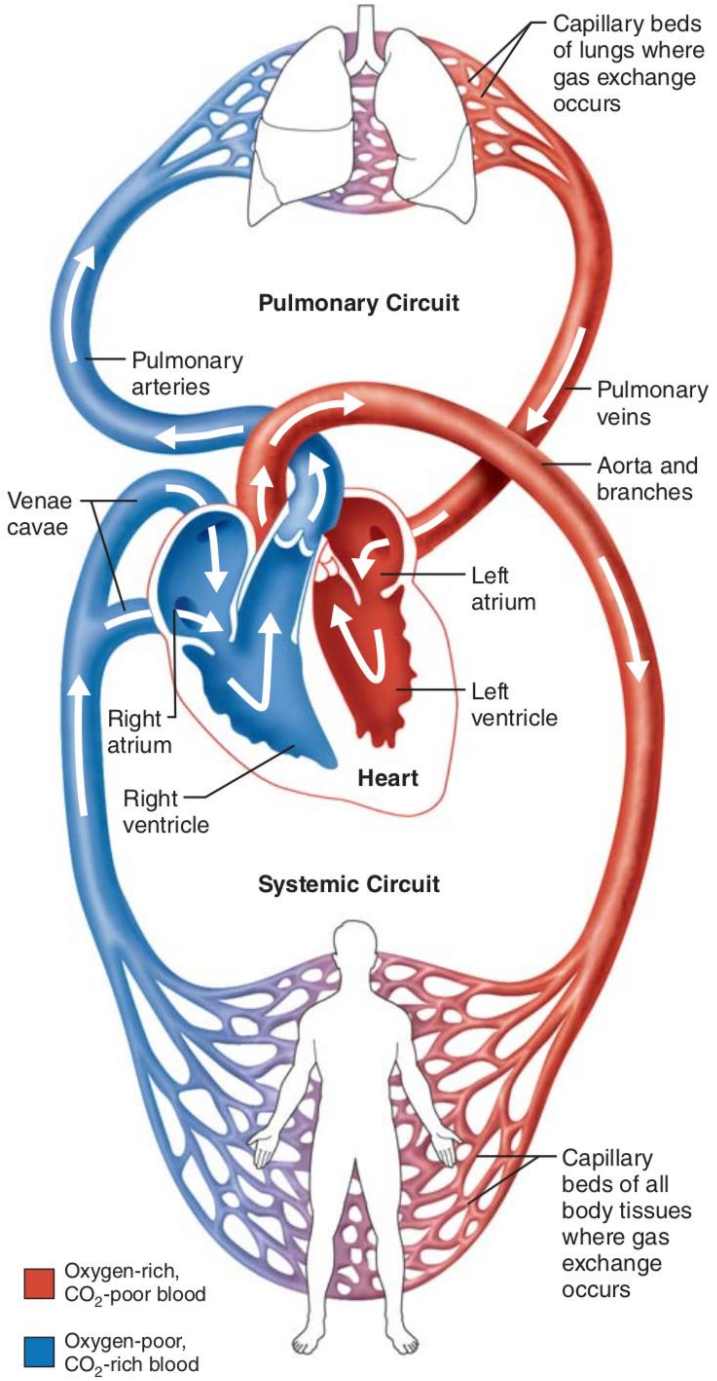
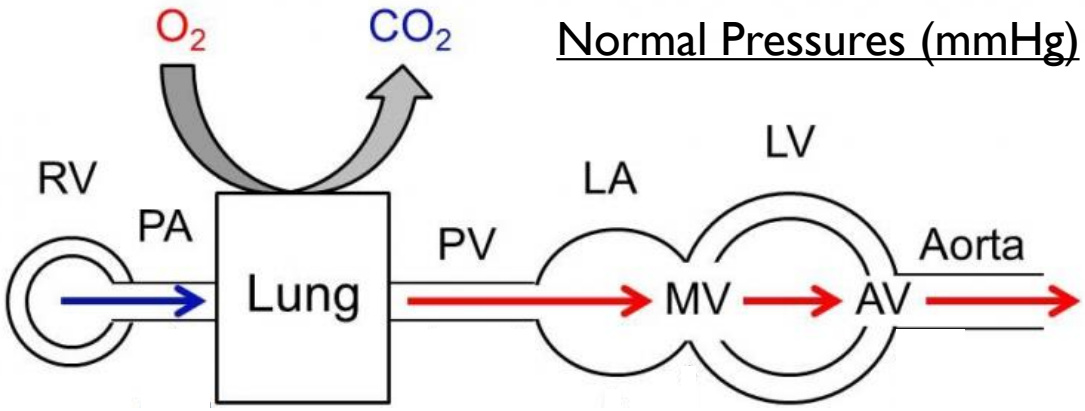
PULMONARY HYPERTENSION IN THE ICU

NEHAL BHATT, MD

ATHENS PULMONARY AND SLEEP





Normal Pressures (mmHg)

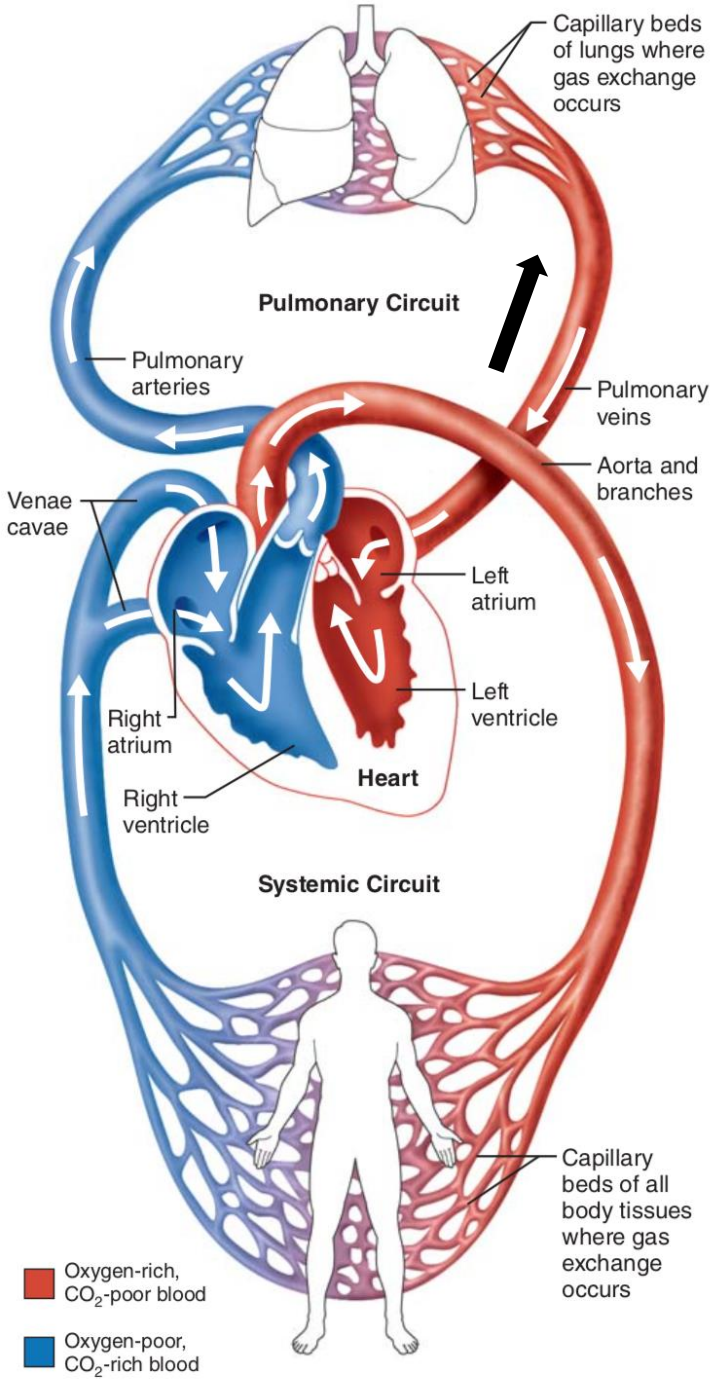
mPAP =15

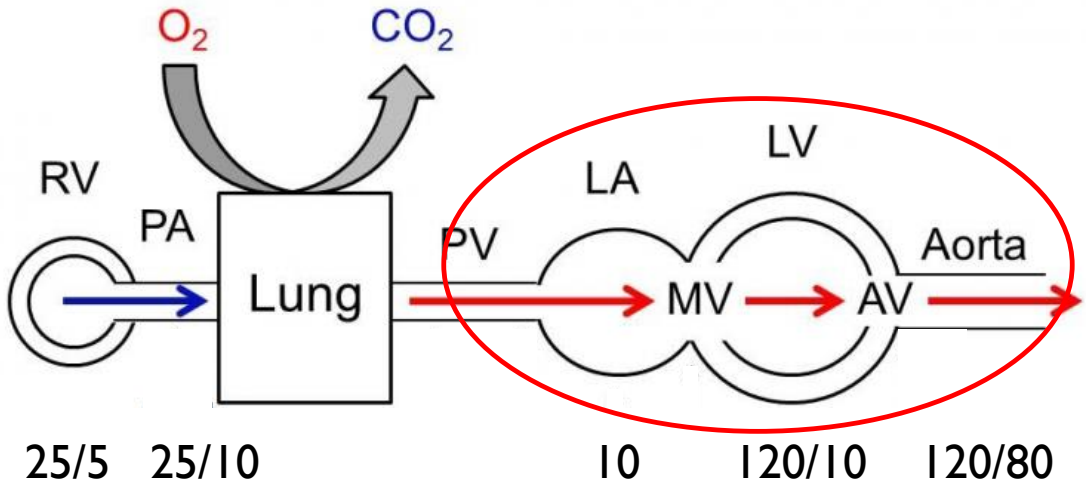
LVEDP = 10

Pulmonary Hypertension (PH)

mPAP >25 mmHg

(usually sPAP or RVSP > 40 mmHg)





mPAP =15

LVEDP = 10

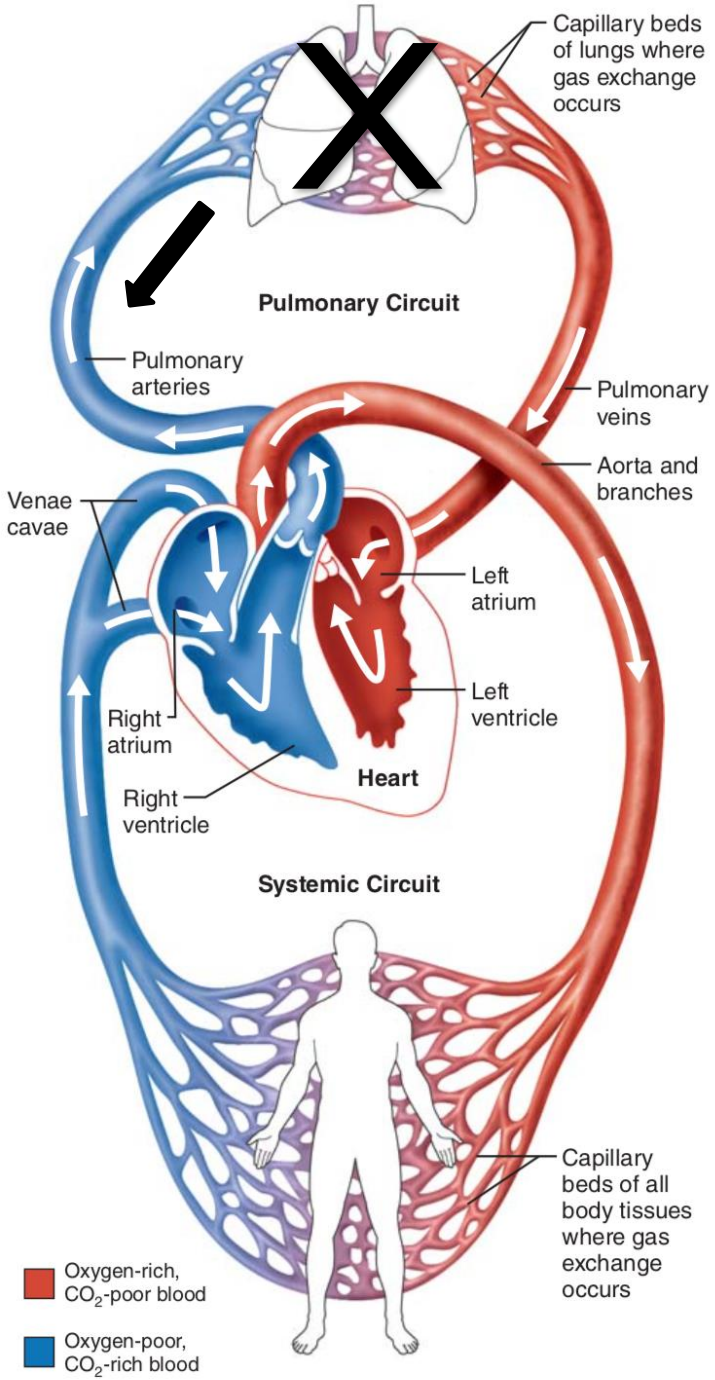
40/15

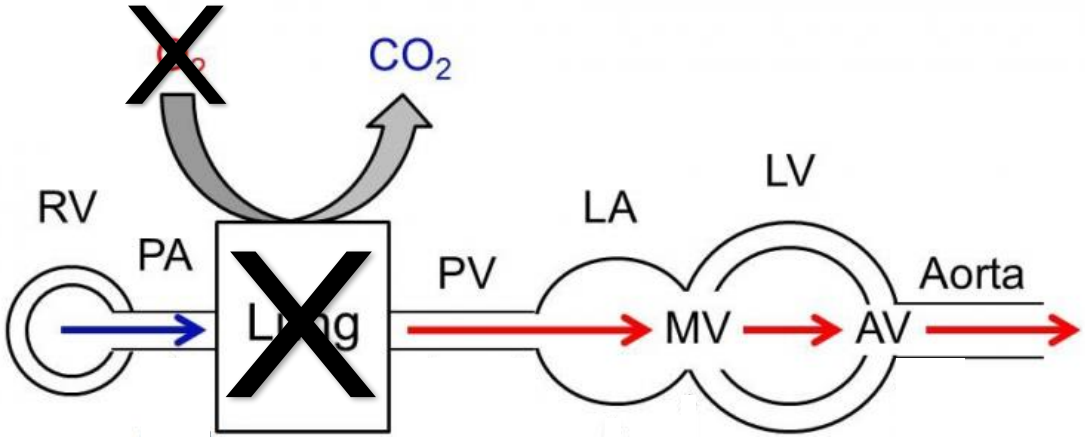
mPAP > 25

LVEDP > 15

Post-Capillary PH
or
Pulmonary Venous Hypertension

(Due to Left Heart Disease)



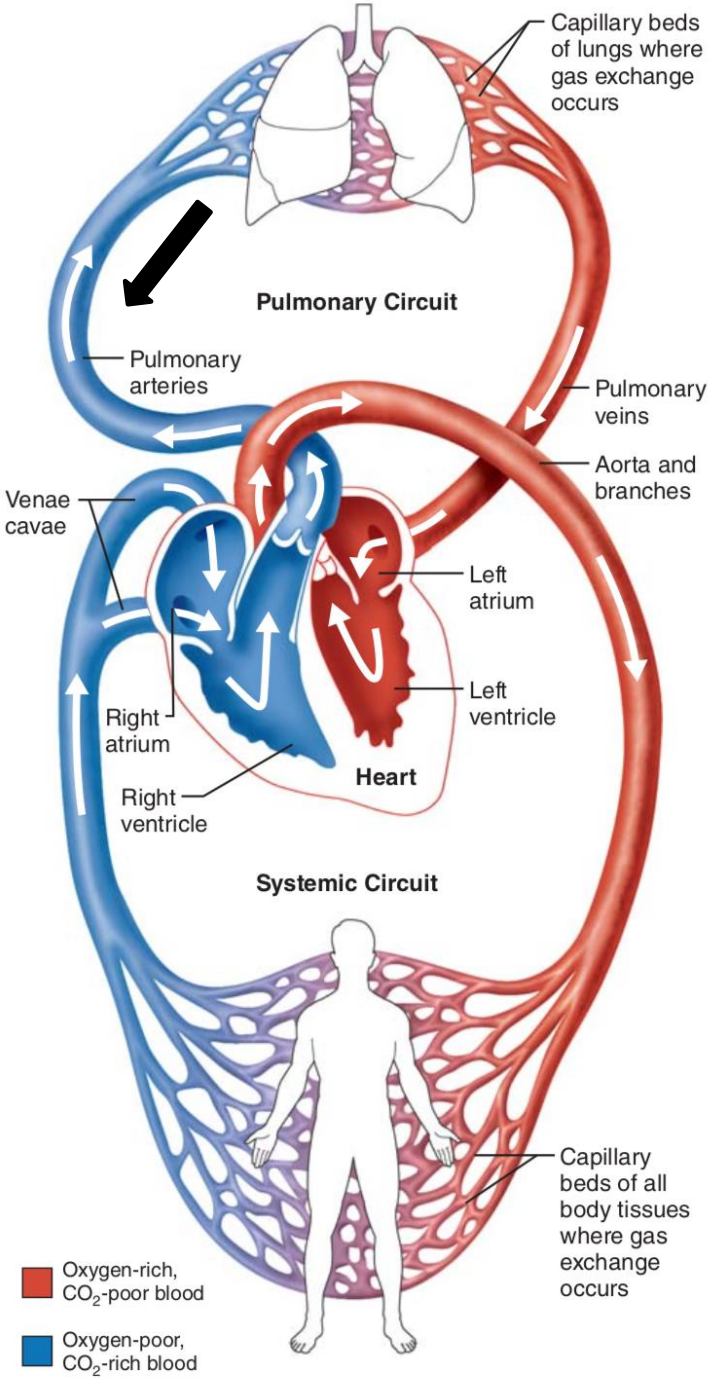


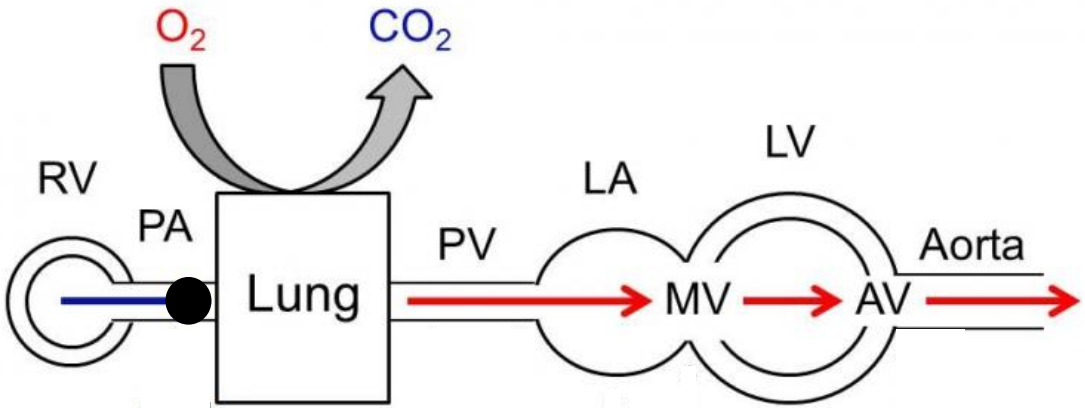
mPAP =15

LVEDP = 10

mPAP > 25

PH Due to Lung Disease and/or Hypoxia





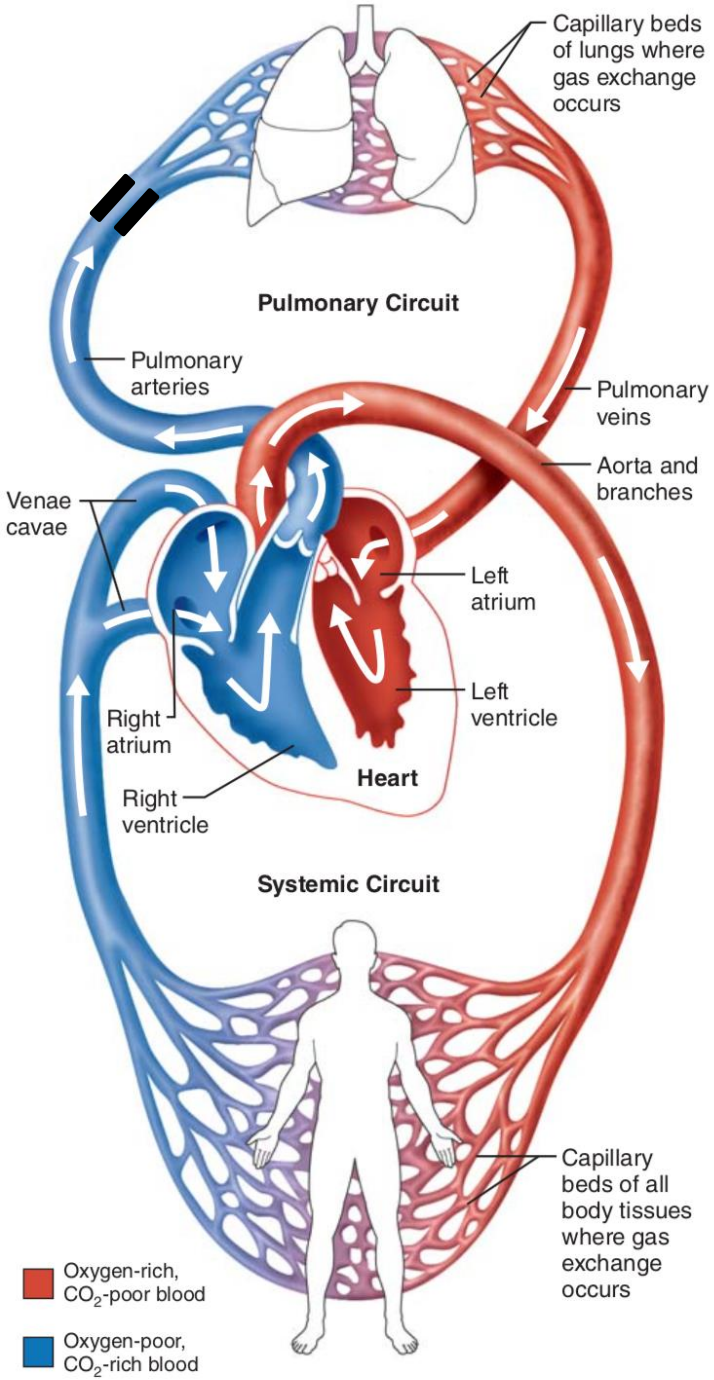
mPAP =15

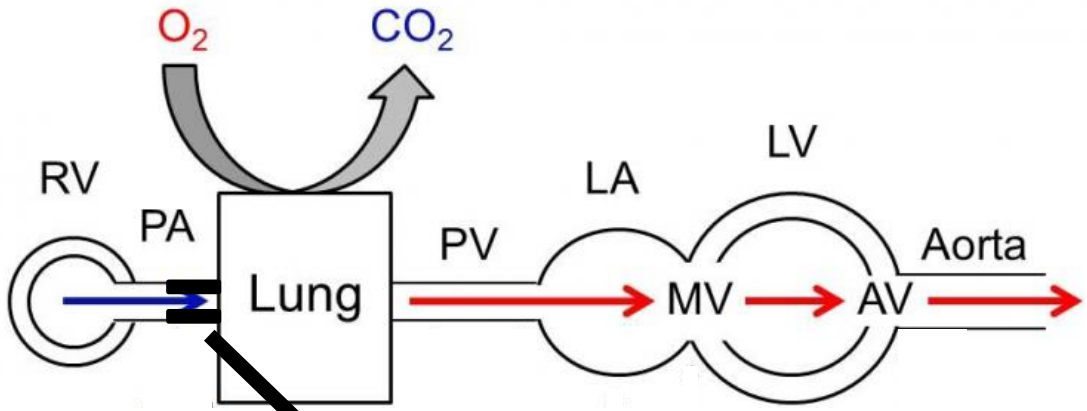
LVEDP = 10

mPAP > 25

PH Due to Thromboembolism

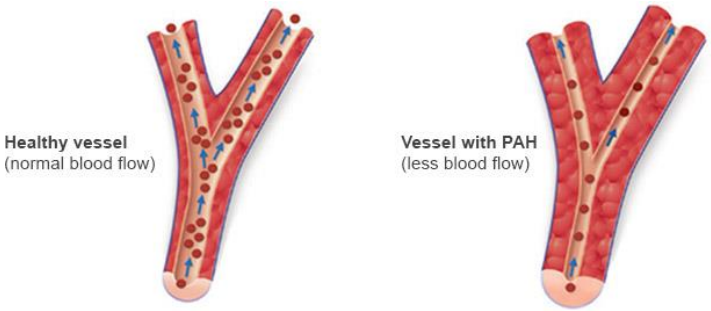
(Acute PE or CTEPH)





mPAP =15

LVEDP = 10



Pulmonary Arterial Hypertension = PAH

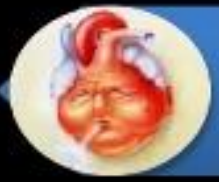
mPAP > 25 mmHg

PCWP or LVEDP < 15 mmHg

PVR > 3 wu

Pulmonary Hypertension Classification
Dana Point 2008 (WHO)

Group 1: Primary vessel problem
(pulmonary arterial hypertension, PAH)



Group 2: Problems with left heart & valves

Group 3: Problems with lungs/hypoxia

Group 4: Thromboembolic

Group 5: Anything else e.g. sarcoid

Group 1 Pulmonary Arterial Hypertension

- Idiopathic
- Familial
- Associated conditions
  - *Connective tissue diseases e.g. scleroderma*
  - *Congenital systemic-pulmonary shunts*
  - *Portal hypertension*
  - *HIV*
  - *Drugs and toxins*
  - *Other e.g. thyroid disease, myeloproliferative or glycogen storage diseases*
- Significant venous or capillary involvement
  - *Pulmonary veno-occlusive disease (PVOD)*
  - *Pulmonary capillary hemangiomatosis (PCH)*
- Persistent pulmonary hypertension of the newborn

Non-PAH PH in the ICU

- Acute/chronic PE
- Acute respiratory distress syndrome
- Chronic lung disease
- Acute/chronic left heart failure
- Mitral/aortic stenosis
- Severe sepsis
- Post cardiac or thoracic surgery
- ESRD

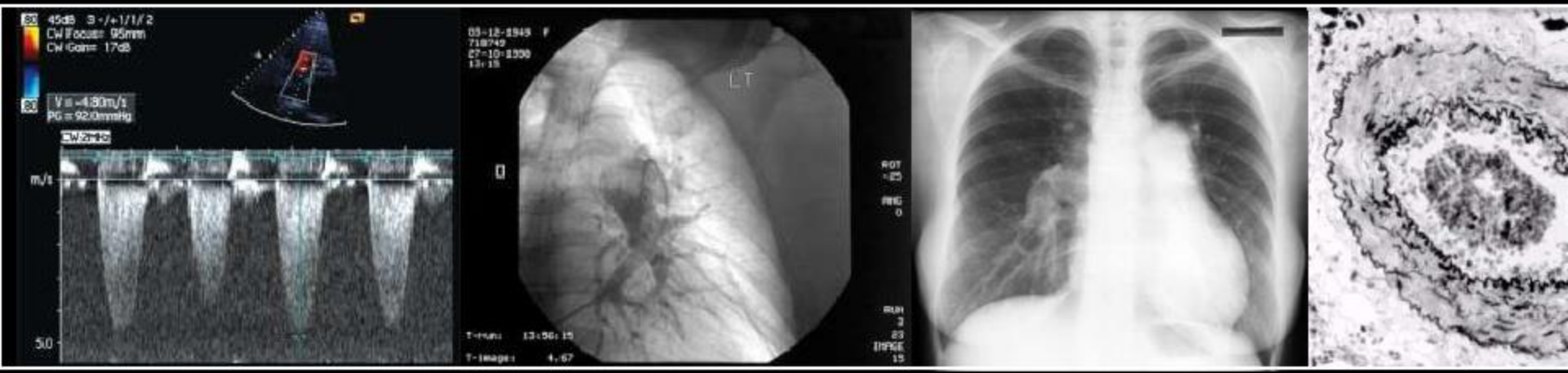
Thromboembolism

Lung disease

Heart disease

Speed of onset determines tolerance to insult

- RV copes poorly with the acute insult
- acute cor pulmonale has very poor outcome



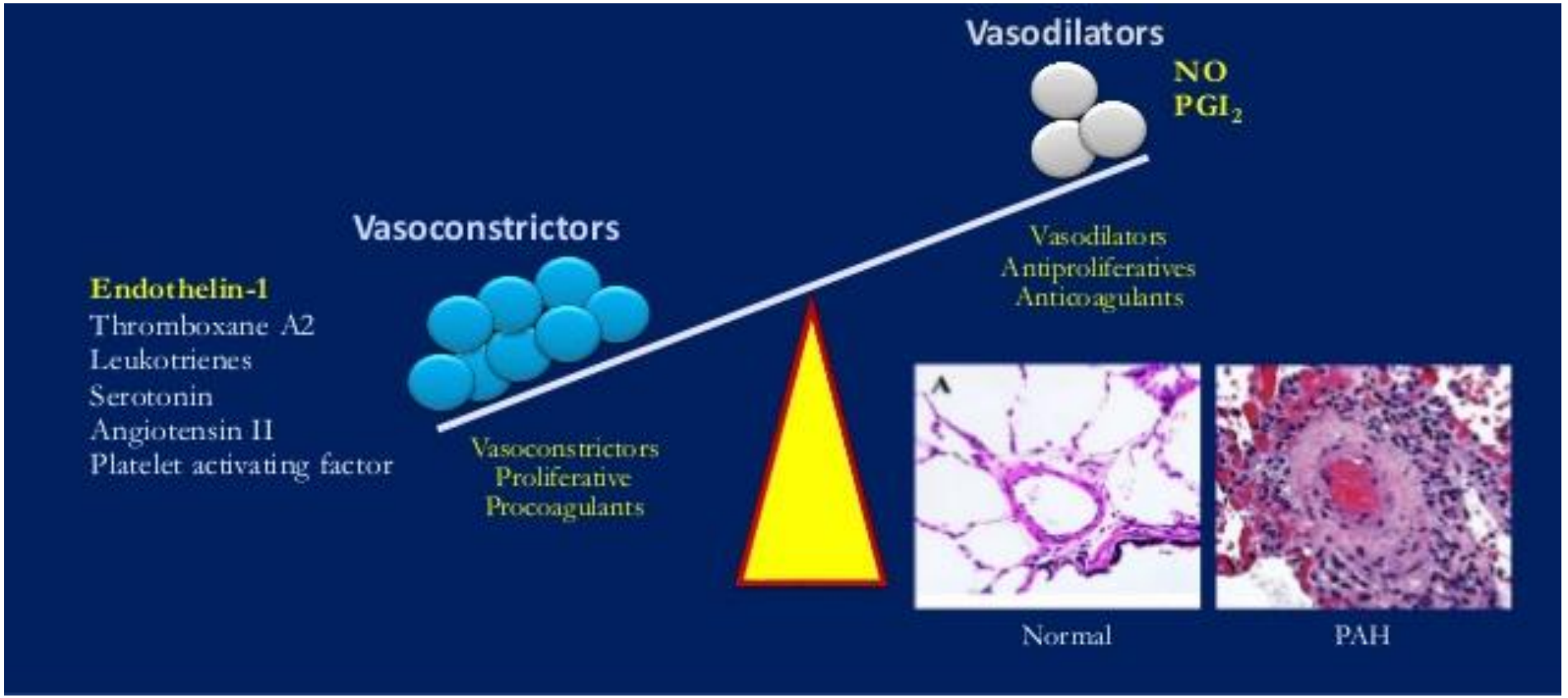
PATHOPHYSIOLOGY

Pathophysiology

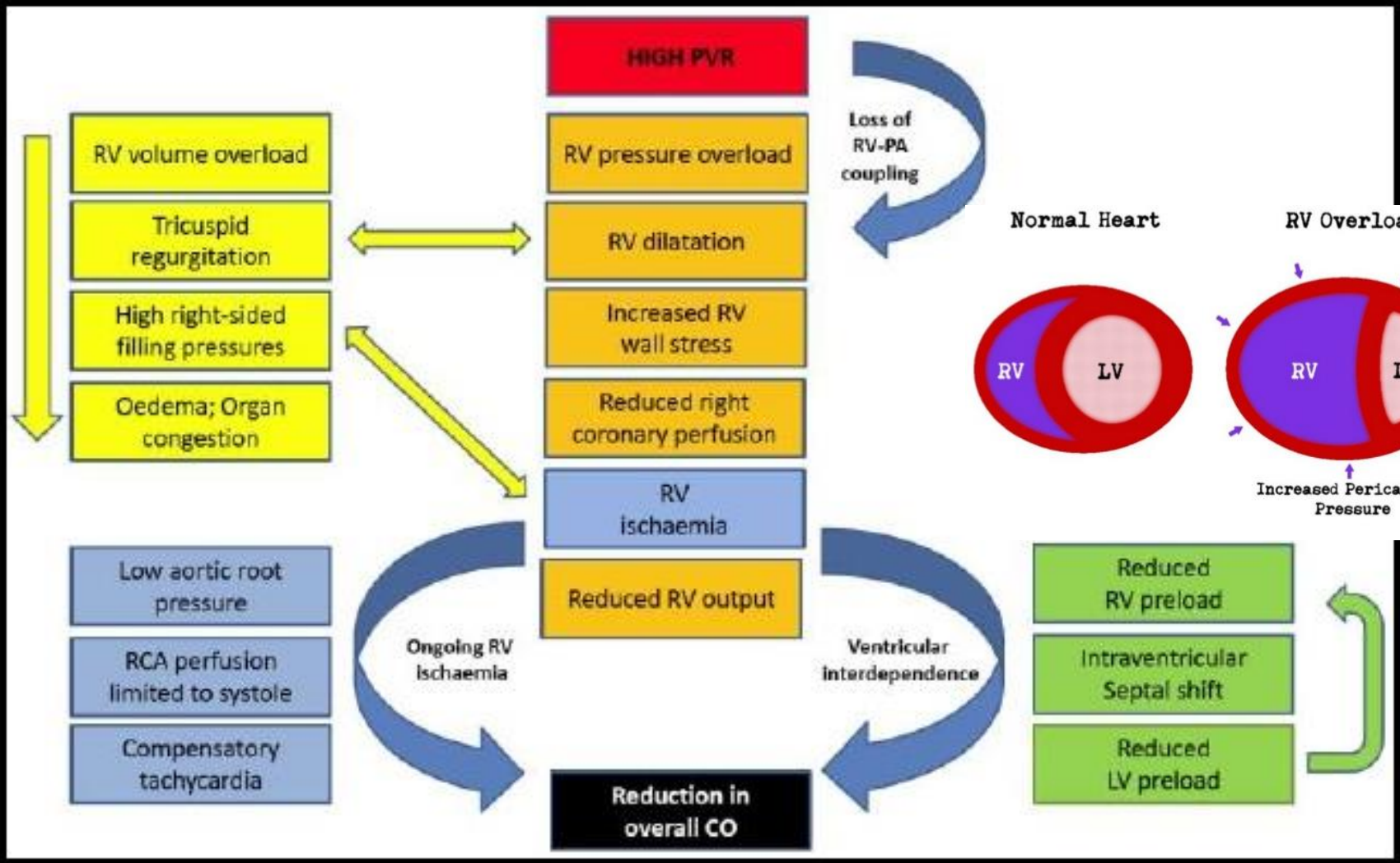
- PAH
  - Mainly pre-capillary arteries and arterioles
  - Increased vasoconstriction (ET-1 etc.)
  - Vascular remodeling (smooth muscle proliferation/neointima)
  - In situ thrombosis
  - Endothelial dysfunction
- Lung disease with hypoxia e.g. ILD, COPD
  - Hypoxic vasoconstriction
  - Vascular destruction
- ALI/ARDS
  - Hypoxic vasoconstriction
  - Increased vasoconstriction (ET-1 etc.)
  - Intravascular fibrin and cell debris

Pathophysiology of PAH

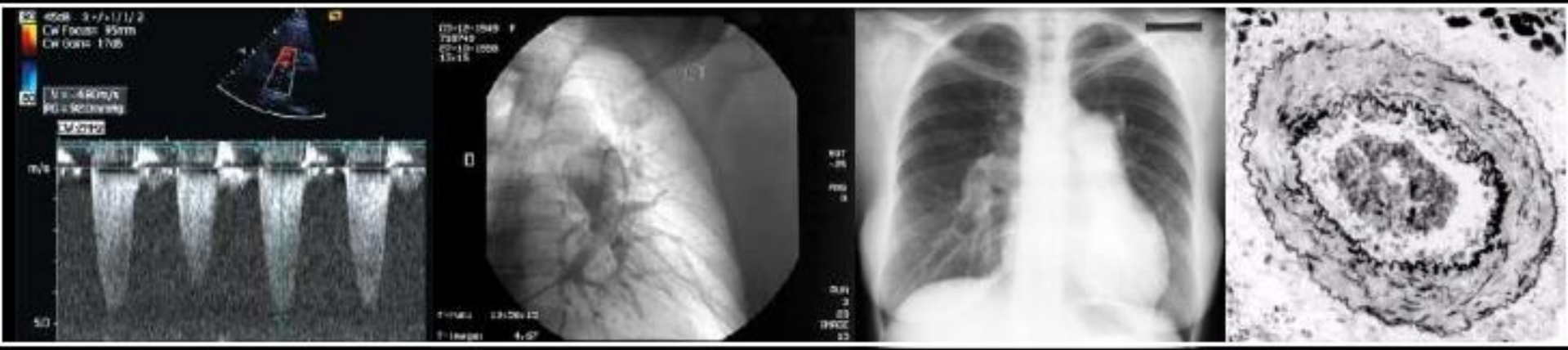
Imbalance of Vasoconstrictors and Vasodilators



Hemodynamic Impact of PH

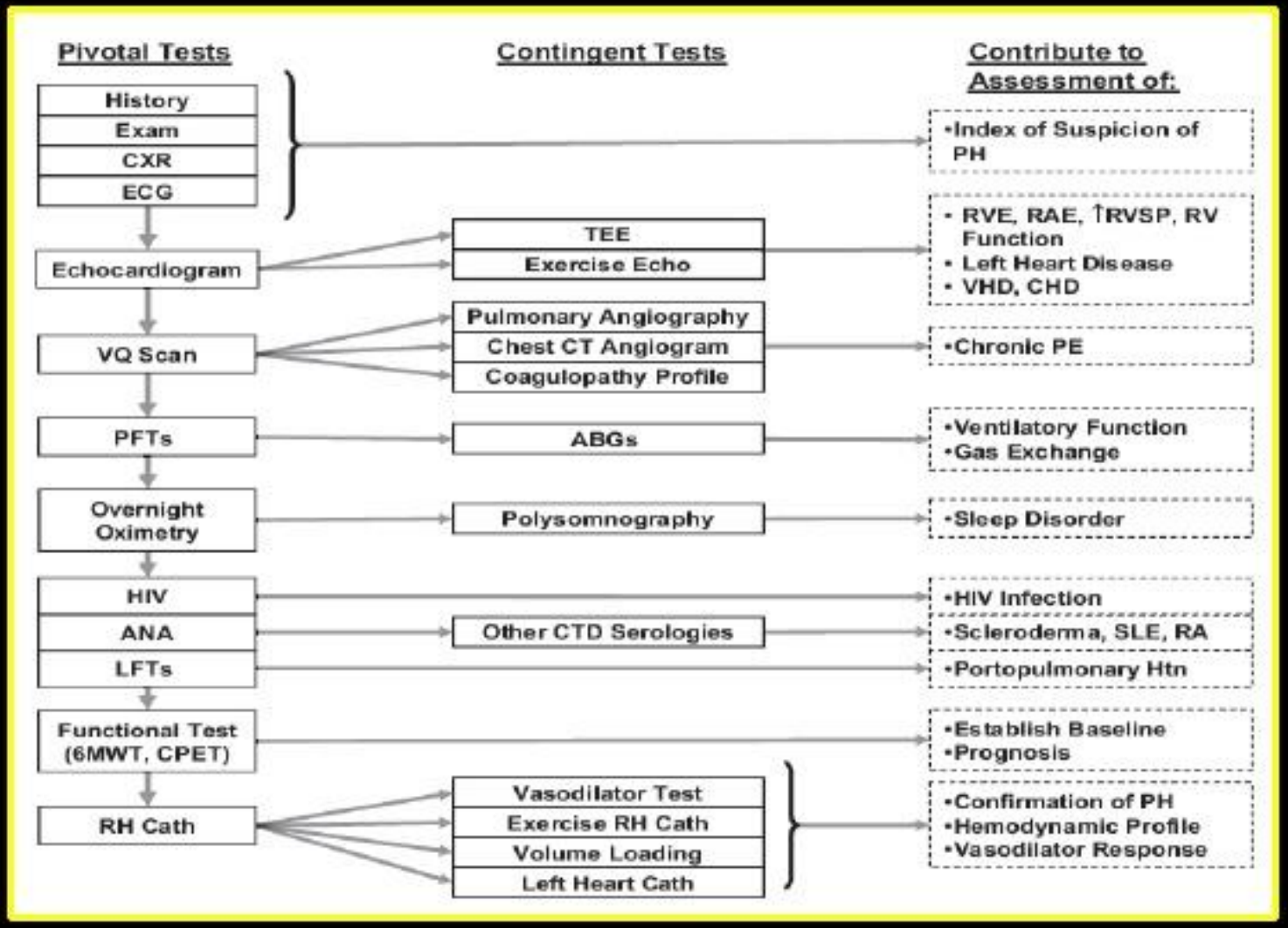


Price LC et al. *Critical Care* 2010, **14**:R169 doi:10.1186/cc9264

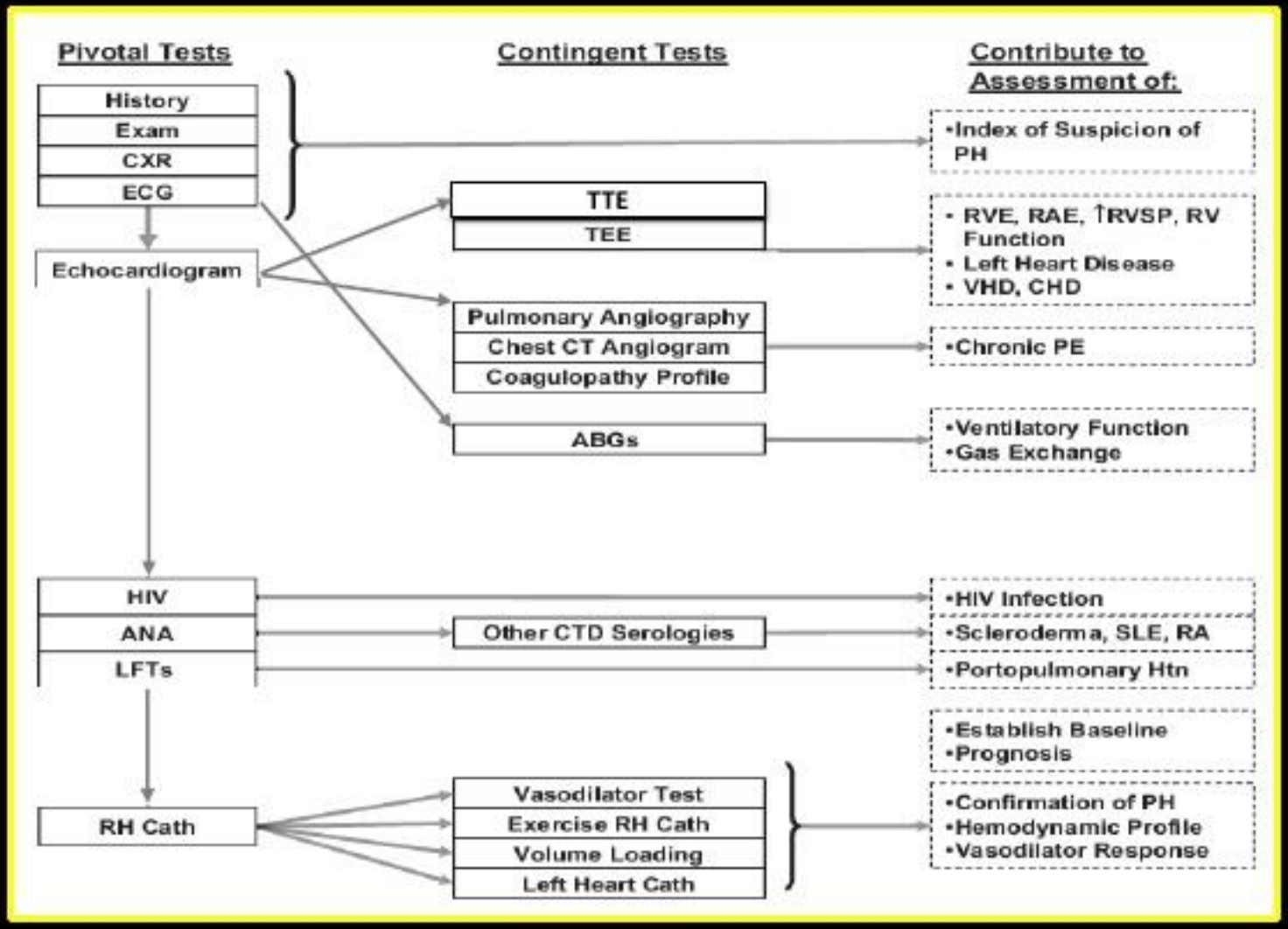


DIAGNOSTIC WORK-UP

Diagnostic evaluation of chronic PH



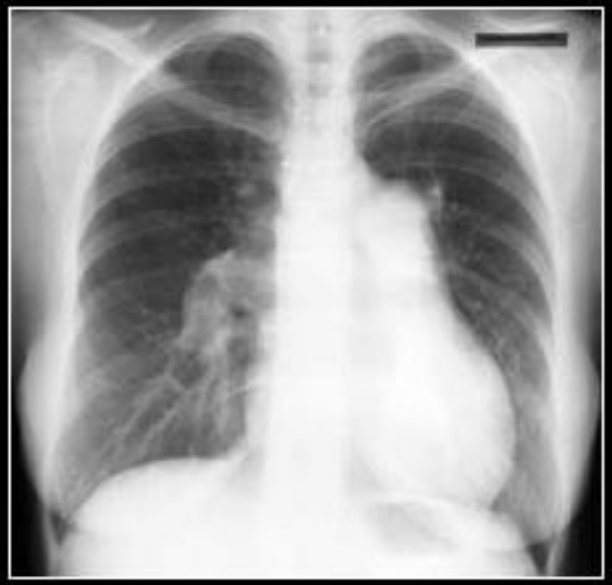
Diagnostic evaluation of PH in ICU

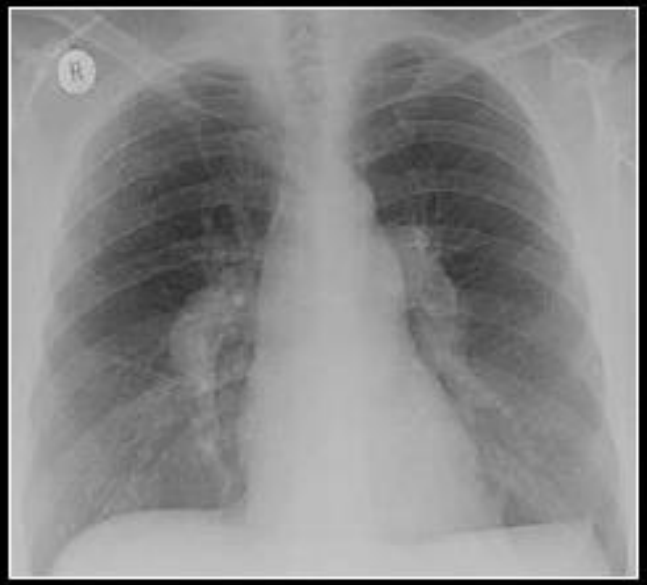


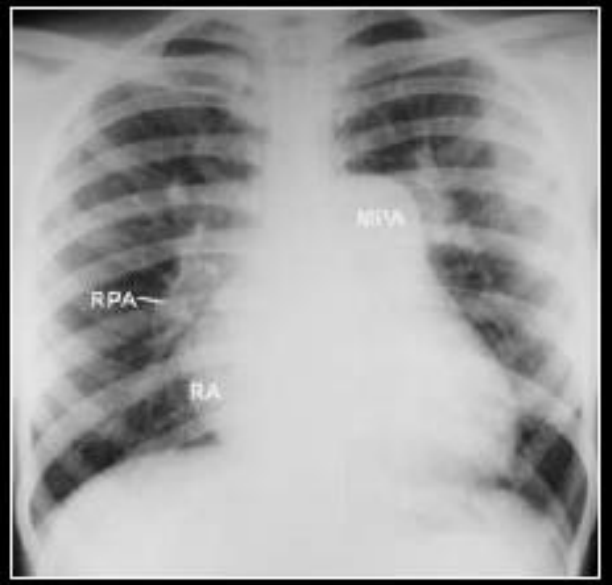
PH HISTORY AND EXAM

- Clinical History = symptoms
- Clinical Exam: PH severity
  - Prominent S2(P2), RV heave, JVD, murmurs (TR), Hepatojugular reflux, Hepatosplenomegaly, Peripheral edema, Ascites,
  - low CO state (low BP, diminished pulse pressure, cool extremitie)s
- Clinical Exam: find underlying cause or association of PH
  - Central cyanosis, clubbing, other murmurs, rales/dullness/diminished breath sounds
  - Obesity, kyphoscoliosis, Mallampati airway III-IV
  - CREST syndrome, thrombophlebitis, signs of portal hypertension

Chest X-ray Features





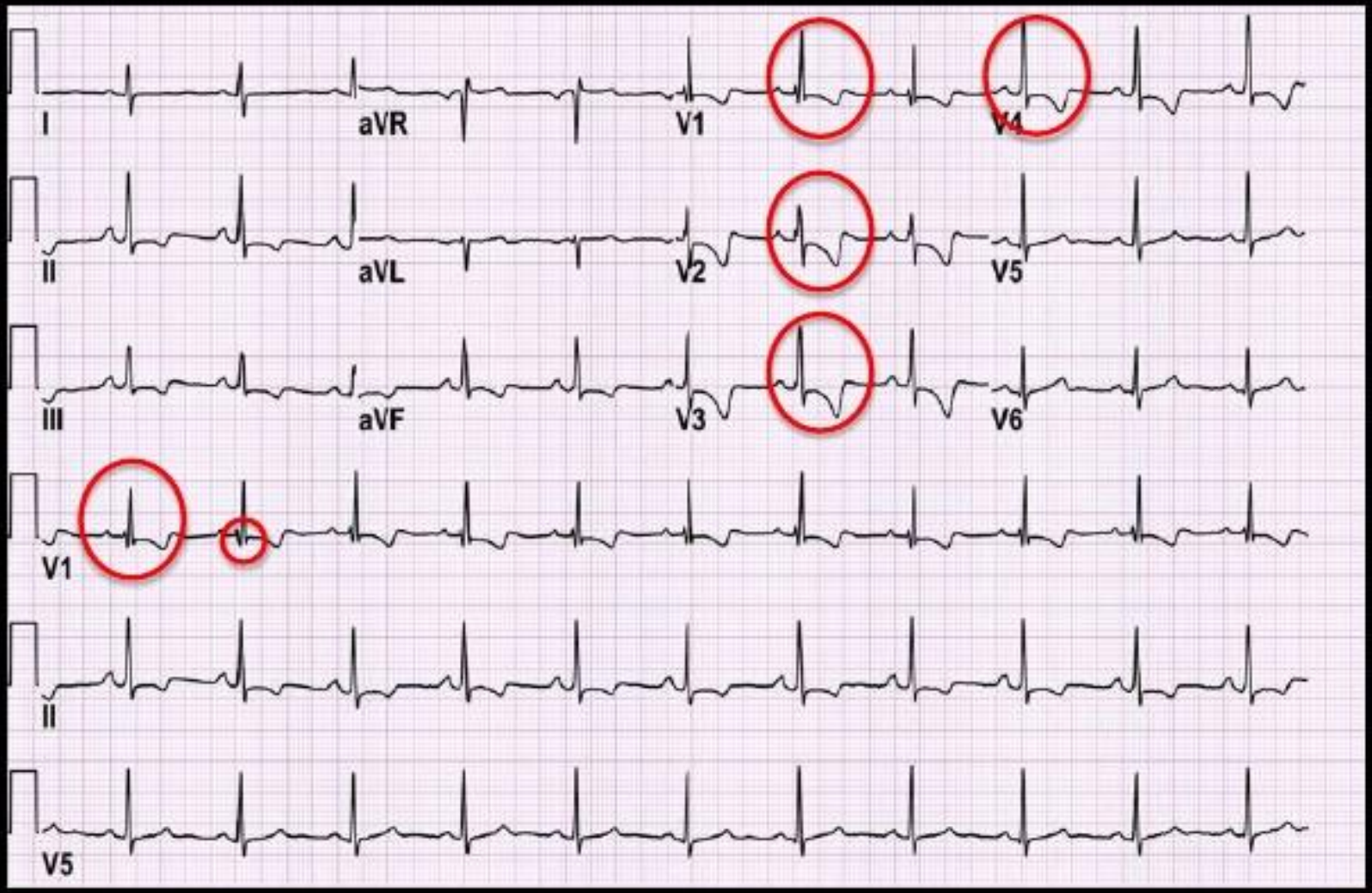


- Enlargement of the main, right and left pulmonary arteries
  - Main PA diameter > 29 mm, right PA > 16 mm and left PA > 15 mm
- Tapering of the pulmonary vasculature ('peripheral pruning')
- Heart size - normal or enlarged e.g. right atrial contour
- Underlying causes, e.g. COPD, cardiac disease
- Loss of aortico-pulmonary window

ECG Features (insensitive)

- Right atrial enlargement
  - P wave >2.5 mm tall in II and/or >1.5 mm in V1 (P pulmonale)
- Right ventricular hypertrophy or strain
  - R/S ratio > 1 in lead V1
  - R/S > 1 in V3R or V4R
  - R wave lead V1 >_7mm
  - qR in V1
  - rSR' in V1 with R' >10mm
  - Incomplete RBBB
  - ST depression or T inversion in V1-3 +/- II, III, aVF (if STRAIN)
- Right axis deviation of QRS
  - Right axis deviation of > +90 degrees

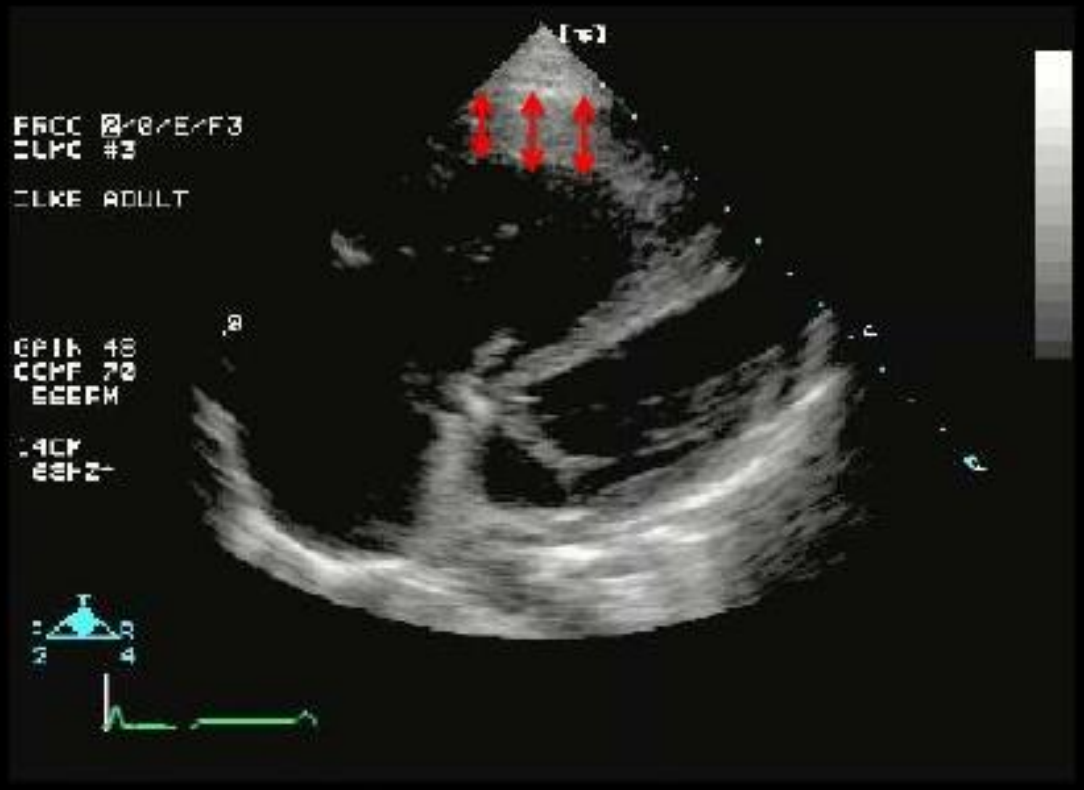
ECG with RVH/strain



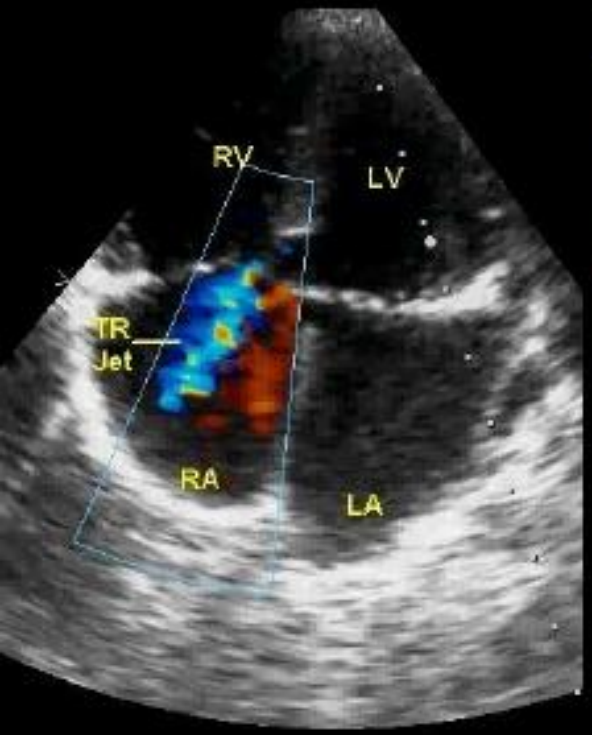
Echo Features of Pulmonary Hypertension

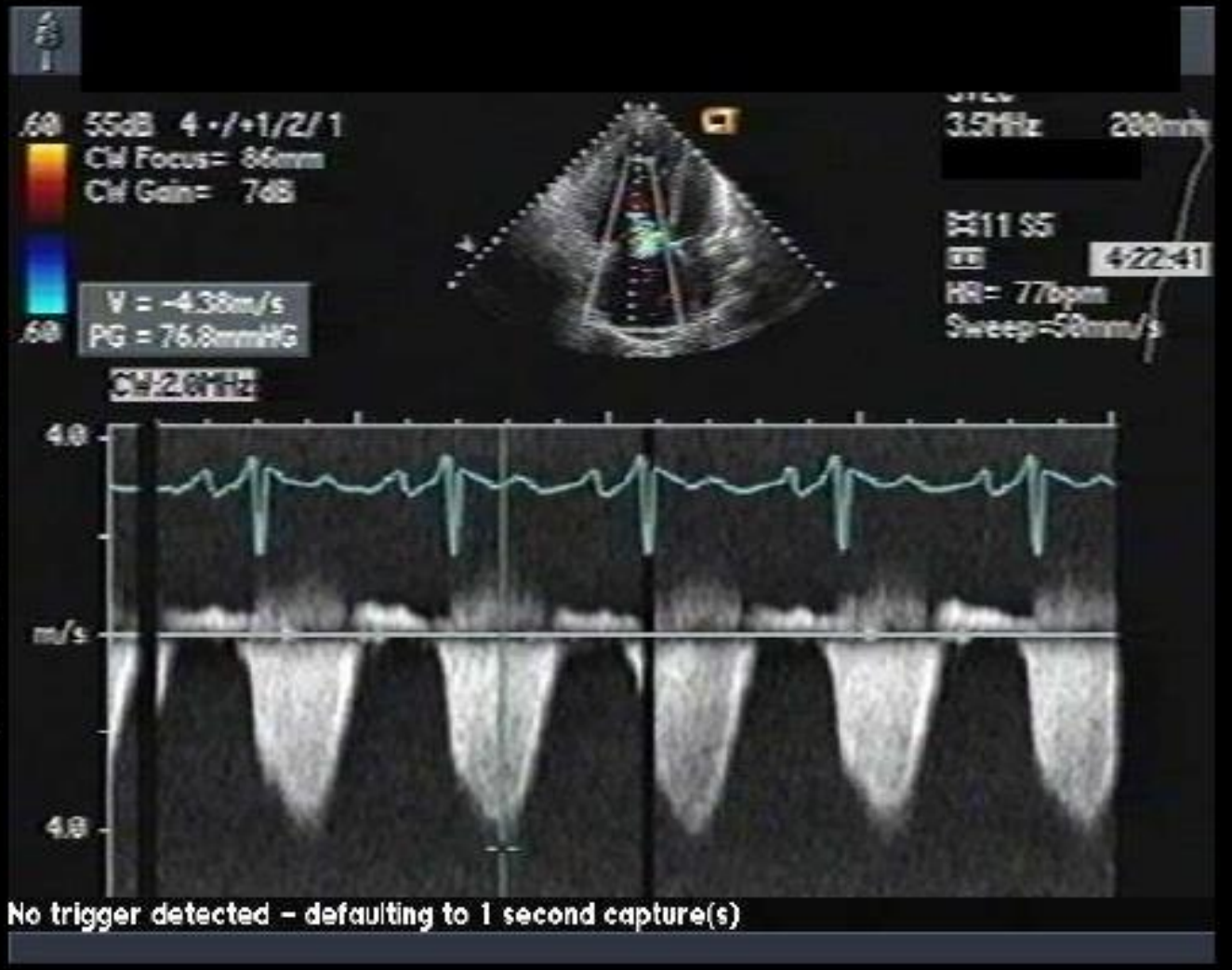
Right ventricular hypertrophy
Significant tricuspid regurgitation - Using TR jet estimated RVSP is $4V^2$ + RAP
Right atrial enlargement
Right ventricular enlargement/dilatation - D-shaped LV on short axis
Right ventricular dysfunction
Pulmonary regurgitation - Using PR jet estimated PAEDP is $4V^2$ + RAP
Reduced RV outflow tract velocity, short acceleration time
Dilated IVC not collapsing with respiration (if patient not ventilated)
Patent foramen ovale (bubble contrast used)
Pericardial effusion
Dilated pulmonary arteries

Right ventricular hypertrophy



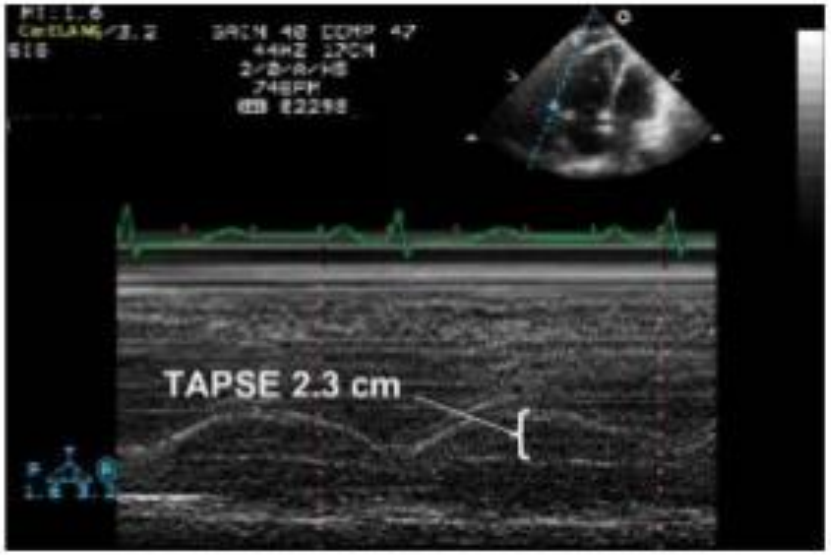
Tricuspid regurgitation

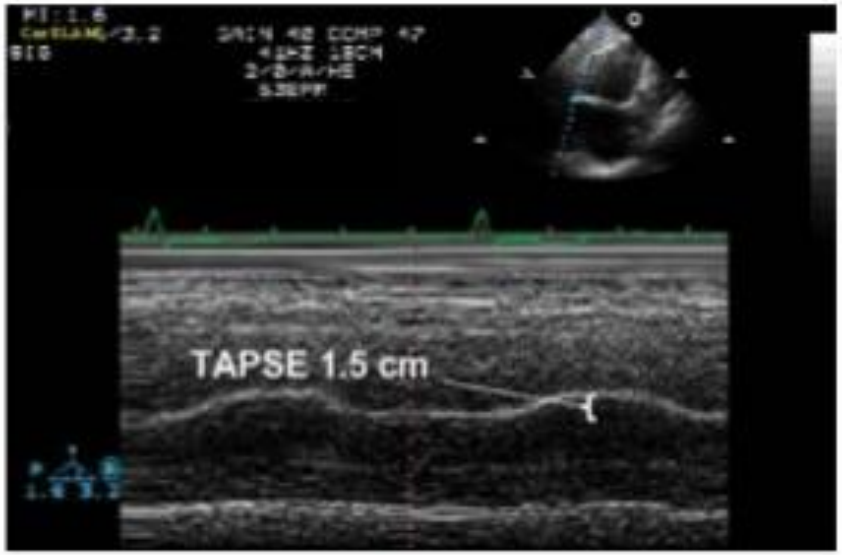




Tricuspid Annular Plane Systolic Excursion (TAPSE)

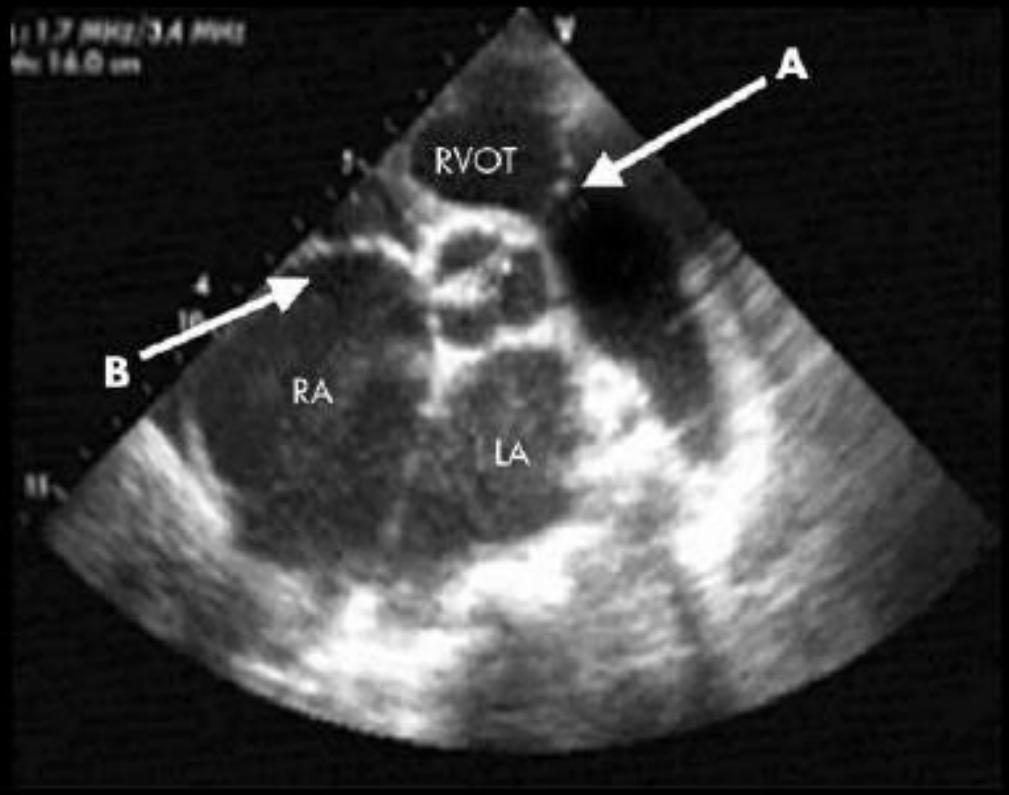
- Contraction of the RV is mainly longitudinal, and the tricuspid annulus displaces toward apex during systole
- Imaging through lateral RV free wall with M-mode assesses longitudinal displacement (excursion) of the tricuspid annulus
- Less TAPSE occurs when RV function declines
- Baseline TAPSE < 1.8 cm has negative prognostic implications

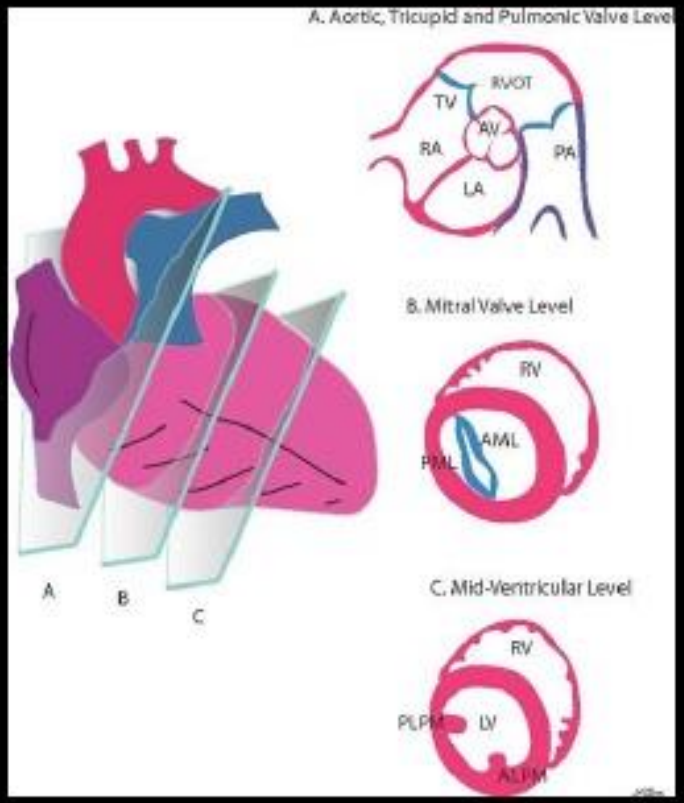




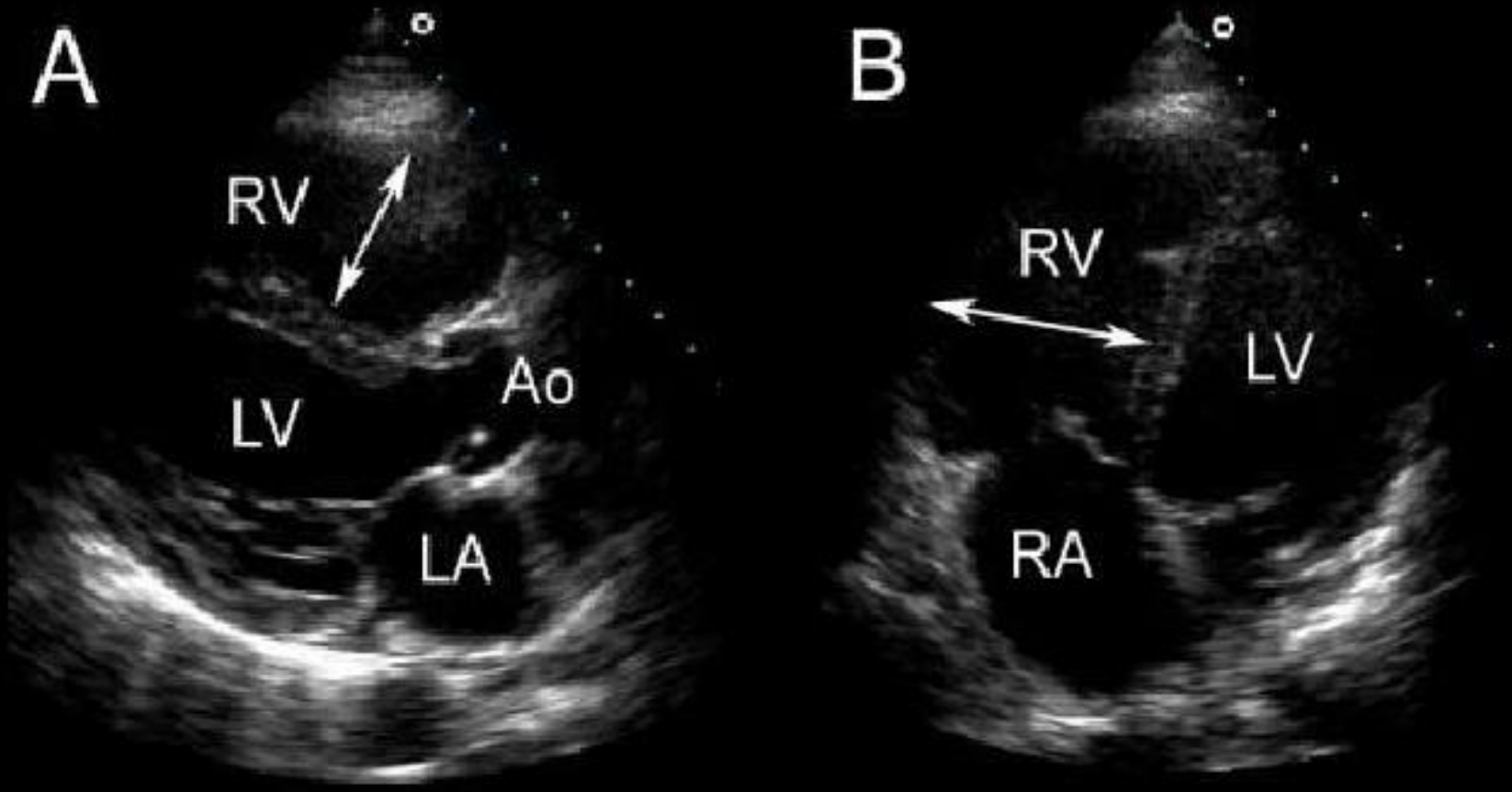
Forfia PR, et al. *Am J Respir Crit Care Med*. 2006;174:1034-1041.

Right atrial enlargement





Right ventricular enlargement



Normal RV:LV ratio < 0.6, severe dilation at 1:1

Right ventricular dysfunction

- Hypokinesis
- Akinesis
- Septal dyskinesia
- McConnell's sign: severe hypokinesis of RV mid-free wall, with normal apical contraction seen in acute PE

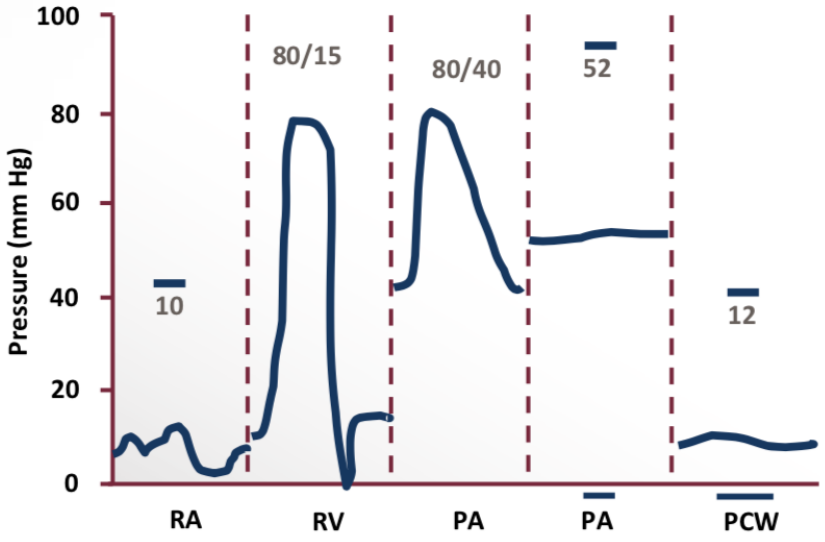
Right Heart Catheterization

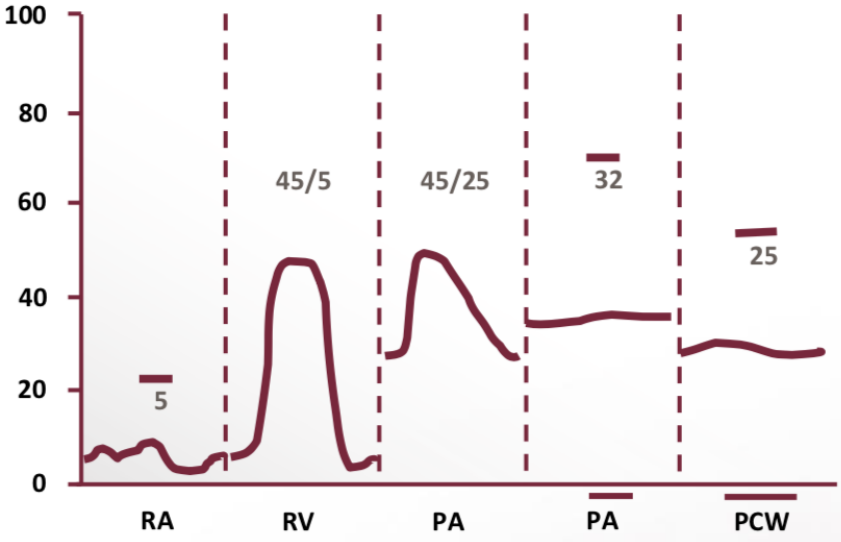
- YES!
- Challenging!
  - Severe TR
  - Elevated PAP
  - CO measurement may be inaccurate (TR & low CO)
  - Tachyarrhythmias (even AF) can be disastrous!
- One time when it may actually help!

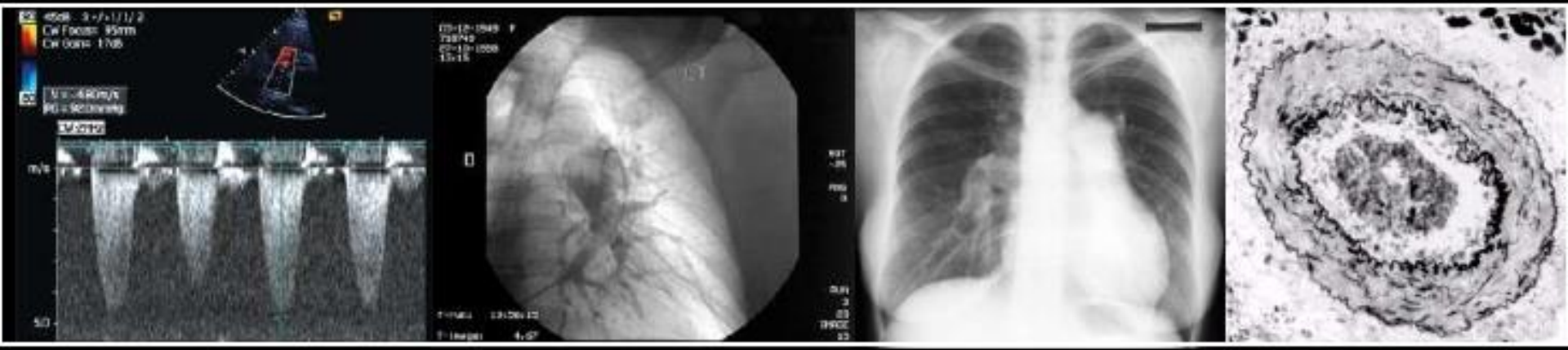
RHC Pressure Tracings: PAH vs PVH[1-4]

PAH	
CO	5 L/min
TPG	40 mm Hg
PVR	8 WU

PVH	
CO	4 L/min
TPG	7 mm Hg
PVR	1.75 WU







CLINICAL IMPACT

Why do we care?

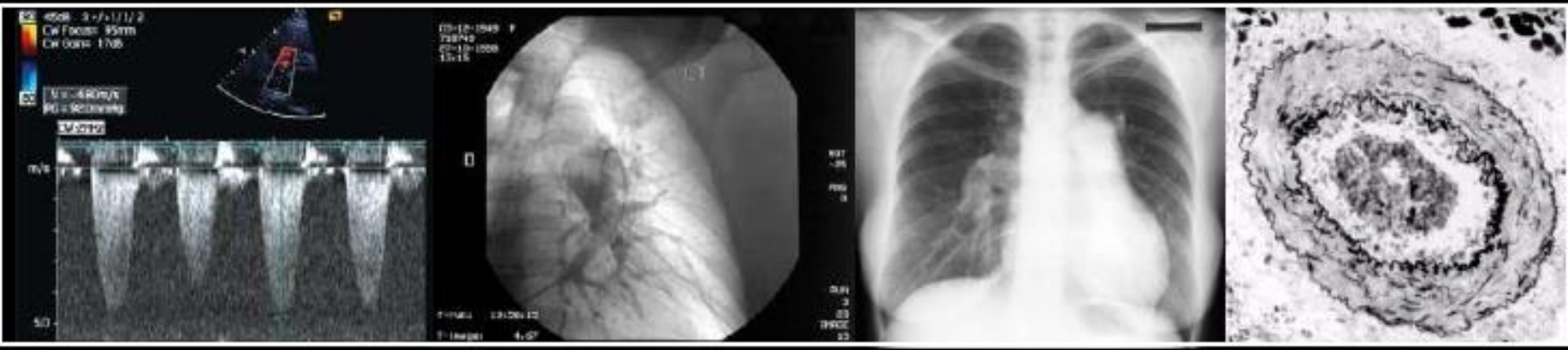
- More patients have it in ICU than you think!
- Almost any typical ICU insult can tip them over
- They can deteriorate VERY rapidly
- Too much or too little fluid = BIG changes in cardiac index and gas exchange
- Altered LV shape causes diastolic dysfunction and reduces LV stroke volume
- Develop interstitial edema at lower PCWP

Severe PH = Independent Risk Factor for Death

Prognostication in Group 1 (PAH)

Determinant	Low risk (good prognosis)	High risk (bad prognosis)
Clinical RV failure	NO	YES
WHO functional class	II/III	IV
6 min walk distance	> 400m	< 300m
CPET results	VO_2 max > 10.4 ml/kg/min	VO_2 max < 10.4 ml/kg/min
Echo	Minimal RV dysfunction	Pericardial effusion RV enlarged or dysfunction RA enlarged
Haemodynamics	RAP < 10 mmHg CI > 2.5 L/min/m^2	RAP > 20 mmHg CI < 2.0 L/min/m^2
BNP	Minimal elevation	Significant elevation

McLaughlin VV, McGoon MD. Pulmonary arterial hypertension. Circulation. 2006;114:1417–31.



THERAPY

Therapeutic goals

- *"Reduce pulmonary artery pressure" (PAH vs PH)*
- Reduce pulmonary vascular resistance
- Improve RV function
- Improve CI
- BEFORE RV failure becomes irreversible
- Maintain adequate preload
- Maintain SVR
- Avoid acidosis, hy[ercapnia, hypothermia, hypoxia

Established Medical Therapy for PH

- Treat hypoxia and left heart failure
- Diuretics if right heart failure
- Calcium channel blockers
  - Diltiazem if HR > 100 bpm
  - Nifedipine if HR < 100 bpm
- Prostacyclin analogs (mortality benefit in chronic)
  - iv epoprostanol, inhaled iloprost, s/c Trepostinil
- Phosphodiesterase (PDE-5) inhibitors
  - Sildenafil, Tadalafil
- Endothelin receptor antagonists e.g. Bosentan
- Nitric oxide (inhaled, continuous)

AGENTS USED TO REDUCE PULMONARY VASCULAR RESISTANCE

- Intravenous
  - Prostacyclin (Treprsotinol, Epoprostenol).
    - Half-life = 3-4 minutes. SE = hypotension, V/Q mismatch, HA, Flushing, jaw pain
  - Sildenafil 0.05-0.43 mg/kg.
    - Half-life = 3-5 hours. SE = Hypotension, V/Q mismatch, HA
  - Milrinone 0.375-0.75 ug/kg/min infusion
    - Half-life = 1-2 hours. SE = Tachyarrhythmias, hypotension
  - Adenosine 50-350 ug/kg/min
    - Half-life = 5-10 seconds. SE = Bradycardiac, Bronchospasm, chest pain
- Inhaled
  - Prostacyclins (Iloprost, Tyvasso) 2.5-5 ug 6-9 times per day. Half-life = 30 min.
  - NO 5-40 ppm SE = methemoglobinemia
- Oral
  - Sildenafil 20-80mg TID, can titrate up further

Inotropes & pressors in RV dysfunction

- Dobutamine (best studied)
  - Up to 5 μg/kg/min PVR falls, CI climbs
  - 5-10 μg/kg/min tachycardia with no change in PVR
  - Can combine with NO inhalation
- Norepinepherine
  - Increases mPAP and PVR
  - Sustains CI
  - May be needed to offset hypotension with dobutamine
- Dopamine
  - No convincing benefit on PVR
  - Tachycardia dangerous
- Phenylephrine
  - Increases mPAP and PVR
  - Drops CO and HR therefore AVOID IT!
- Epinepherine
  - Not widely studied although fairly widely used
- Vasopressin
  - Not studied in low doses (as used in sepsis)
  - Doses > 1 unit/kg/hour increase mPAP and PVR
- Milrinone
  - Decreases mPAP and PVR (but less than PDE-5 inhibitors)
  - Increases CO BUT often causes hypotension
- Levosimendan
  - Decreases mPAP and PVR
  - Improves RV/PA coupling

Recommendations

- Volume management
  - Close monitoring of fluid status according to effects on RV function is recommended. Initial carefully monitored limited volume loading may be useful after acute PE, but may also worsen RV performance in some patients with pulmonary vascular dysfunction, and vasoactive agents may be required (very-low-quality evidence, WEAK recommendation).
- Vasopressors
  - Noradrenaline may be an effective systemic pressor in patients with acute RV dysfunction and RV failure, as it improves RV function both by improving SVR and by increasing CO, despite potential increases in PVR at higher doses (mostly low-quality evidence,WEAK recommendation).
  - In patients with vasodilatory shock and pulmonary vascular dysfunction, low-dose AVP (vasopressin) may be useful in difficult cases that are resistant to usual treatments, including norepinephrine (low-quality evidence, WEAK recommendation).

Price LC et al. *Critical Care* 2010, **14**:R169 doi:10.1186/cc9264

Recommendations

- Inotropes
  - Low-dose dobutamine (up to 10 µg/kg/min) improves RV function and may be useful in patients with pulmonary vascular dysfunction, although it may reduce SVR (Low-moderate-quality evidence, a WEAK recommendation)
  - Dopamine may increase tachyarrhythmias and is not recommended in the setting of cardiogenic shock (STRONG recommendation based on high-quality evidence level)
  - PDE III inhibitors improve RV performance and reduce PVR in patients with acute pulmonary vascular dysfunction, although systemic hypotension is common, usually requiring co-admininstration of pressors (Moderate-quality evidence, a STRONG recommendation)
  - Inhaled milrinone may be useful to minimize systemic hypotension and V/Q mismatch in pulmonary vascular dysfunction (Based on low-quality evidence, a WEAK recommendation)
  - Levosimendan may be considered for short-term improvements in RV performance in patients with biventricular heart failure (low-quality evidence, a WEAK recommendation)

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Surgical Therapy (Refractory PH)

- Pulmonary Endarterectomy
- Lung transplant (single or bilateral)
- Heart-lung transplant
- Atrial septostomy – make R to L shunt
- Right ventricular assist device (RVAD)
- ECMO

Mechanical ventilation in PH

- RV afterload and pulmonary vascular resistance increased by
  - High lung volumes/over-distension
  - Decreased functional residual capacity/underinflation/atelactasis
- Inadequate recruitment/PEEP can be just as bad as overinflation, risking fatal decreases in cardiac output
- PEEP 3-8 cmH_2O better than < 3 or > 8 in one small study
- Suggests best approach is low tidal volume with minimum PEEP consistent with acceptable balance of FiO_2 and PaO_2
- Permissive hypercapnia is problematic as it increases PVR and may decrease cardiac output e.g. post-cardiac surgery hypercapnia increased PVR by 54% and mPAP by 30%

Summary

- Critical clinical problem to understand
- Index of suspicion and early diagnosis needed
- Treat underlying causes where possible
- Consider right heart catheterisation
- Vasodilator options (evidence lacking in ICU)
- Aggressive treatment of RV dysfunction
- Mortality remains high

THANK YOU!

QUESTIONS?