Pulmonary Hypertension

Pretest Probability Assessment via Echocardiography (some numbers are rounded for ease of use)		
Probability of PH	ESC/ERS 2015 guidelines recommend TRV	Older 2009 guidelines and ISHLT use PASP
Low	TRV < 2.8 m/s	PASP <35 and TRV <2.8
Medium	TRV ~ 3 – 3.5 m/s	PASP and TRV and in-between low and high + other PH signs on echo
High	TRV~3 – 3.5 with other PH signs on echo	PASP > 50 and TRV > 3.5
	TRV > 3.5 m/s	

What are "other signs of PH on echo" ?

- RV:LV basal diameter ratio > 1.0, flattening of the septum
- PA diameter > 25
- IVC > 21 mm with decreased inspiratory collapse

Who to screen for pulmonary hypertension – high risk groups	
Systemic sclerosis	Congenital heart disease
HIV	HHT, family history of HHT, other heritable etiologies
Portopulmonary hypertension	Sickle cell disease

If you have a medium to high risk of pulmonary hypertension on echocardiography

1. Determine if there is left heart disease sufficient to explain the pulmonary hypertension
2. If there is no left heart disease or insufficient left heart disease, consider the following work up:
    - **Chronic lung disease evaluation** with PFTs, CT chest, 6 minute walk; overnight oximetry/PSG if needed
    - **Venous thromboembolism evaluation** with VQ scan; rare cases may require angiography
3. Consider HIV and serologic testing
4. If one of these etiologies is identified, you do not necessarily need a RHC but it may be indicated, especially in mixed disease or to assess for treatment effect

Primary Therapy for Pulmonary Hypertension (AKA – treat the underlying disease)

- In all patients, consider the following: diuretics, oxygen, anticoagulation, digoxin (particularly in group 3 with COPD and biventricular failure), exercise
- Anticoagulation seems beneficial in idiopathic PAH, not in CTD-associated PAH (Khan MS, et al. Circulation. 2018; 11)

A special note on oxygen in Group 3 PH – the only modality with proved mortality benefit

- PaO2 < 60 on oxygen for 15 hrs/day - decreased 5 year mortality but only after 500 days of therapy (lancet 1981)
- NOTT showed improved 3 year mortality in continuous oxygen vs nocturnal oxygen (Ann Int Med 1980)

Broad Review of Drug Therapies – This is mostly for Group 1 PAH

Calcium channel blockers – use for those who are vasoreactive on RHC (mean PAP decreases at least 10 and to a value less than 40 mmHg). **Nifedipine** has been shown to increase 5 year survival (Rich S, et al. NEJM 1992)

Prostacyclin agonists – epoprostenol, treprostinil, selexipag

- Epoprostenol improves hemodynamics, functional capacity and survival in idiopathic PAH, but no known survival benefit in other types of Group 1 - Consider for idiopathic, CTD, portal hypertension, HIV, congenital heart disease

Endothelin receptor antagonists – bosentan, macitentan, ambrisentan - improved exercise capacity, dyspnea, and hemodynamics (not survival); adverse effects are hepatotoxicity and peripheral edema

- **Note**: ambrisentan is associated with disease progression and hospitalizations in patients with IPF

PDE5 inhibitors – sildenafil, tadalafil, vardenafil – improves functional class for group 1, no role in lung disease, benefit in left heart disease "unclear" according to Cochrane review 2019

Guanylate cyclase stimulant – riociguat – benefit in inoperable CTEPH, maybe benefit in group 1 (Ghofrani HA. NEM 2013)

Combination therapy with tadalafil plus ambristentan shows decreased hospitalizations and increased exercise capacity (Galie N. NEJM 2015)