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No Disclosures

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Objectives

- **Definition and Groups of PH**
- Pathophysiology
- Symptoms, screening & diagnosis
- Treatment

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Definition of PH – Hemodynamic and Pathologic

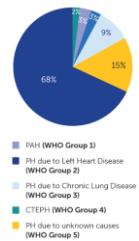
PAH: mPA pressure > 20, wedge ≤ 15 and PVR > 2 Wood

Group 2 PH: mPA pressure > 20 & wedge > 15

Group 3: mPA > 20 due to lung disease

Group 4: mPA > 20 due to chronic clot

Group 5: mPA > 20 due to multifactorial reasons



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Group 1

- GROUP 1** Pulmonary arterial hypertension (PAH)
- 1.1 Idiopathic
 - 1.1.1 Non-responders at vasoreactivity testing
 - 1.1.2 Acute responders at vasoreactivity testing
 - 1.2 Heritable^a
 - 1.3 Associated with drugs and toxins^a
 - 1.4 Associated with:
 - 1.4.1 Connective tissue disease
 - 1.4.2 HIV infection
 - 1.4.3 Portal hypertension
 - 1.4.4 Congenital heart disease
 - 1.4.5 Schistosomiasis
 - 1.5 PAH with features of venous/capillary (PVOD/PCP) involvement
 - 1.6 Persistent PH of the newborn

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PAH Epidemiology

Rare disease, prevalence of iPAH and heritable PAH around 5-15 per million, higher when you factor in associated PAH

Affects everyone, most prevalent in 4th and 5th decades of life and more common among women

Survival has been improving over time but very heterogeneous disease

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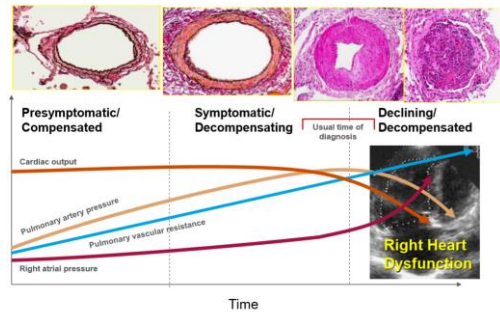
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Pathophysiology of PAH



Genetics

BMPR2 mutation identified in 2000

Since then others including SMAD9, ENG, CAV1, ALK1, KCNK3 and the gene associated with PVO/PCH EIF2AK4 have been identified

Objectives

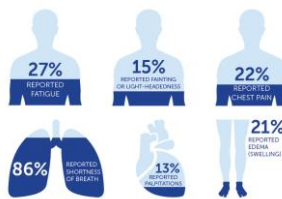
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Symptoms

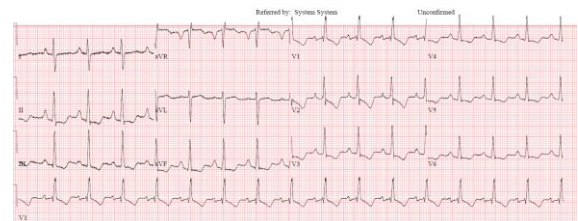
Progressive exertional dyspnea

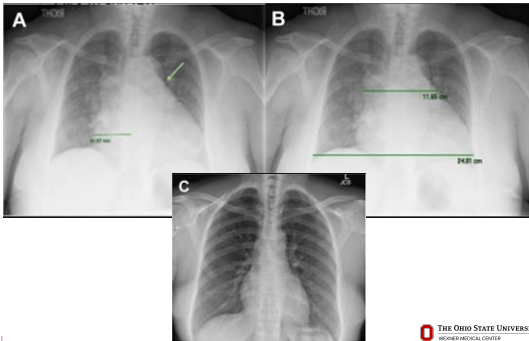
Right heart failure → Fluid retention, exertional chest pain

Low output state → Lightheadedness and syncope



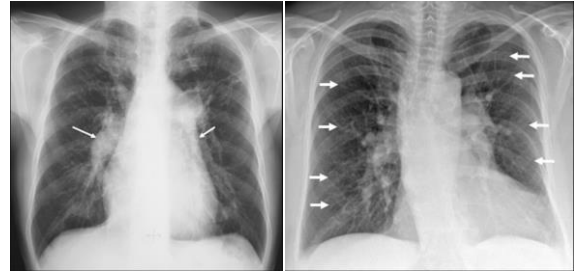
Think PH - EKG



Think PH - CXR

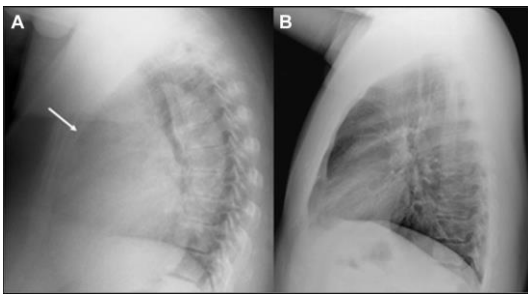
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Think PH - CXR

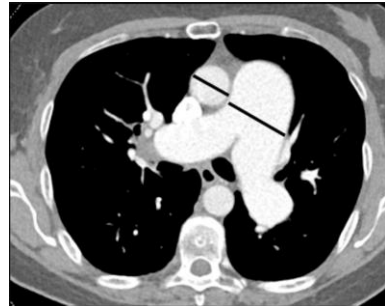
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Think PH - CXR

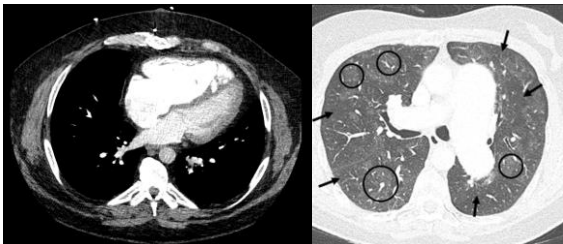
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Think PH - CT

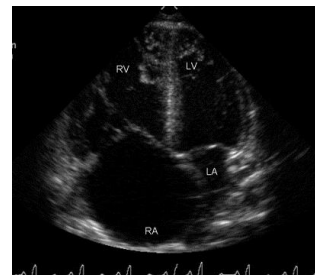
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Think PH - CT

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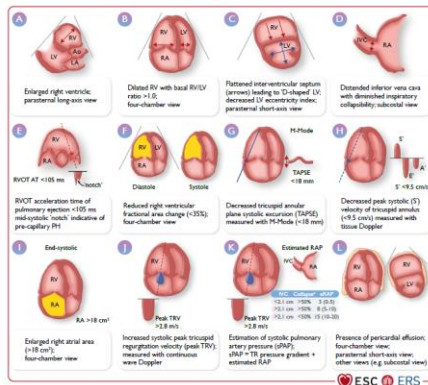
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The only true screening test

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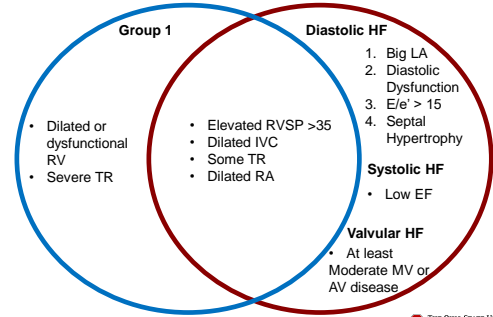
TTE



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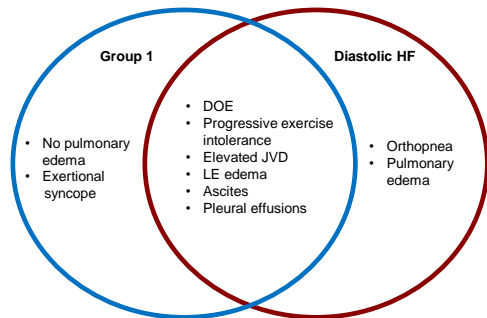
PAH vs Diastolic Heart Failure on TTE



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Signs and Symptoms of PAH vs Diastolic HF



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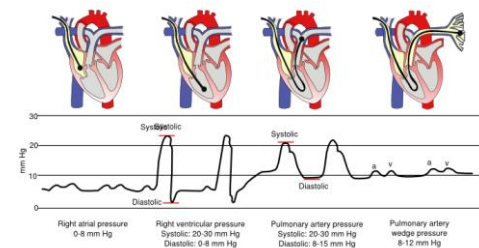
Risk Score for Diastolic HF

Clinical Variable	Values	Points
H₂ Heavy	Body mass index > 30 kg/m ²	2
H Hypertensive	2 or more antihypertensive medicines	1
F Atrial Fibrillation	Paroxysmal or Persistent	3
P Pulmonary Hypertension	Doppler Echocardiographic estimated Pulmonary Artery Systolic Pressure > 35 mmHg	1
E Elder	Age > 60 years	1
F Filling Pressure	Doppler Echocardiographic E/e' > 9	1
H₂FPEF score		Sum (0-9)
Total Points		
Probability of HFpEF		

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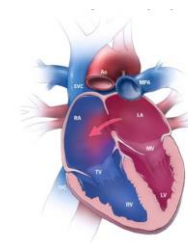
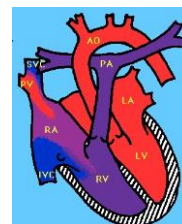
Next step if there is concern for PH – Have to do a RHC



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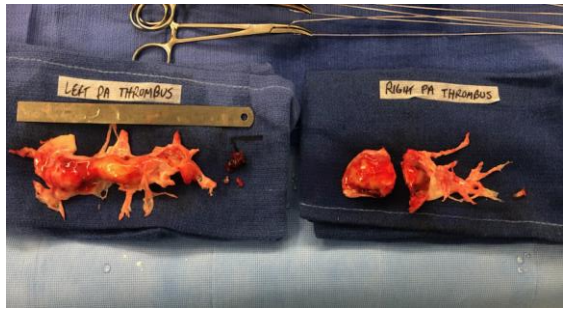
RHC – Must do the saturation study



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Precapillary PH Diagnosed – Next testing



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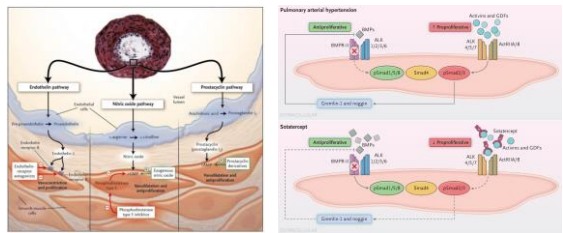
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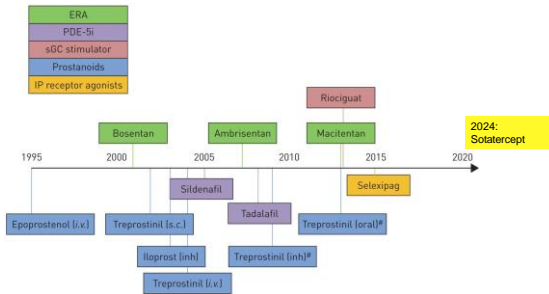
Pharmacology



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The Pulmonary Vasodilators



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Risk Assessment - 2022

Determinants of prognosis (estimated 1-year mortality)	Low risk (<5%)	Intermediate risk (5-20%)	High risk (>20%)
Clinical observations and modifiable variables			
Signs of right HF	Absent	Absent	Present
Progression of symptoms and clinical manifestations	No	Slow	Rapid
Syncope	No	Occasional syncope ^a	Frequent syncope ^a
WHO-FC	I, II	III	IV
6MWD ^b	≥440 m	165-440 m	<165 m
CPET	Peak VO ₂ ≥15 mL/min/kg (≥45% pred) VE/VCO ₂ slope ≤36	Peak VO ₂ 11-15 mL/min/kg (35-45% pred) VE/VCO ₂ slope 36-44	Peak VO ₂ <11 mL/min/kg (<35% pred) VE/VCO ₂ slope >44
Biomarkers BNP or NT-proBNP ^c	BNP <30 ng/L NT-proBNP <300 ng/L	BNP 30-400 ng/L NT-proBNP 300-1100 ng/L	BNP >400 ng/L NT-proBNP >1100 ng/L
Echocardiography	RA area <18 cm ² TAPSE/LAP >0.22 m/min/mg No pericardial effusion	RA area 18-26 cm ² TAPSE/LAP 0.19-0.22 m/min/mg Minimal pericardial effusion	RA area >26 cm ² TAPSE/LAP <0.19 m/min/mg Moderate or large pericardial effusion
CPET	RVEF ≥45% SVI ≥40 mL/m ² RVESVI <42 mL/m ²	RVEF 37-45% SVI 26-40 mL/m ² RVESVI 42-54 mL/m ²	RVEF <37% SVI <26 mL/m ² RVESVI >54 mL/m ²
Hemodynamics	RAP <8 mmHg CI ≥2.5 L/min/m ² SVI ≥30 mL/m ² SaO ₂ ≥95%	RAP 8-14 mmHg CI 2.0-2.4 L/min/m ² SVI 21-30 mL/m ² SaO ₂ 88-95%	RAP >14 mmHg CI <2.0 L/min/m ² SVI <21 mL/m ² SaO ₂ <88%

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2022 Simplified 4 Strata Model

Determinants of prognosis	Low risk	Intermediate-low risk	Intermediate-high risk	High risk
Points assigned	1	2	3	4
WHO-FC	I or II ^a	-	III	IV
6MWD, m	≥440	320-440	165-319	<165
BNP or NT-proBNP ^a ng/L	<50 <300	50-199 300-449	200-800 450-1100	>800 >1500

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Treatment Simplified

- Only treat WHO group 1, 4 and sometimes 5. Within group 3 have FDA approval for Tyvaso for ILD. Almost never 2.
- No specific guidelines but in general, triple therapy for high risk and mostly dual therapy for the others.
- All take weeks to have an effect. Specialty pharmacy.
- Prostacyclin side effects – Headache, flushing, nausea, diarrhea, myalgias. Systemic hypotension and high output.
- Avoid sildenafil or tadalafil with riociguat. Avoid nitrates with these medications.
- Riociguat, ERAs are teratogenic and require REMS. Must ensure adequate birth control for females with reproductive potential.
- All pills can be crushed except for oral prostacyclins.
- For refractory patients refer for double lung transplant.

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Parenteral prostacyclins



Remunity pump



CADD Solis pump

Doses are in ng/kg/min – typical infusion rate is on the order of 0.03ml/min

Do not flush their lines or interrupt infusions!

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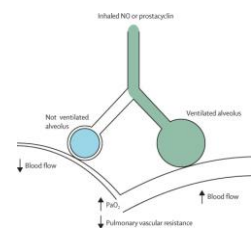
Subcutaneous Site



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Tyvaso approved for PH-ILD in 4/2021



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Sotatercept – Approved 2024

- Subcutaneous injection every 3 weeks.
- Can cause increased bleeding, polycythemia, thrombocytopenia and telangectasias.
- Likely increased risk to embryo so must use contraception. Possible effects on fertility.

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Treatment

Ultimately the goal of PH therapy (but really all therapy) is to reduce a patient's degree of risk and improve their quality of life and symptoms, while also balancing comorbidities, side effects and patient preferences.

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Summary for the PCP

- If you suspect PH please always get a TTE and refer.
- It can be difficult to discern PAH from other types of PH based on TTE alone and the decision to proceed with RHC should be made by a specialist.
- Pulmonary vasodilators come from specialty pharmacies, should not be interrupted, cannot be administered at SNFs.
- Many of our pulmonary vasodilators are teratogenic.
- Avoid nitrates with the PDE5i and riociguat. Otherwise most usual medications are fine but good to check interactions – particularly important during COVID.
- Notify us if patients need procedures.
- Reach out to us anytime if you have any questions!

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Thank You

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