Pulmonary Hypertension

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Symptoms & signs:

- Often **nonspecific** & include fatigue, dyspnea,CP, palpitations, presyncope & syncope.
- Examination may reveal loud P2, TR, an S4, signs of right heart failure, **stigmata** of the underlying aetiology (e.g. telangiectasia and features of CREST syndrome).

Epidemiology:

- PAH is rare: Incidence of **6/million/year**
- Hereditary PAH (HPAH) due to **BMPR2 mutations** are inherited in an autosomal dominant pattern, with incomplete penetrance – which is higher in females (14% men, 42% females).
- CTEPH has identifiable risk factors, **~75%** have a history of prior PE

Risk stratification:

- **ESC/ERS 2015** risk stratification tool typically used in Ireland.
- **Low** (<5%), **Intermediate** (5-10%), **High risk** (>10%) strata predict 1 year mortality.

Investigation checklist

Bloods:
- Baseline FBC/Liver/Renal/Bone
- BNP/NT-proBNP
- TFTs, Iron studies
- HIV, Hepatitis, CTD screen

Lung imaging:
- CXR, CT thorax, VQ Scan*

PFTs
- Spirometry & DLCO

Echocardiogram

Liver doppler ultrasound

*Ventilation perfusion (V/Q) scan
- To screen for CTEPH. If mismatched perfusion defects, refer to PH unit for invasive pulmonary angiogram

Right heart catheterization (RHC):
- With documentation of mPAP, mRAP, PVR, PAWP, CO, CI, SVO2, PA Sats

Classification (5 Groups)	Group 1 (PAH)	Group 2	Group 3	Group 4	Group 5
Subgroups	IPAH, HPAH, Drug-PAH, CTD (connective tissue disease)-PAH	Due to **left heart disease**: PH- HFpEF or PH- HFrEF	Due to **hypoxia or chronic lung disease** e.g. ILD, COPD, OSA	Pulmonary vascular obstruction e.g. **CTEPH**	Miscellaneous, including **sarcoidosis**
Pattern on RHC: Mean pulmonary artery pressure Pulmonary artery wedge pressure Pulmonary vascular resistance	**Precapillary:** • **>20** mmHg • **<15** mmHg • **>3** Wood Units	**Postcapillary:** • >20 mmHg • **>15** mmHg • <3 WU	• >20mmHg • <15mmHg	• >20mmHg • <15mmH • >3 WU	• >20mmHg • <15mmHg
Current role for PAH therapy	**YES**	NO	NO	**YES**	Individualised

Treatment pathways for Group 1 PAH:	Endothelin pathway (ET)	Nitric oxide pathway (NO)	Prostacyclin pathway (PGI_2)
Levels in PAH	↑	↓	↓
Mechanism of action	**Endothelin receptor antagonists** (ERAs) block endothelin receptors and reduce vasoconstriction and proliferation	**Phosphodiesterase type 5 inhibitors** (PD5-) or **soluble guanylate cyclase stimulators** (sGCS) increase cGMP and vasodilation	**Prostacyclin analogues or direct prostacyclin receptor agonists** (below) increase prostacyclin level to vasodilate pulmonary arteries
Examples	Macitentan Ambrisentan Bosentan	PD5-: Sildenafil, Tadalafil sGCS: Riociguat	Selexipag (oral) iloprost (inhaled) Treprostinil (s/c), epoprostenol (IV)
Drug side effects/ monitoring	Monitor BP 3 monthly LFTs (liver toxicity)	Headache common initially Generally well tolerated Monitor BP	Prostacyclin side effects are common: GI (e.g. nausea, diarrhea) Headache, neurological (e.g. jaw sensitivity) etc.

Treatment Group 4 CTEPH:	
Anticoagulation	**Lifelong**: Warfarin or DOACs
Medical therapy	**Riociguat (sGCS) and subcut Treprostinol** Other PH therapies are used off-label
Pulmonary endarterectomy (PEA)	For **proximal disease**. There are very few absolute contraindications to the procedure. **All cases** should be discussed at expert MDT in Papworth, UK
Balloon pulmonary angioplasty (BPA)	For distal disease. Can improve symptoms and hemodynamics if disease is not amenable to PEA. Also performed in Papworth, UK.
Other	IVC filters are **not** recommended routinely.

Supportive measures should be optimized & include (where appropriate):

- Vaccination, supplemental oxygen therapy (P_aO_2 <8kPa), optimize comorbidities, diuretics (if right heart failure), exercise training & **pulmonary rehabilitation** (in stable disease), regular **contraception** for female patients of childbearing age (avoid combined oral contraception due to VTE risk).
- Decisions regarding **anticoagulation** for patients with IPAH/HPAH/APAH who do not have an alternative indication, should be made in expert centers, on an individualized basis.

Advanced disease: **Triple combination therapy** with parenteral prostacyclin**, palliative care, transplant referral** (select cases)

- Suspected case of PH, especially group 1 and 4 should be referred **urgently** to the National PH Unit
- More information is available at **PHA Ireland** website