Pulmonary Hypertension (PH) – an overview

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Disclosures

- I have received speaking fees, consultancy fees, research grants and/or travel grants from Janssen, MSD, Ferrer, AstraZeneca, Chiesi and GSK

Aims

- Pulmonary vascular physiology
- Why look for PH?
- Which forms of PH should you ‘ignore’?
- How do you decide who to refer?

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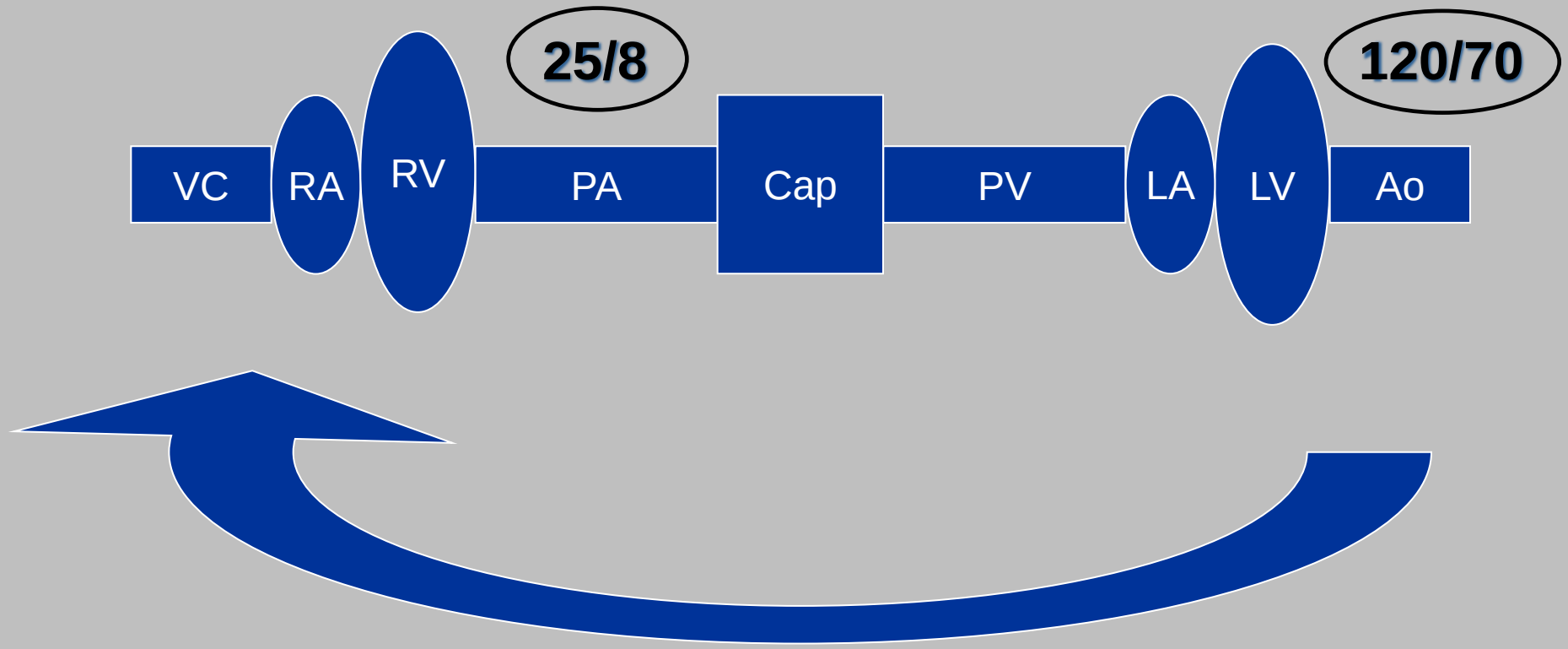
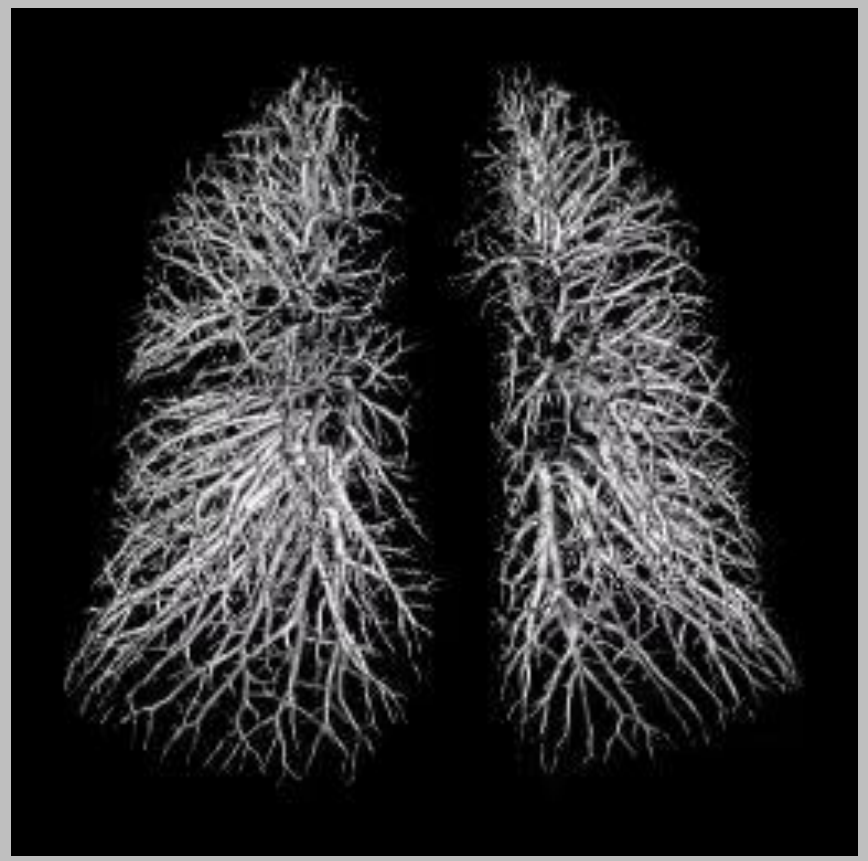
- **Pulmonary vascular physiology**
- Why look for PH?
- Which forms of PH should you ‘ignore’?
- How do you decide who to refer?

The pulmonary circulation - a high flow low pressure circuit



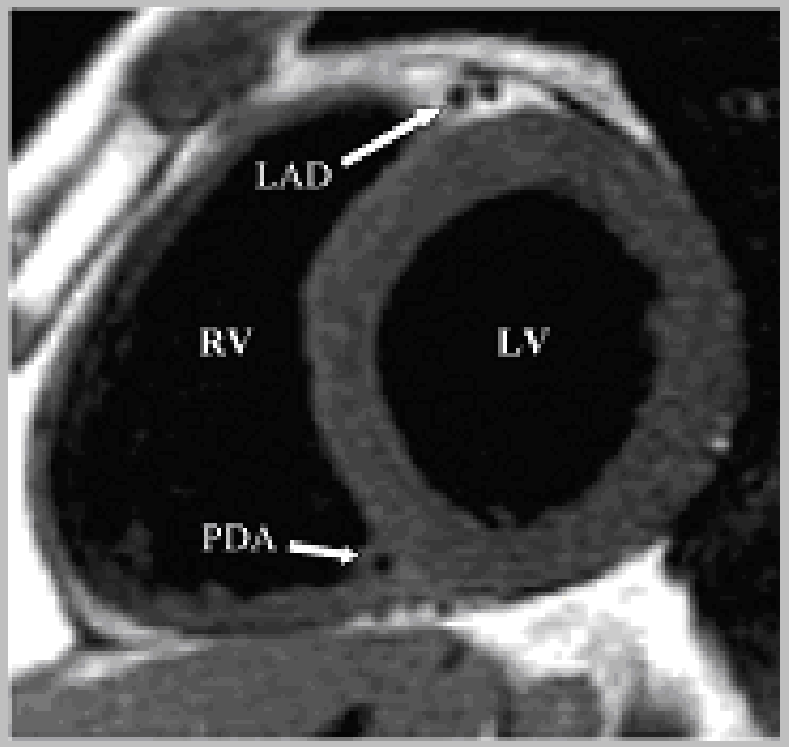
The pulmonary vascular tree

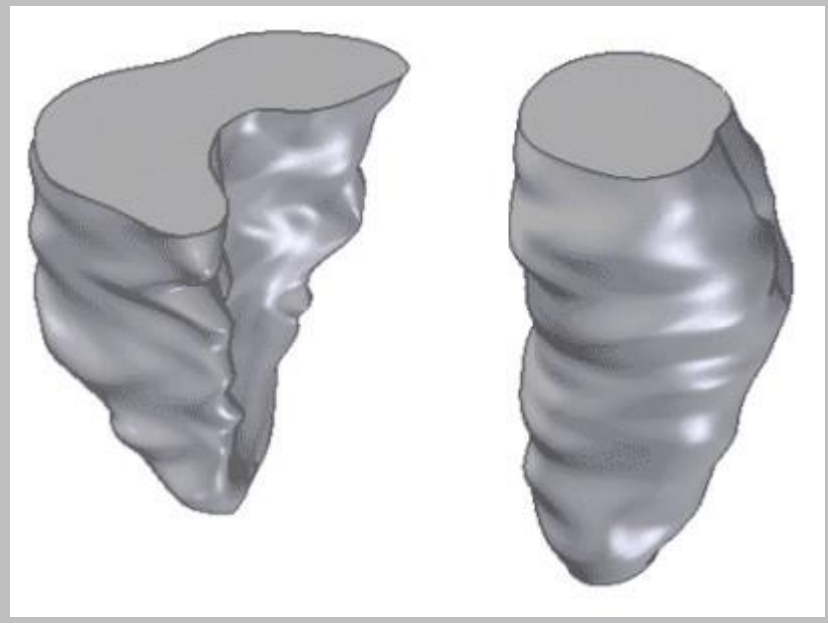


'pulmonary hypertension' - mPAP >20mmHg

With permission Dr Hidenori Shikata

Right versus left ventricles in health





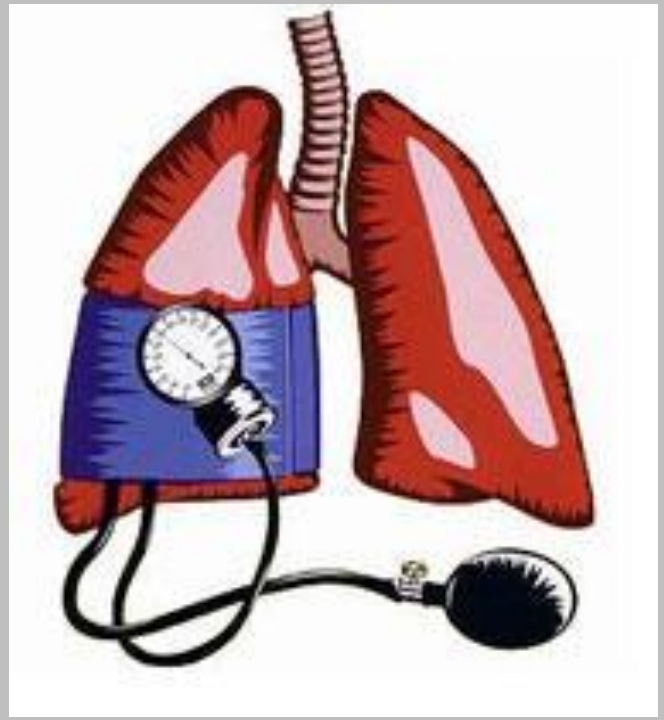
PH symptoms – caused by right heart strain

- Exertional dyspnoea
- Fatigue
- Right ventricular angina
- Pre-syncope/syncope
- Palpitations
- Fluid retention

Aims

- Pulmonary vascular physiology
- **Why look for PH?**
- Which forms of PH should you ‘ignore’?
- How do you decide who to refer?

PH – a syndrome



PH classification

1. Pulmonary Arterial Hypertension
- Idiopathic PAH (IPAH)
- Heritable
- Drugs/toxins
- Associated PAH (APAH)
  - connective tissue diseases
  - HIV infection
  - portal hypertension
  - congenital heart diseases

1*. PVOD/PCH

2. PH 2ry to left heart disease
- systolic and diastolic dysfunction
- valvular

3. PH 2ry to lung disease
- COPD
- interstitial lung disease
- sleep disordered breathing
- developmental abnormalities

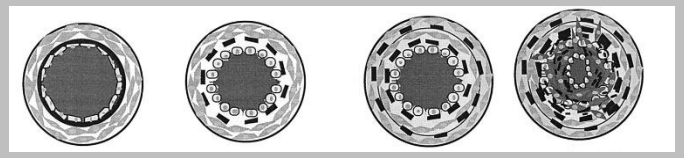
4. PH due to chronic thrombotic and/or embolic disease
- proximal CTEPH
- distal CTEPH
- non-thrombotic embolism

5. Miscellaneous
- sarcoid
- PLCH, LAM
- metabolic disorders

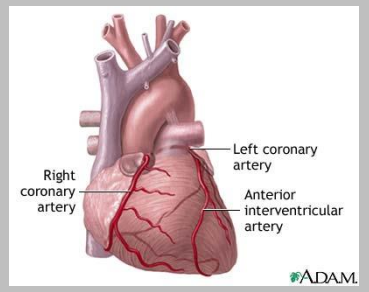
Adapted from Dana Point Classification 2008

PH classification

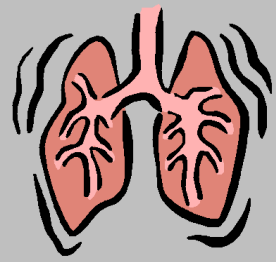
1. Pulmonary Arterial Hypertension



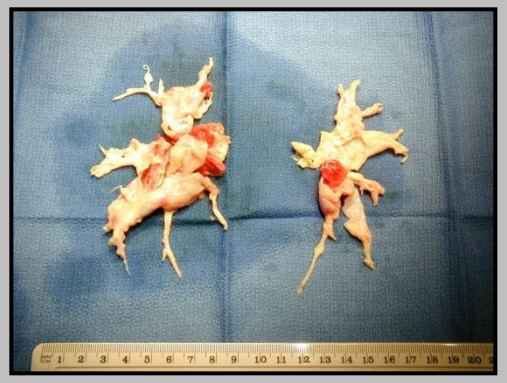
2. PH 2ry to left heart disease



3. PH 2ry to lung disease



4. PH due to chronic thrombotic and/or embolic disease



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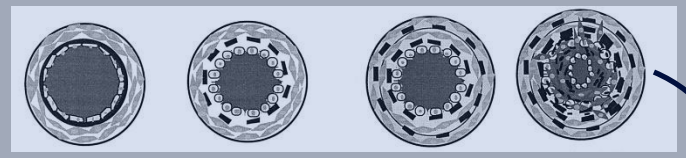
‘Treatable’ PH

1. Pulmonary Arterial Hypertension



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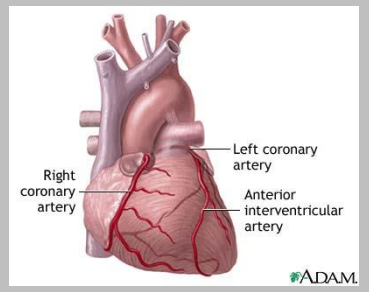

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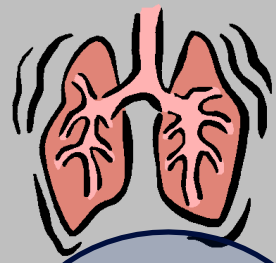

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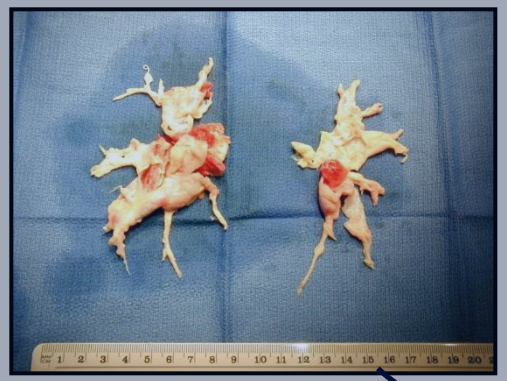

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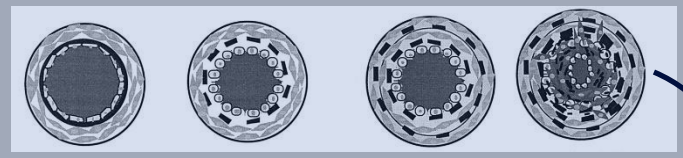
‘Treatable’ PH - PAH

1. Pulmonary Arterial Hypertension



Case - Lucy

- 42 year old ♀ office worker

IPAH tends to affect younger women
- **Average age = 50's**
- **F:M = 8:1**

Case - Lucy

- 42 year old ♀ office worker
- PMHx - migraines

‘Pure’ IPAH patients should have no significant cardiorespiratory comorbidities and a minimal smoking history

Case - Lucy

- 42 year old ♀ office worker
- PMHx – migraines
- 12-18 months worsening SOBOE – attributed to ‘long Covid’ – ET now 100 yards

IPAH patients typically take >1 year to be referred to secondary care, and a further >1 year to be referred to a specialist PH centre

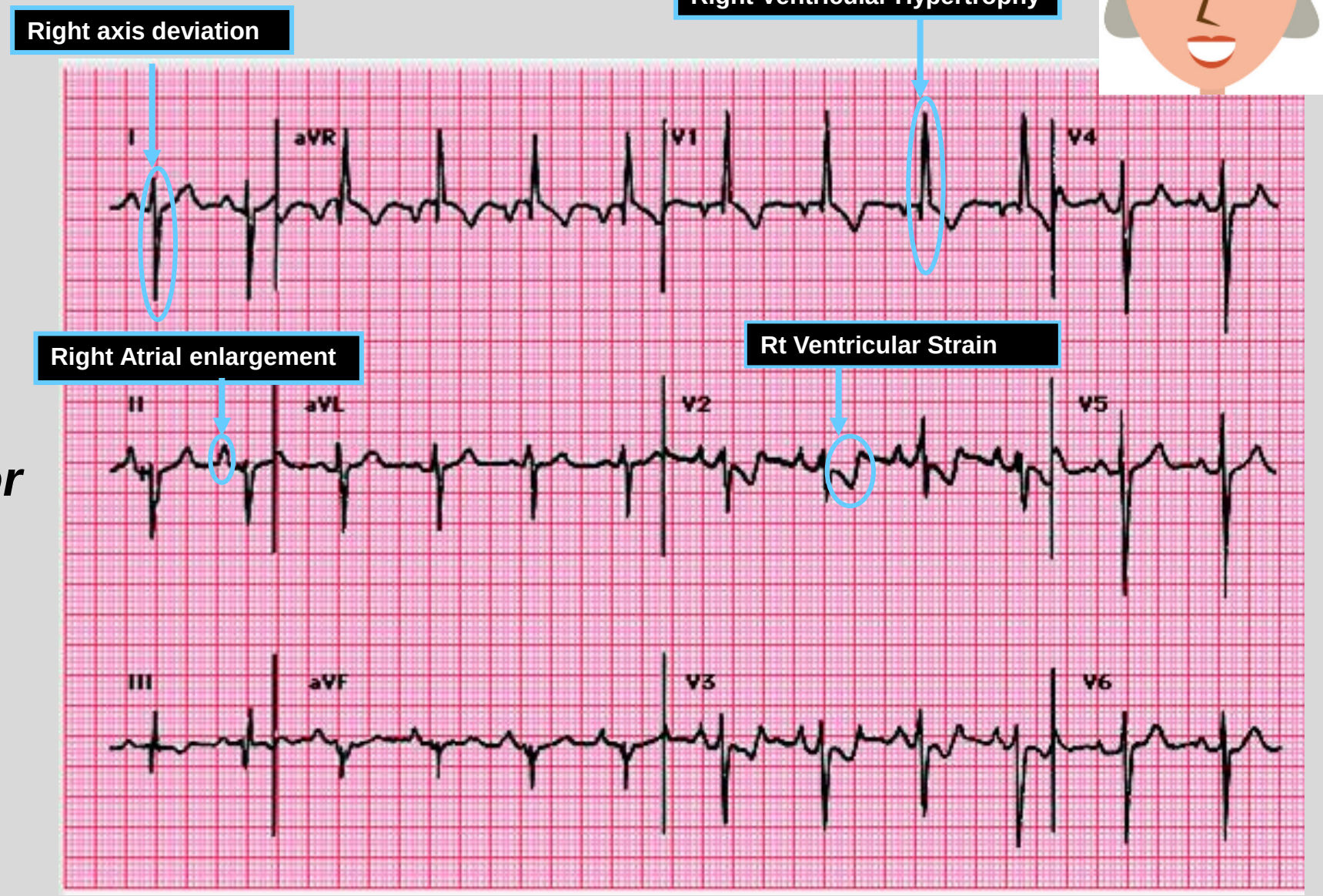
Case - Lucy

- 42 year old ♀ office worker
- PMHx – migraines
- 12-18 months worsening SOBOE – attributed to ‘long Covid’ – ET now 100 yards
- Presents on medical take with syncopal episode after rushing up two flights of stairs at work

Exertional syncope in PH is a marker of severe disease

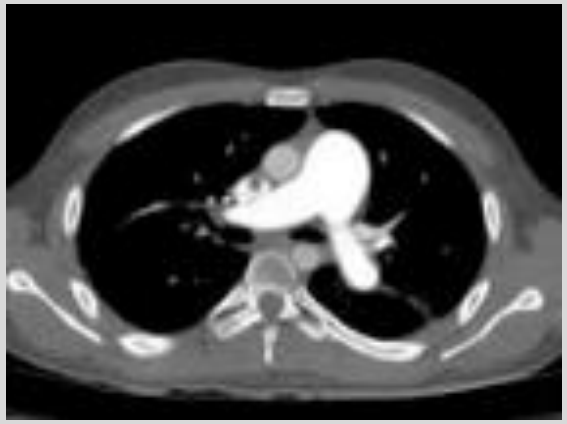
Case - Lucy

ED clerking –
‘Ischaemic ECG
Needs admission for
?NSTEMI workup’

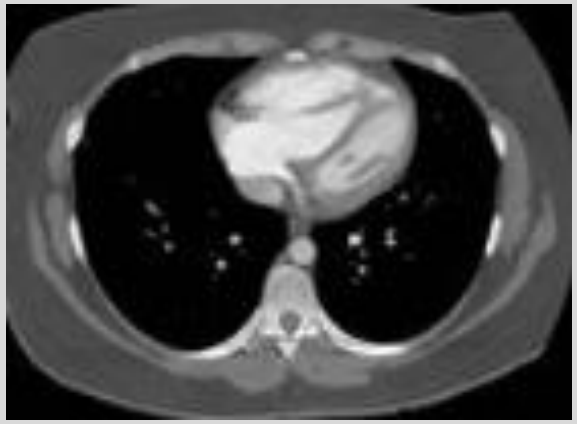


Case - Lucy

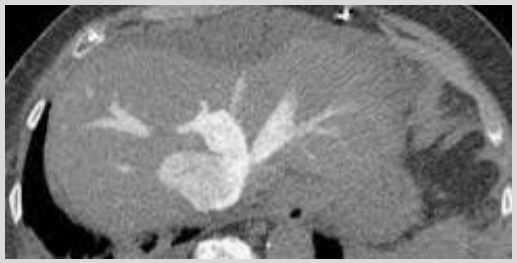
- CTPA
  - *'No PE – normal study'*



Enlarged PA



Increased RV:LV



Hepatic reflux

Case - Lucy

- Echo
  - Preserved LV systolic function (EF>55%) with septal flattening
  - Normal LA
  - Severely dilated RA
  - Dilated RV with severely impaired function
  - PASP 80mmHg +JVP
  - Moderate pericardial effusion
  - ‘High probability of PH’

Case - Lucy

- Echo
  - Preserved LV systolic function (EF>55%) with **septal flattening**
  - Normal LA
  - **Severely dilated RA**
  - **Dilated RV** with severely **impaired function**
  - **PASP 80mmHg** +JVP
  - **Moderate pericardial effusion**
  - ‘High probability of PH’

How to interpret an echo report (as a non-Cardiologist)

✓

Clinically relevant PH more likely

- Dilated right sided chambers
- Poor RV function
- Paradoxical septal wall motion
- +/- elevated PASP

✗

Clinically relevant PH less likely

- Dilated LA (+/- biatrial dilatation)
- Normal RA
- Preserved RV function
- Modestly elevated PASP in isolation

Case - Lucy

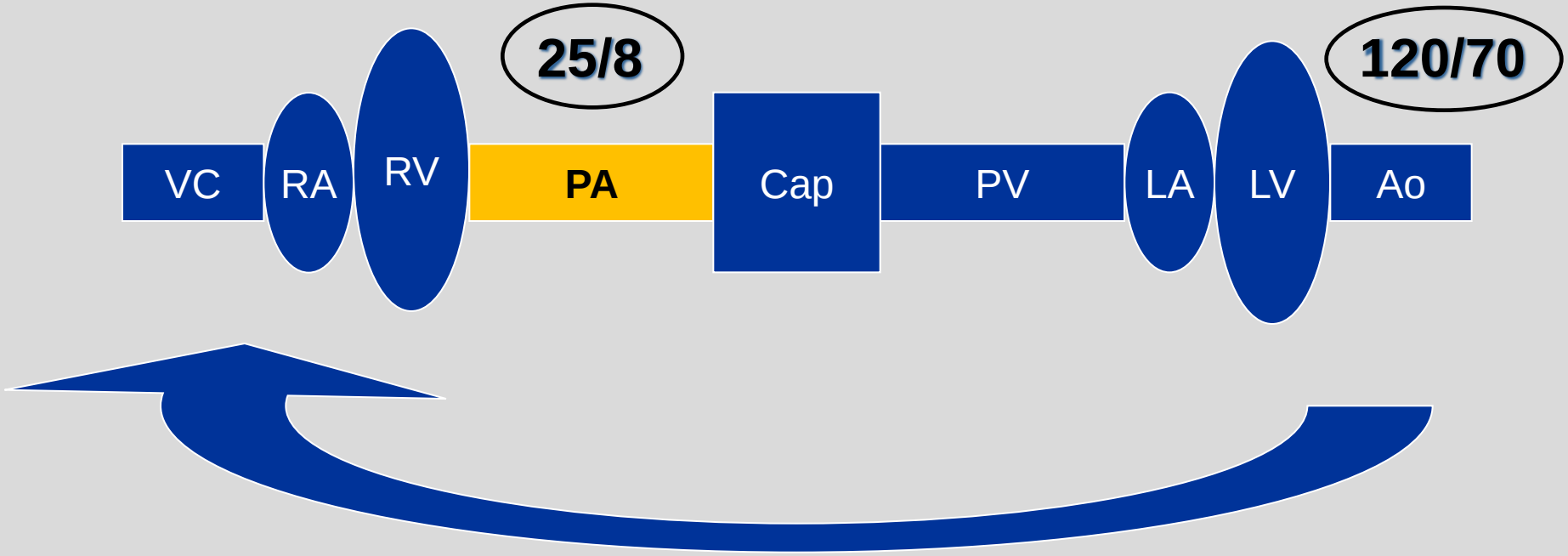
- Right heart catheterisation
  - RA 15mmHg (<8mmHg)
  - RVEDP 15mmHg
  - **mPAP 61mmHg (<20mmHg)**
  - PCWP 13mmHg (<15mmHg)
  - CO 2.38l/min
  - CI 1.65l/min/m (2.8-4.2L/min/m)
  - **PVR 18.9WU (<2WU)**

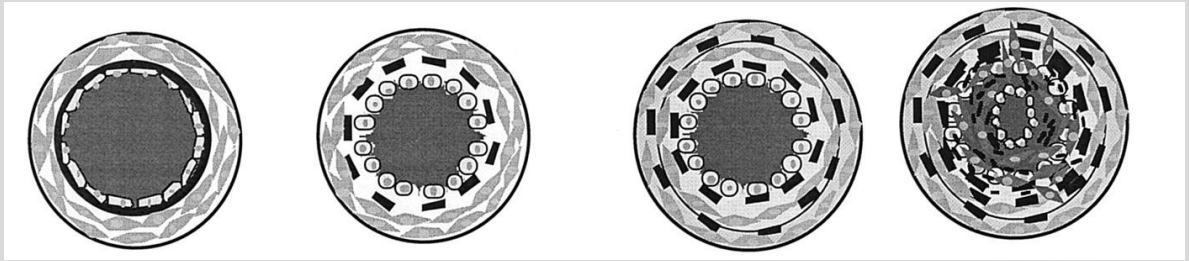
- NT-proBNP 4394 pmol/L

Case - Lucy

- Δ Idiopathic Pulmonary Arterial Hypertension (IPAH)

The pulmonary circulation - a high flow low pressure circuit

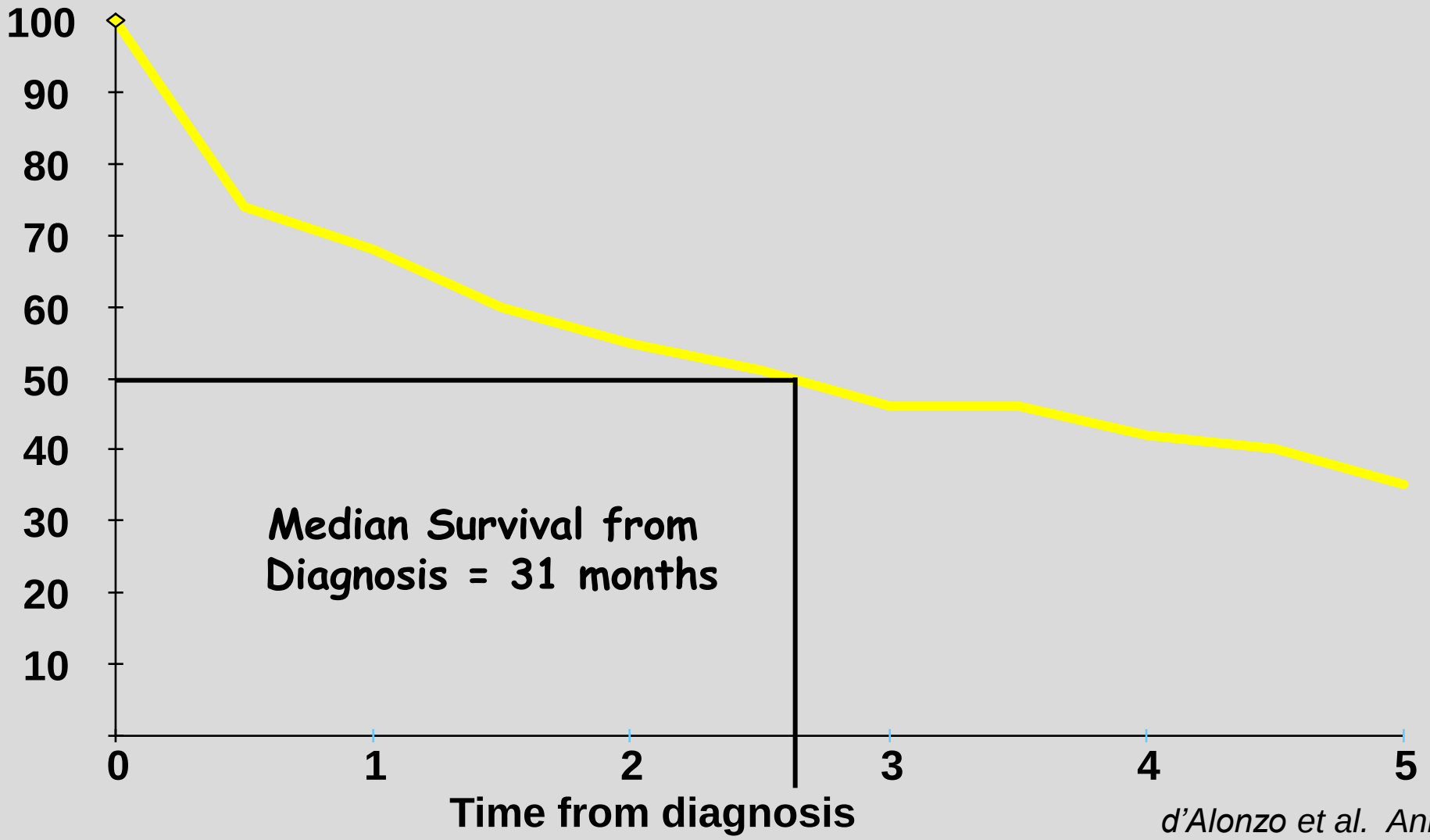




Case - Lucy

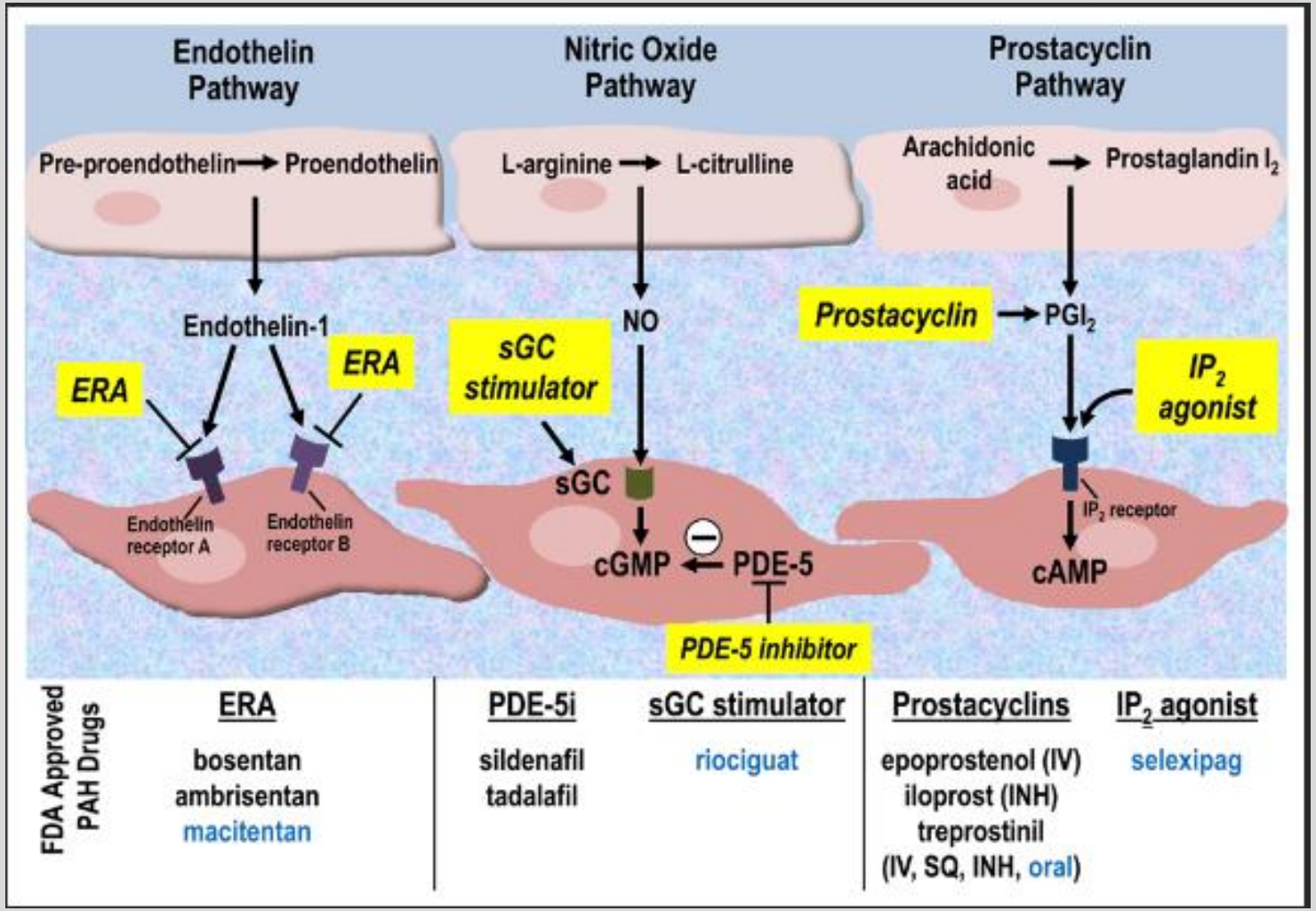
- Δ Idiopathic Pulmonary Arterial Hypertension (IPAH)
  - iv furosemide infusion
  - spironolactone
  - digoxin

Survival in IPAH with supportive treatment alone is poor



d'Alonzo et al. Annals Int Med 1991

PAH treatment - many treatment options now available



Case - Lucy

- Δ Idiopathic Pulmonary Arterial Hypertension (IPAH)
  - iv furosemide infusion
  - spironolactone
  - digoxin
  - ambrisentan (Endothelin Receptor Antagonist)
  - tadalafil (PDE5 inhibitor)

Case - Lucy – FU @ 3/12

• NYHA FC	II	(IV)
• 6MWD	432m	(90m)
• NT-proBNP	182ng/L	(4394)
• RHC		
– RA	7mmHg	(15)
– **mPAP**	**34mmHg**	**(61)**
– PCWP	8mmHg	(13)
– **CO**	**4.8l/min**	**(2.4)**
– **PVR**	**5.4WU**	**(18.9)**

Case – Lucy at 8 yr FU

- Remains on tadalafil & ambrisentan
- Selexipag added in 4 years ago
- Remains ‘Low risk’
- Enjoys a good QOL

Pulmonary Arterial Hypertension (PAH)

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   - Drugs/toxins
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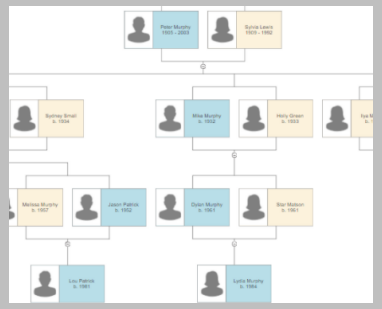
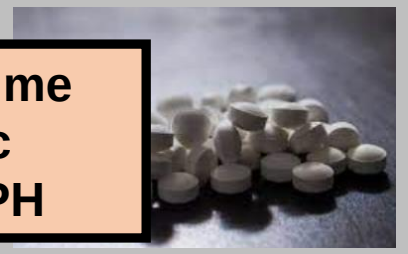
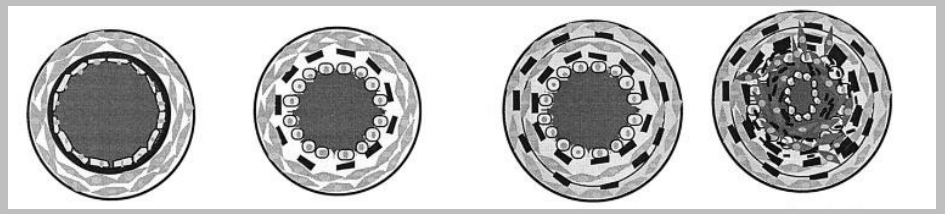
     connective tissue diseases



10-15% patients with SSc can develop PAH during their lifetime
SSc-PAH can often represent the first presentation of SSc
Always consider sending an AIP in patients with possible PH





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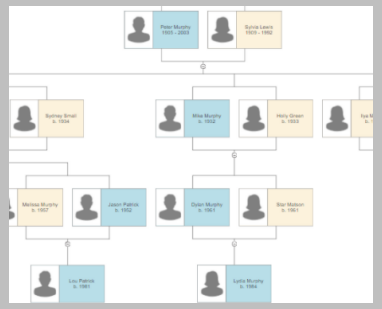

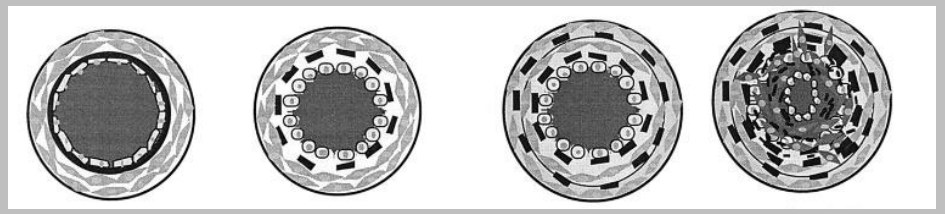

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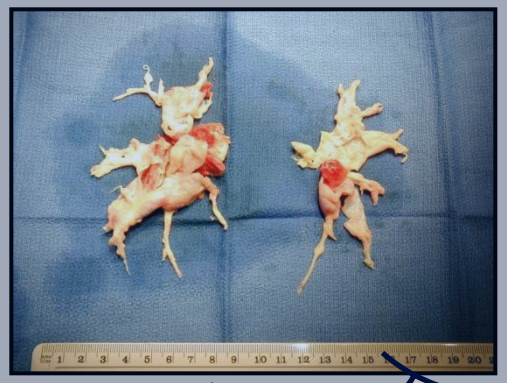
‘Treatable’ PH - CTEPH

4. PH due to chronic thrombotic and/or embolic disease



Adapted from Dana Point Classification 2008

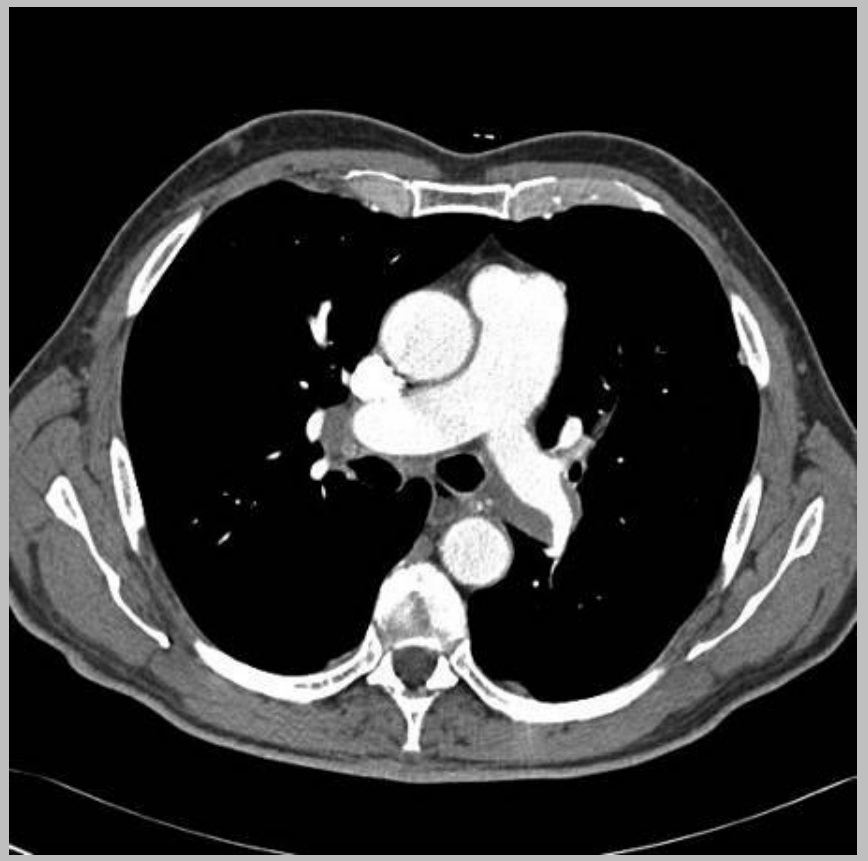
Case - Rex

- 72 year ♂
- 20 pack year smoking history
- HTN & OA knees
- Unprovoked DVT ~10 years ago
- Progressive dyspnoea for 3 years ΔCOPD
  - ET currently 20-30m
  - Admitted with worsening SOB ‘Δexacerbation of COPD’
  - RESPECT discussion – ‘DNACPR in view of severity of COPD’

Case - Rex

- D2 hospital admission
  - Syncopal episode whilst transferring to commode
  - Medical team fast bleeped
  - CTPA requested to rule out PE

Case - Rex



Echo – dilated RA, dilated RV with poor function, septal embarrassment, PASP 56mmHg

Case - Rex

- D2 hospital admission
  - Syncopal episode whilst transferring to commode
  - Medical team fast bleeped
  - CTPA requested to rule out PE

- Anticoagulated and started on diuretics
- Reassessed with repeat CTPA, echo and RHC at 6/52

Case - Rex

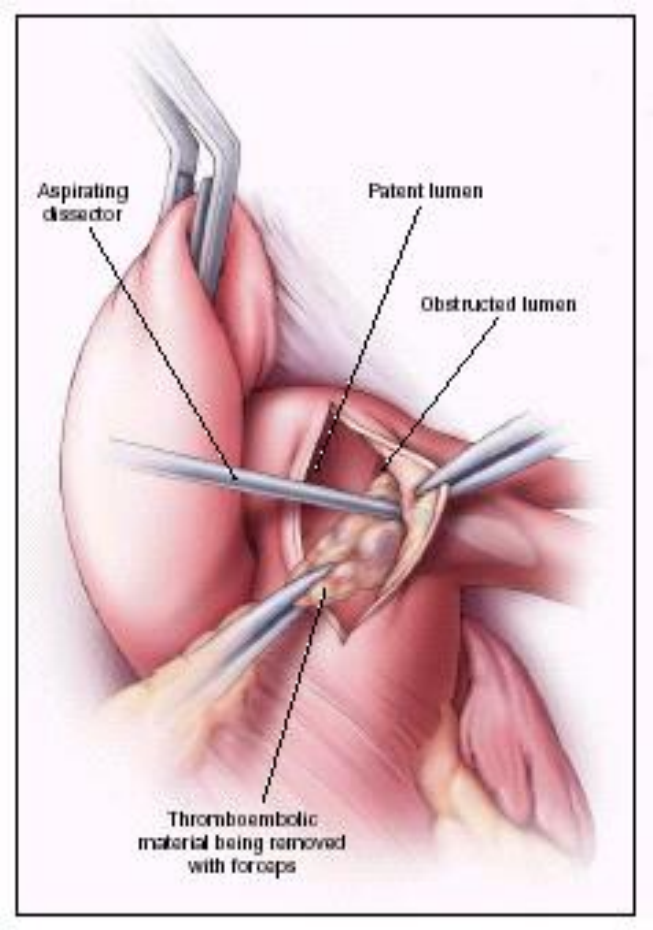
- Repeat CTPA – unchanged persistent thrombus
- Echo – persistent right heart strain
- Right heart catheterisation
  - RA 12mmHg
  - **mPAP** **51mmHg**
  - PCWP 14mmHg
  - CO 3.1l/min
  - **CI** **1.5l/min/m^2**
  - **PVR** **11.9WU**
  - PA sats 51.6%

Δ CTEPH

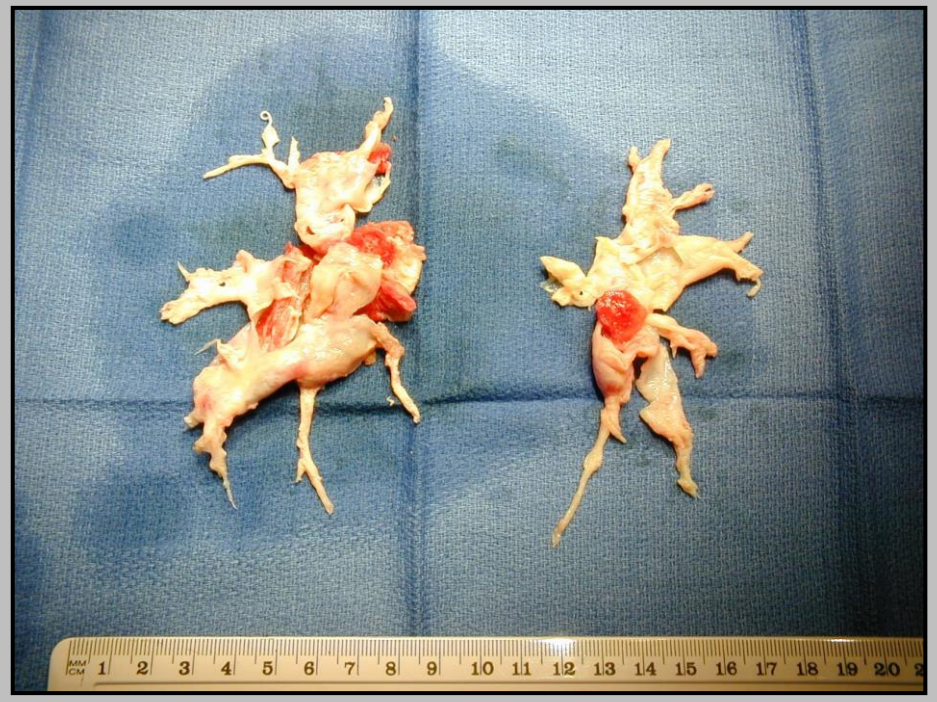
CTEPH affects both men and women equally – broad age range

CTEPH presents similarly to PAH and cannot be distinguished on echo or RHC

Case - Rex



Pulmonary Endarterectomy (PEA) surgery at Papworth



Case - Rex

- 3/12 post op – walking 4-500m
- Right heart catheterisation

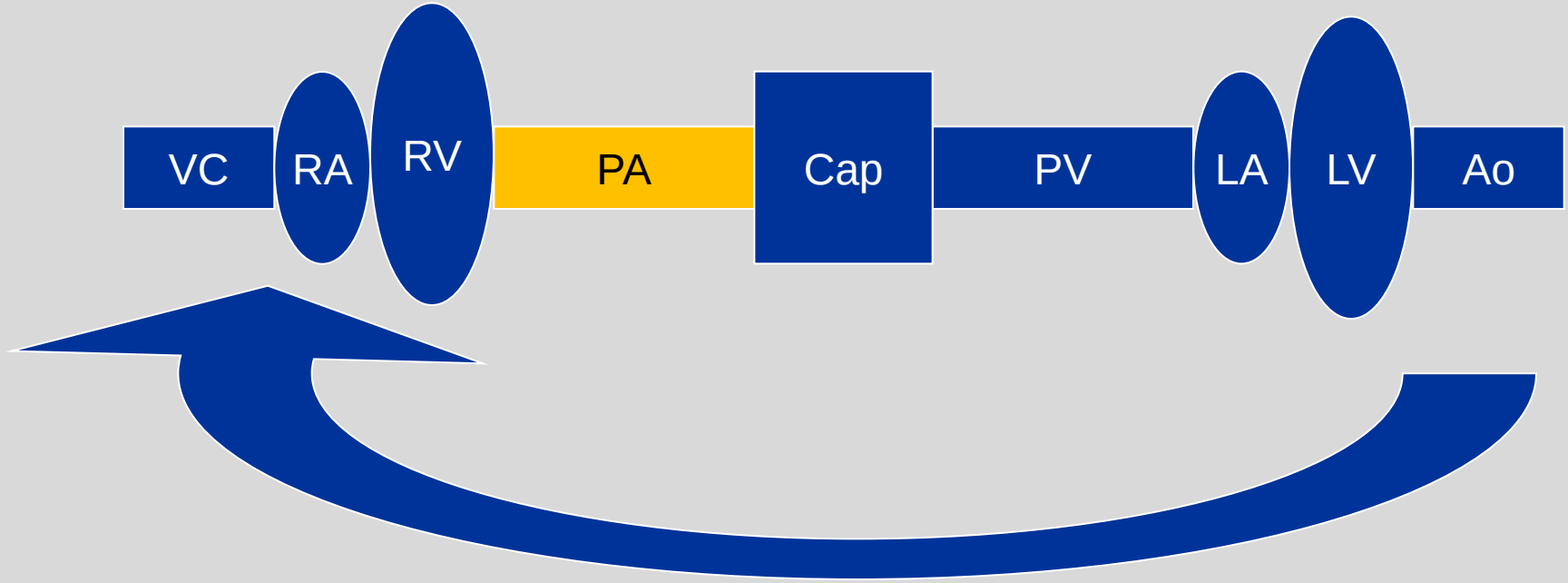
– RA	12mmHg	5mmHg
– RVEDP	14mmHg	
– **mPAP**	**51mmHg**	**19mmHg**
– PCWP	14mmHg	9mmHg
– CO	3.1L/min	6.5L/min
– **CI**	**1.5L/min/m²**	**3.2L/min/m²**
– **PVR**	**11.9WU**	**1.5WU**
– PA sats	51.6%	71%

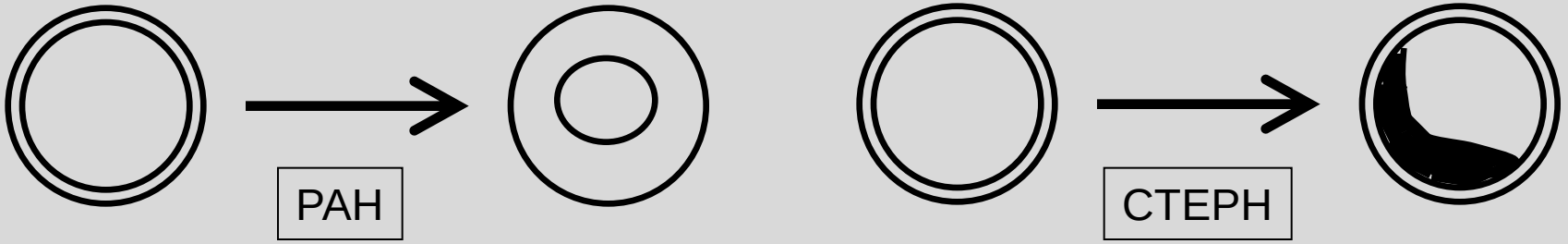
Pulmonary endarterectomy surgery can be curative in selected patients

Case - Rex

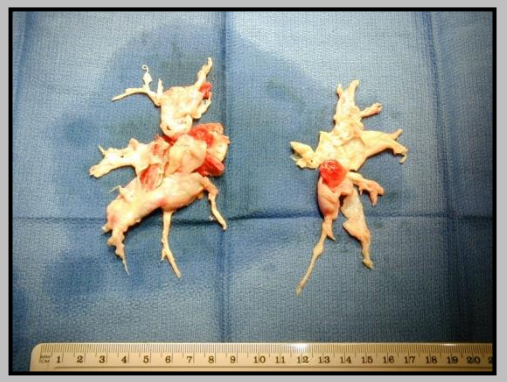
- 1 year post op
  - walking 2 miles every day to play tenpin bowling
- 5 years post op - discharged

CTEPH



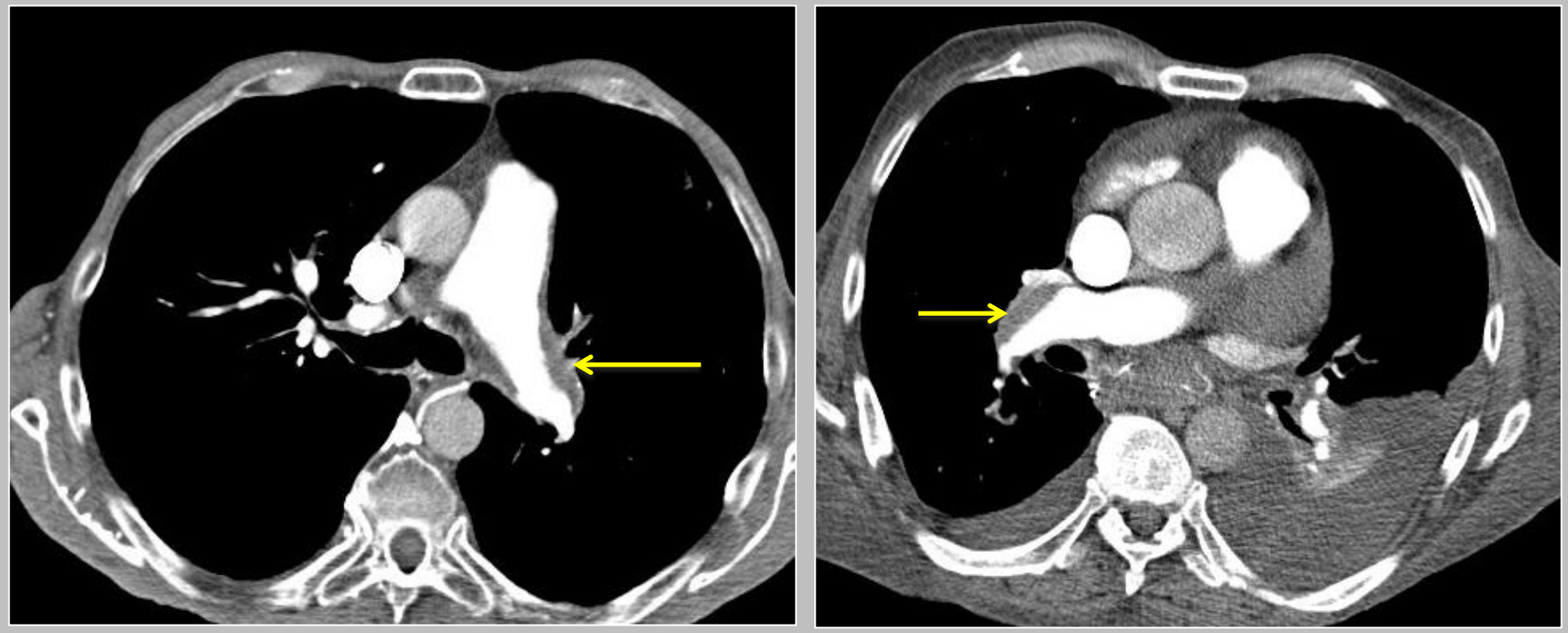


How can CTEPH present?



- **1. Masquerading as ‘acute PE’**
  - **prolonged history**
  - **symptoms & signs suggestive of PH on admission**
  - **elevated PASP on ‘acute’ echo**
  - **chronic-looking changes on initial CTPA**

CTEPH – chronic clot has a different appearance to acute clot



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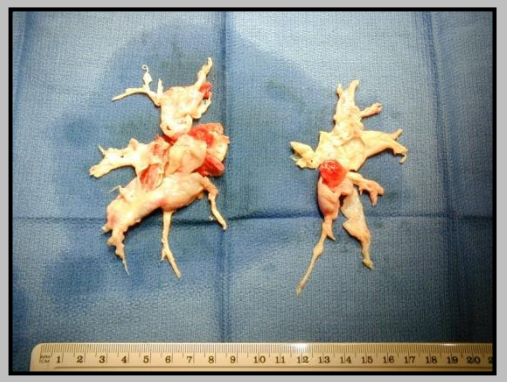
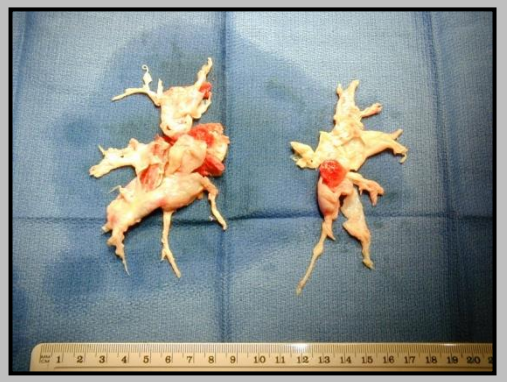


- 1. Masquerading as ‘acute PE’
- **2. Post PE screening**
  - **unprovoked initial event**
  - **high burden disease initially**
  - **residual genuine SOBOE following anticoagulation, with no alternative cardiorespiratory causes**

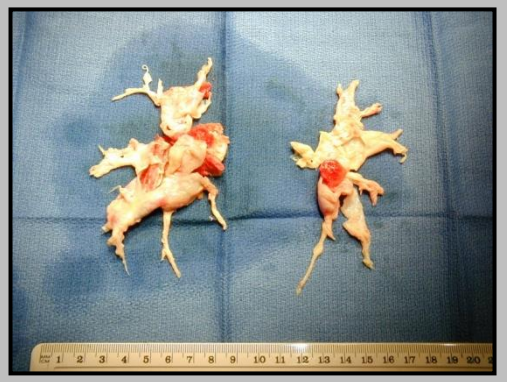
How can CTEPH present?



- 1. Masquerading as ‘acute PE’
- 2. Post PE screening
- **3. Exertional dyspnoea with previous acute PE history**
  - **unexplained SOBOE**
  - **previous DVT/PE**
  - **risk factors**
    - **APLS**
    - **Splenectomy**
    - **VA shunt**
    - **PPM**
    - **IBD**

Consider repeat imaging in patients with a prior history of thromboembolic disease

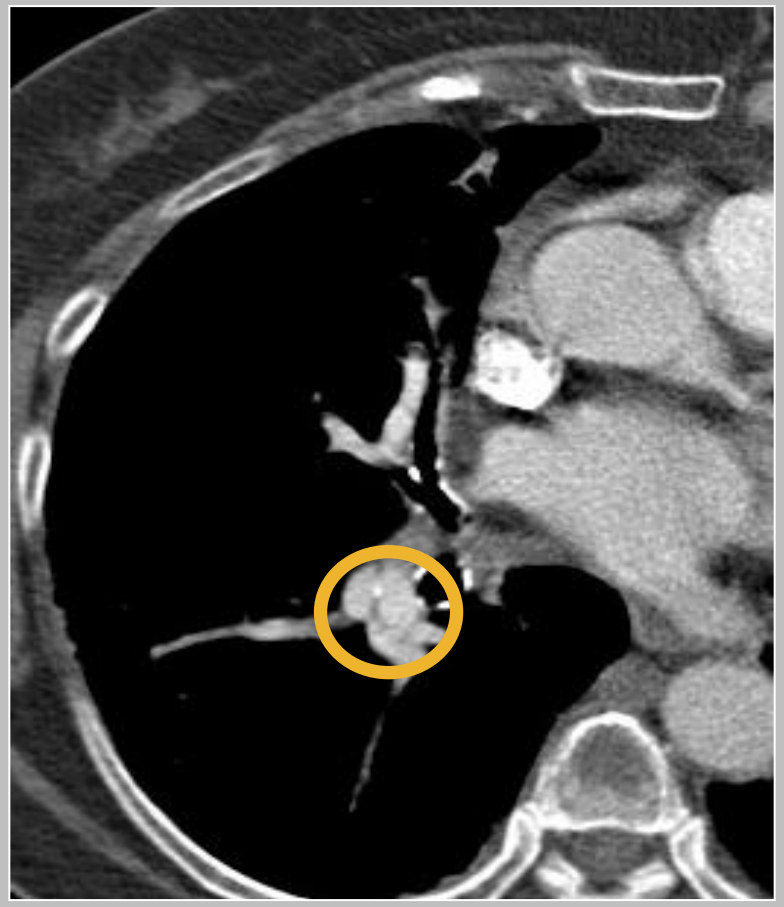
How can CTEPH present?

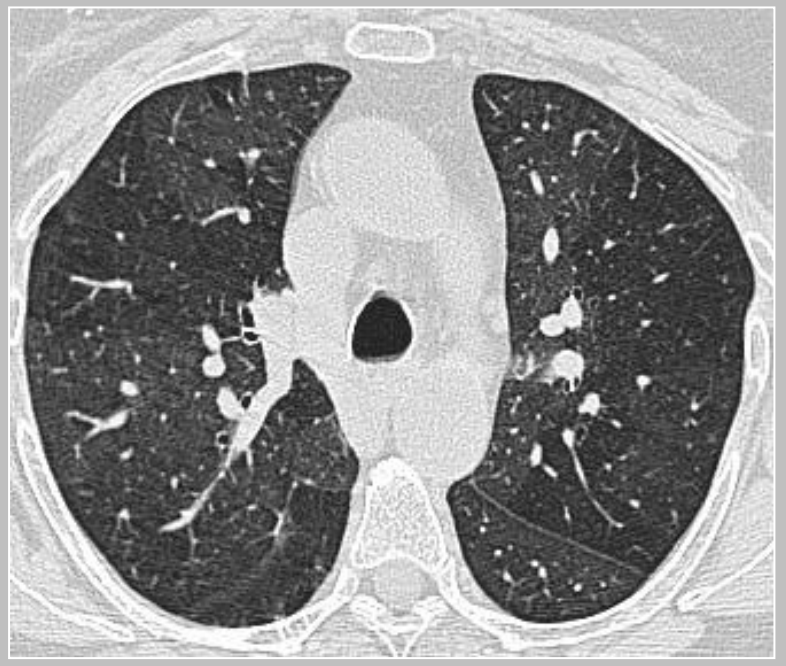


- 1. Masquerading as ‘acute PE’
- 2. Post PE screening
- 3. Exertional dyspnoea with previous acute PE history
- **4. Exertional dyspnoea in absence of previous PE**

40-50% of CTEPH cases have no documented history of a prior thromboembolic event

What if your CTPA is reported as ‘normal’ but you’re still suspicious?



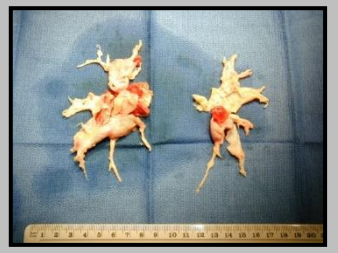


CT changes can be subtle, and can be missed by non-specialist radiologists

Has your Radiologist been primed correctly?

Respiratory Specialist requests CTPA *'?CTEPH'*

Cardiothoracic Radiologist looks specifically for CTEPH



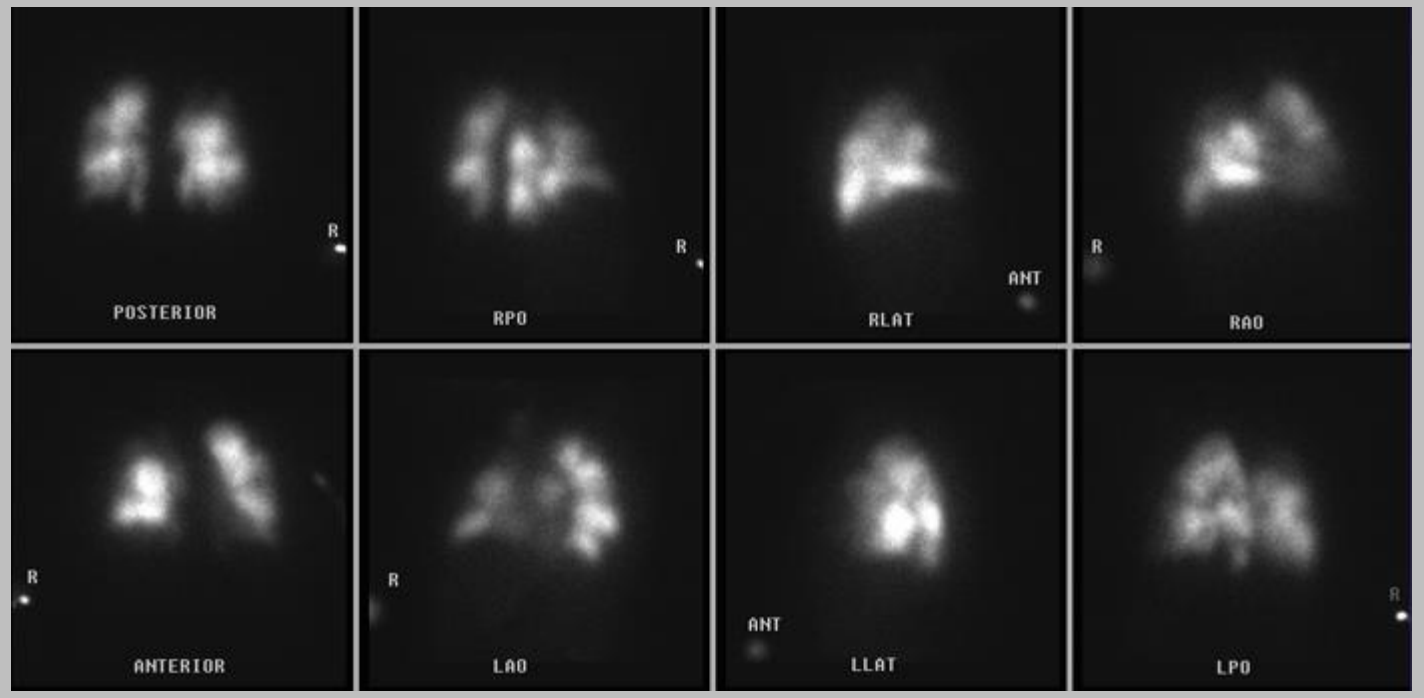
CTEPH confirmed or excluded

MAU F1 requests CTPA – *'SOB ?cause'*

Outsourcing Radiologist reports scan '*No PE*'

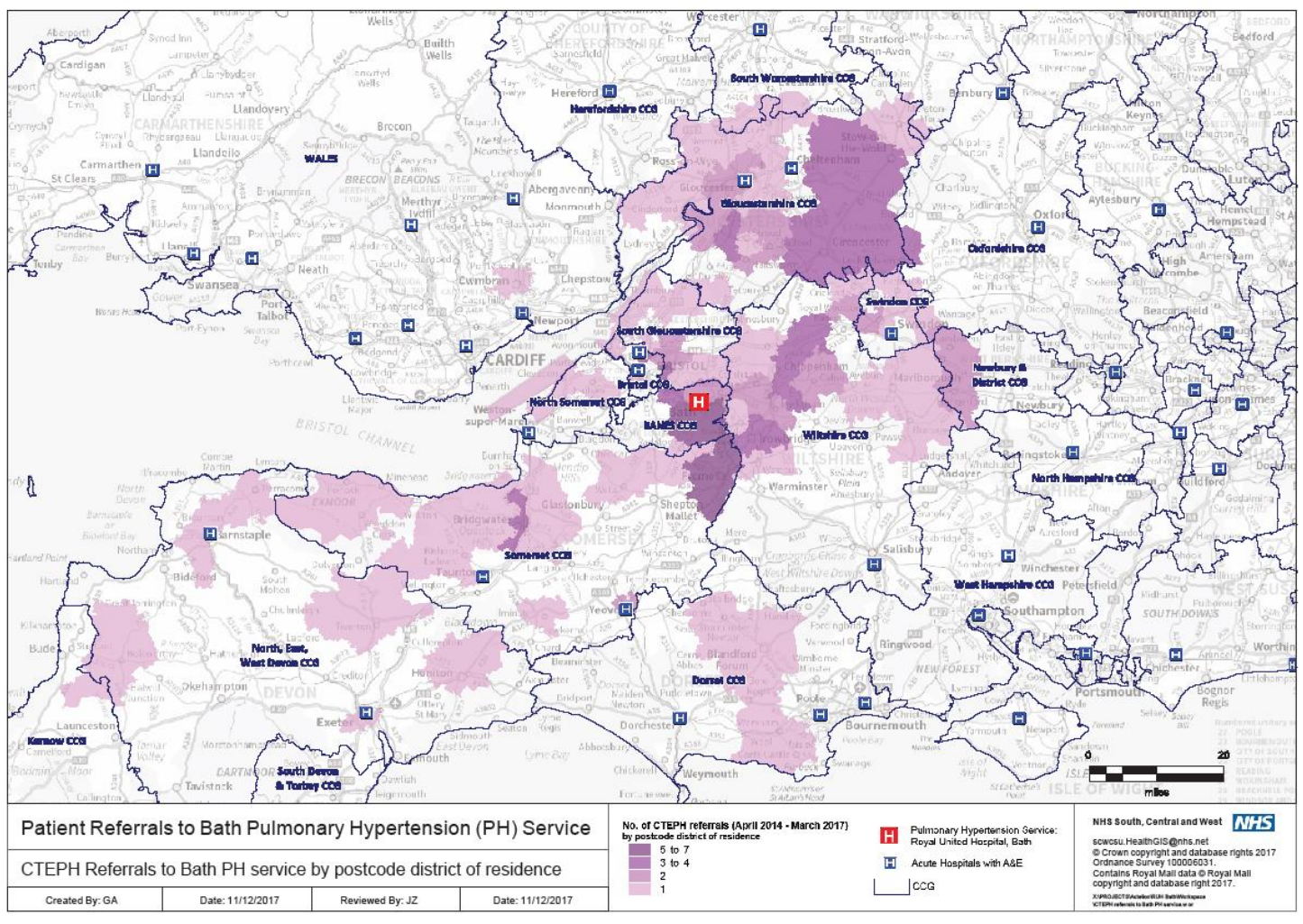
CTEPH never considered again

If in doubt…….VQ is more sensitive for detecting CTEPH



....or alternatively, ask us to review the CTPA at our weekly Radiology MDT

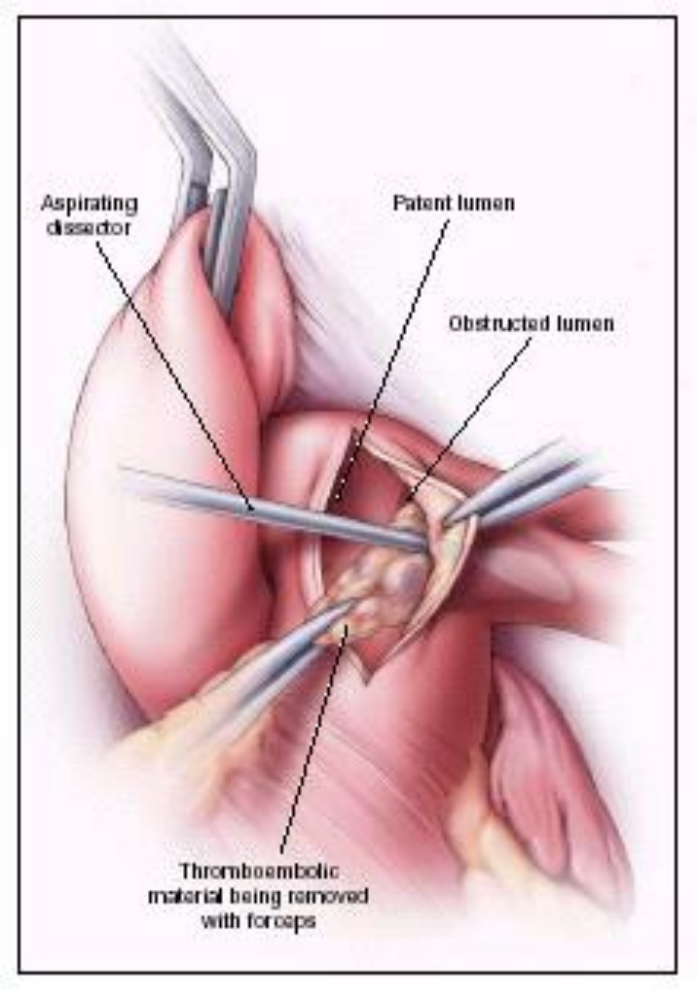
CTEPH – more common than we may appreciate

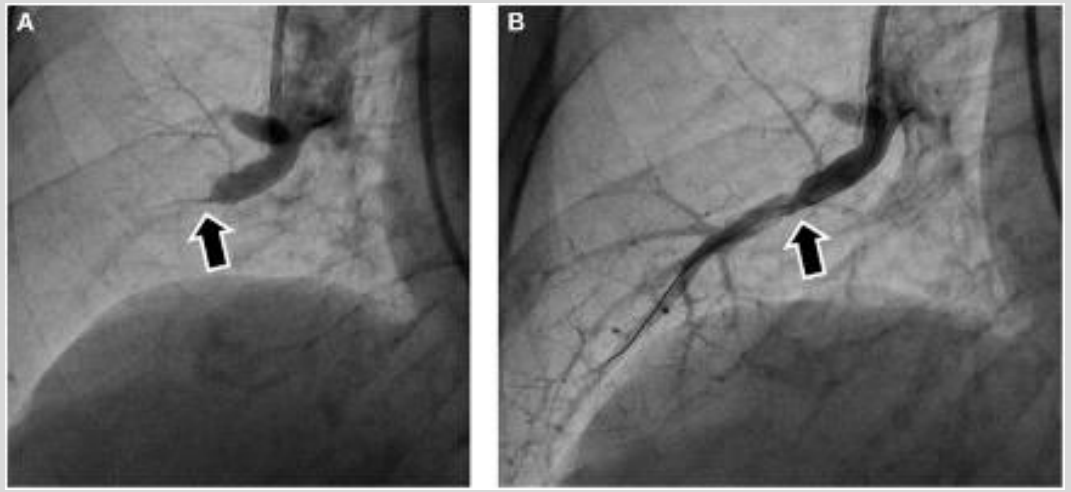


Bath local operated CTEPH prevalence
73 cases/million

UK operated CTEPH prevalence
44 cases/million

CTEPH – other treatment options available for inoperable patients





Aims

- Pulmonary vascular physiology
- Why look for PH?
- **Which forms of PH should you ‘ignore’?**
- How do you decide who to refer?

Even if you find PH it may not be appropriate to refer

1. Pulmonary Arterial Hypertension
- Idiopathic PAH (IPAH)
- Heritable
- Drugs/toxins
- Associated PAH (APAH)
  - connective tissue diseases
  - HIV infection
  - portal hypertension
  - congenital heart dise

1*. PVOD/PCH

2. PH 2ry to left heart disease
- systolic and diastolic dysfunction
- valvular

3. PH 2ry to lung disease
- COPD
- interstitial lung disease
- sleep disordered breathing
- developmental abnormalities

4. PH due to chronic thrombotic embolic disease
- proximal CTEPH
- distal CTEPH
- non-thrombotic embolism

5. Miscellaneous
- sarcoid
- PLCH, LAM
- metabolic disorders

~97-98% of PH

Adapted from Dana Point Classification 2008

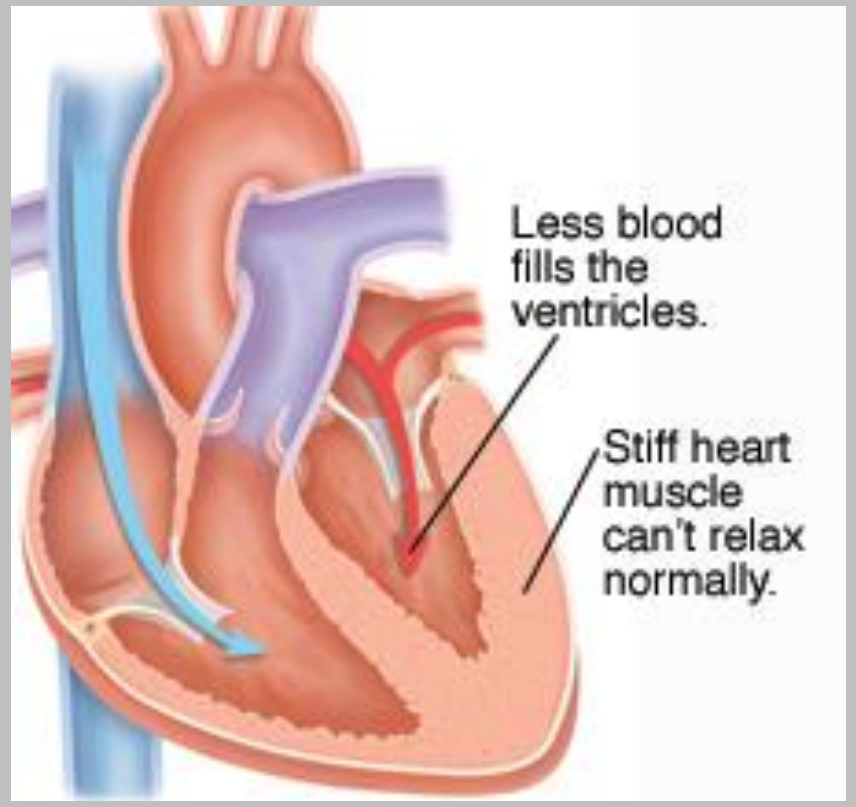
Even if you find PH it may not be appropriate to refer

2. PH 2ry to left heart disease
- systolic and diastolic dysfunction
- valvular

Case - John

- 72 year old retired accountant
- DM, IHD, HTN, AF, BMI 34
- SOBOE for 12-18 months
- Presents with SOBOE, SOA and elevated NT-proBNP
- Echo – '*Good LV function. PASP 60mmHg. High risk of PH*'

Diastolic LV dysfunction (or HF-pEF)

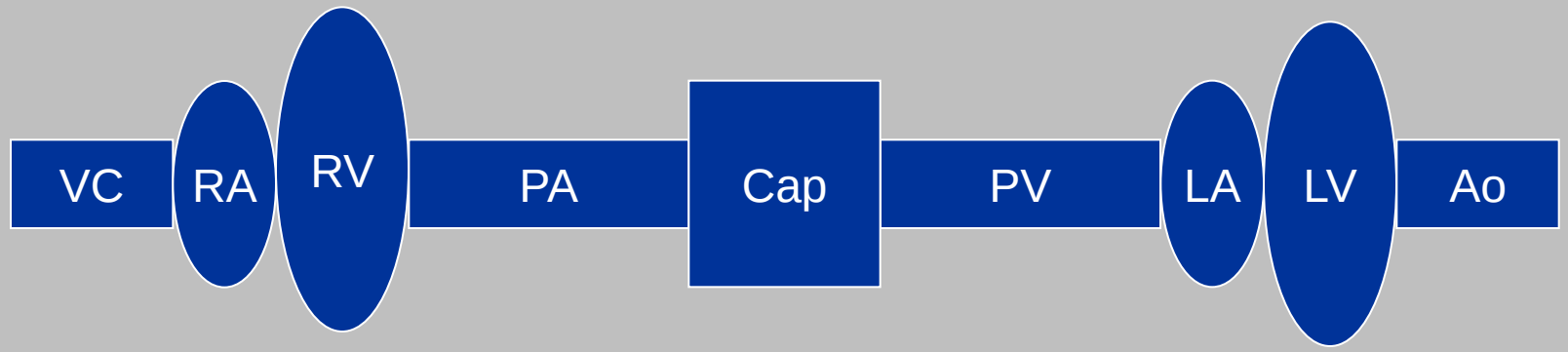


Patients with PAH or CTEPH rarely have a dilated LA on echo

ie ‘Heart Failure with Preserved Ejection Fraction’ or ‘HF-PEF’

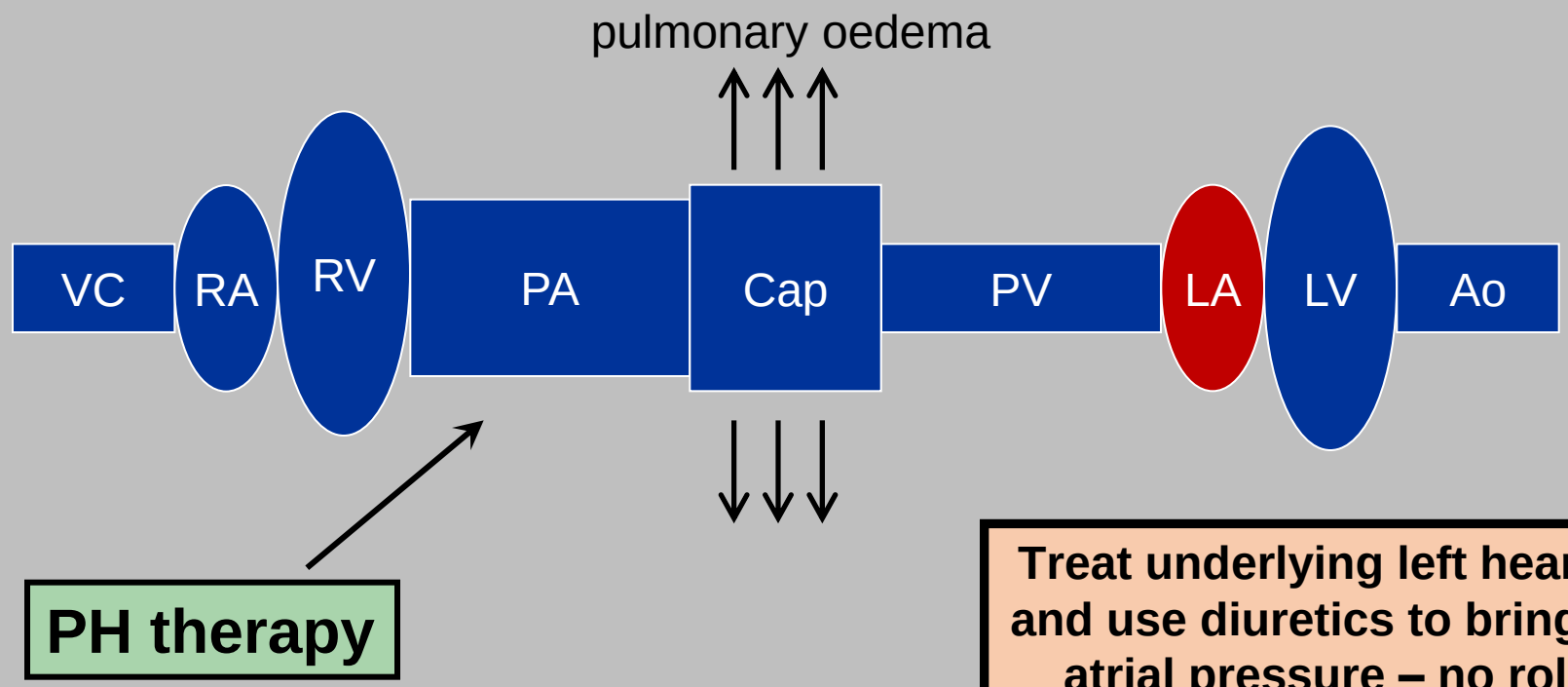
- age>65
- poorly controlled hypertension
- obesity
- diabetes
- CAD
- AF
- **dilated LA**
- LV hypertrophy
- +/- evidence of diastolic dysfunction on echo

PH associated with left heart disease



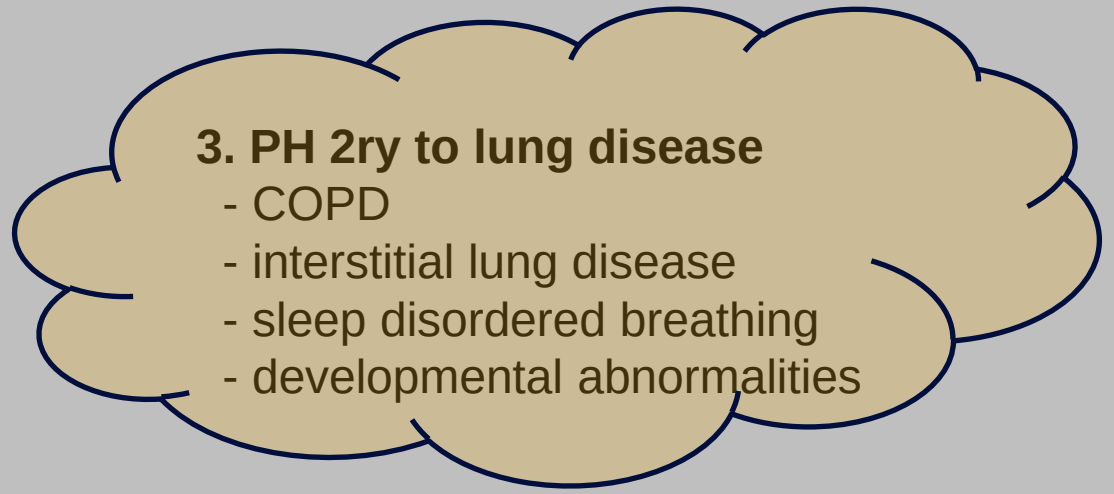
ie a *passive* increase in mPAP

PH associated with left heart disease



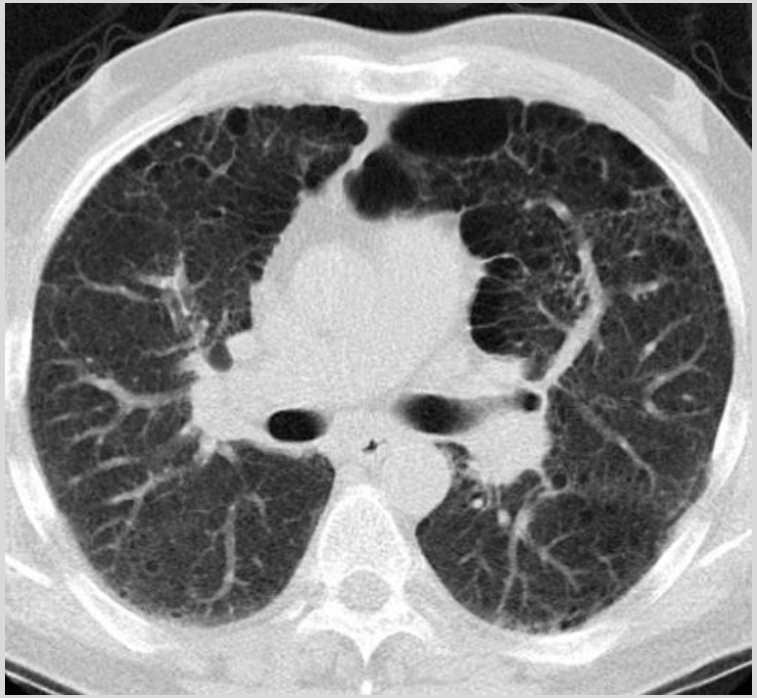
Treat underlying left heart problem and use diuretics to bring down left atrial pressure – no role for PH therapy

Even if you find PH it may not be appropriate to refer



Case - Kevin

- 68 year old retired taxi driver
- SOBOE – ET 200m
- Current smoker – 60 pack year history
- Treated for COPD exacerbation
- Remains hypoxic ++
- '*Echo shows PH*'
- CT – no PE, emphysema ++

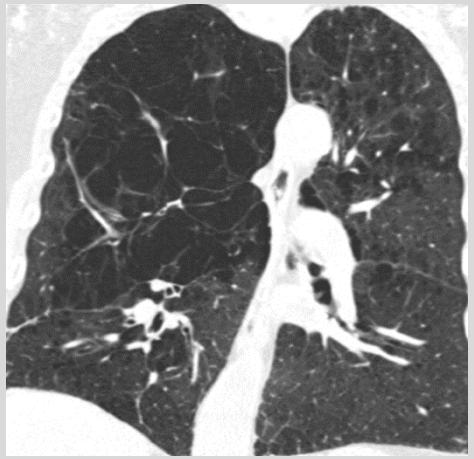


Presence of marked hypoxia in the setting of PH usually signifies co-existent lung disease

PH secondary to lung disease

Disease process

Pulmonary vasculature obliteration



Hypoxia

Hypoxic vasoconstriction

Vascular remodelling

Pulmonary Hypertension

Aims

- Pulmonary vascular physiology
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Finding ‘treatable’ PH

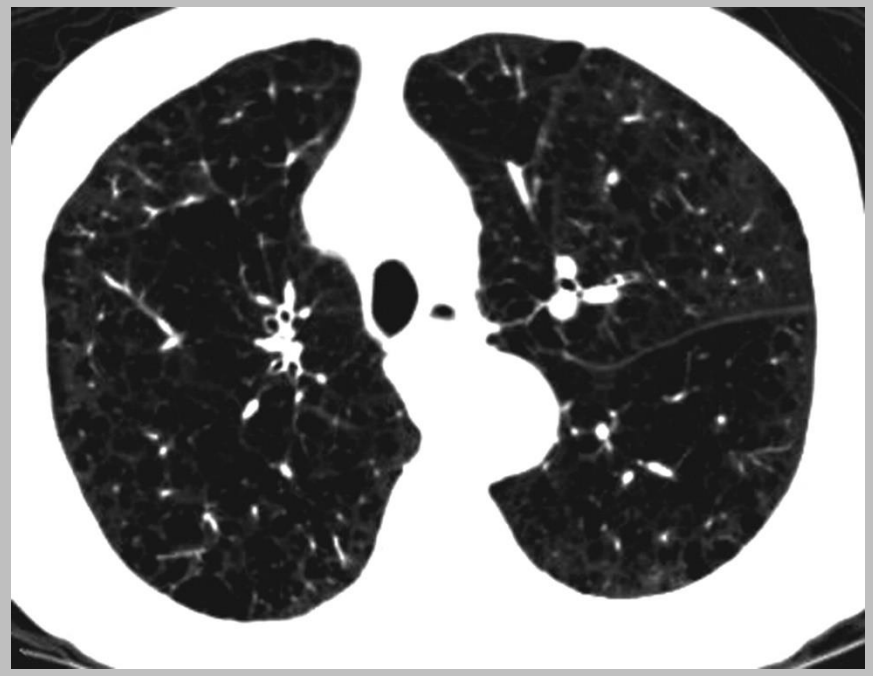
1. PH is rare

2. Not all PH is treatable

3. Some tests such as ECG’s & CTPA’s are often misinterpreted

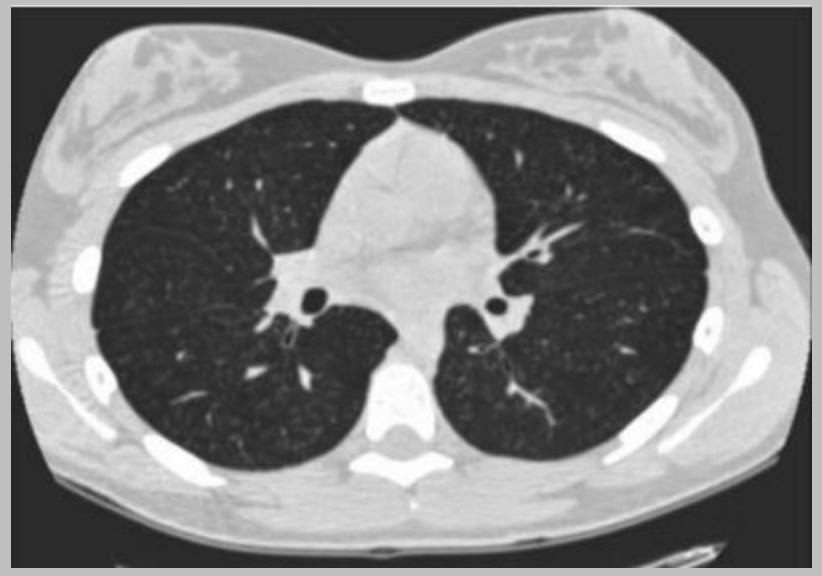
4. The best screening tool we have for PH ie echo carries poor Sensitivity and specificity

PH 2ry to lung disease ie ‘Cor pulmonale’



- 76 yr old ♂ with COPD
- Echo
  - mild RA diln
  - normal sized RV with good systolic function
  - PASP 50mmHg
- PFTs
  - FEV1 45%, FVC 90%
  - TLCO 25%

Likely IPAH



- 52 yr old ‘asthmatic’ ♀
- Echo
  - mild RA diln
  - normal sized RV with good systolic function
  - PASP 50mmHg
- PFTs
  - FEV1 90%, FVC 100%
  - TLCO 70%

It’s all about determining your *pre-test probability*

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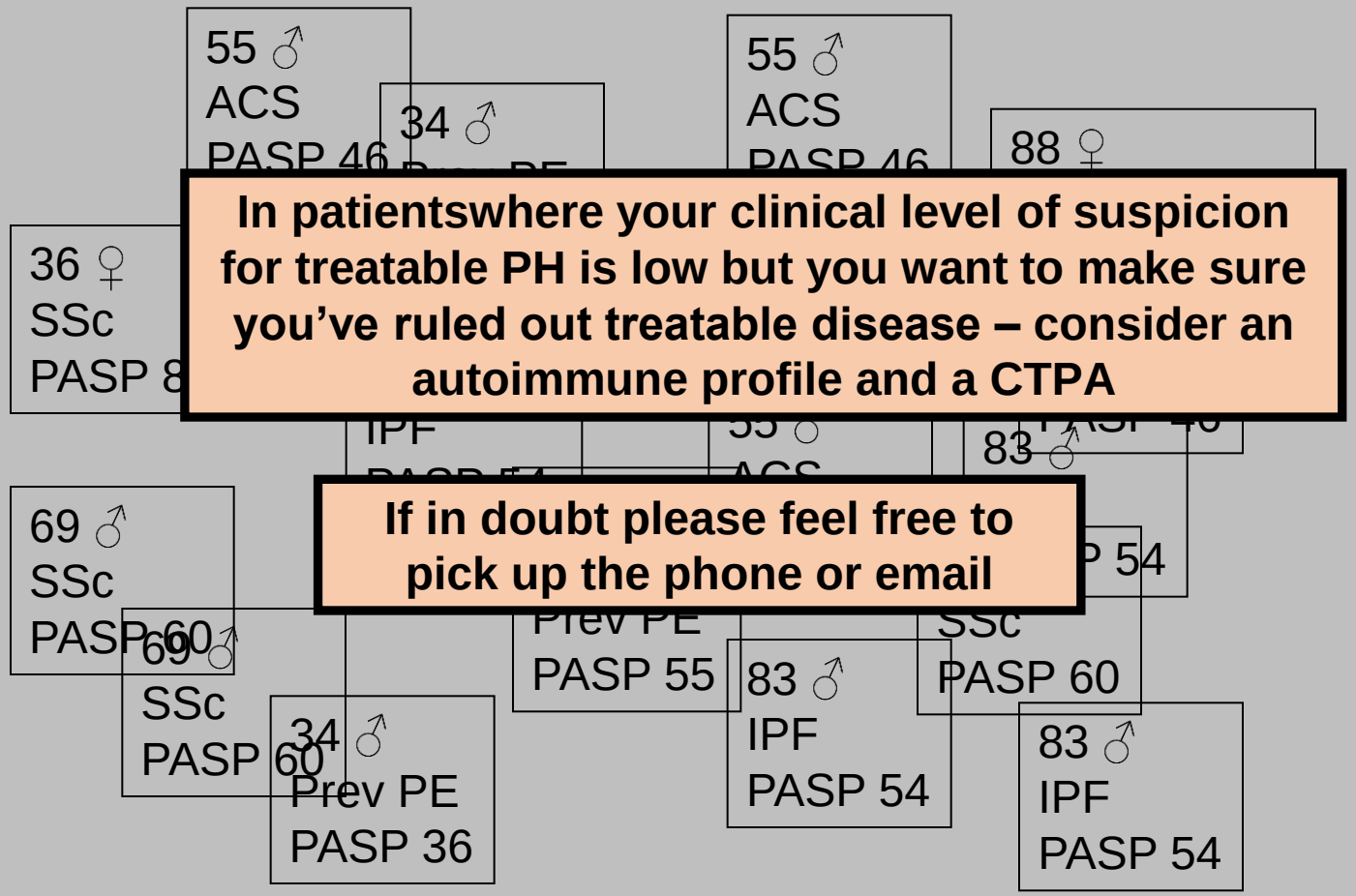
Adapted from Dana Point Classification 2008

…but even then life's not always that simple!



Summary

- Pulmonary vascular physiology
- Why look for PH?
- Which forms of PH should you ‘ignore’?
- How do you decide who to refer?

Shared care PH services in the South West

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