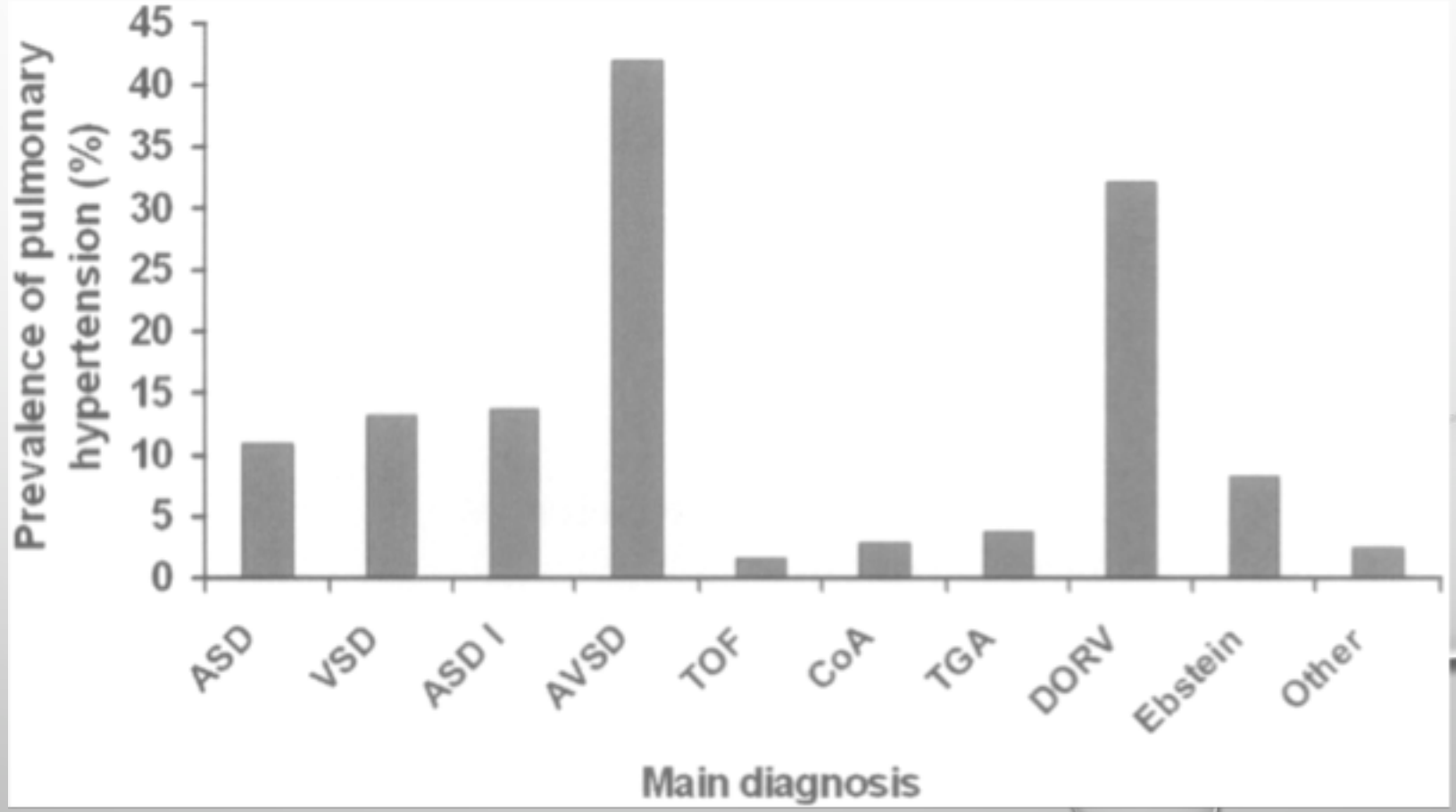
GUGH AND PAH
WICH KIND OF PATIENTS ARE WE TREATING?

G AGNOLETTI

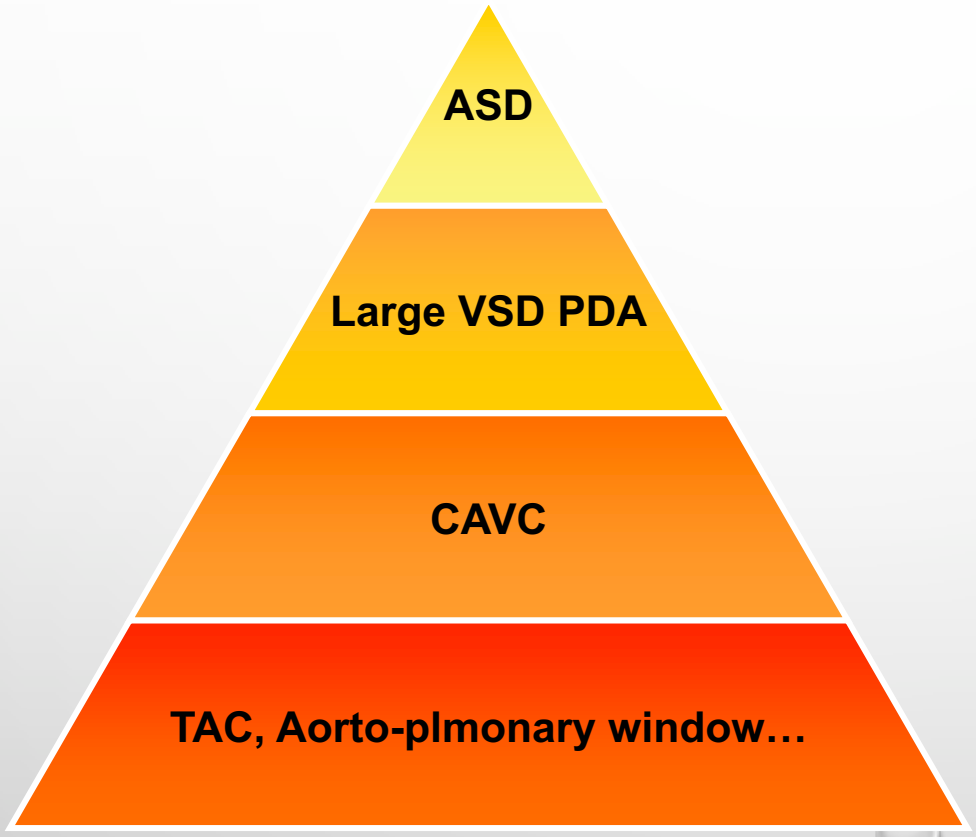
30 GIORNATE CARDIOLOGICHE TORINESI

5-10% OF ACHD DEVELOP PAH

ALL CHD CAN BE ASSOCIATED WITH PAH



RISK OF PVD IN VARIOUS CHD



50 years

1 year

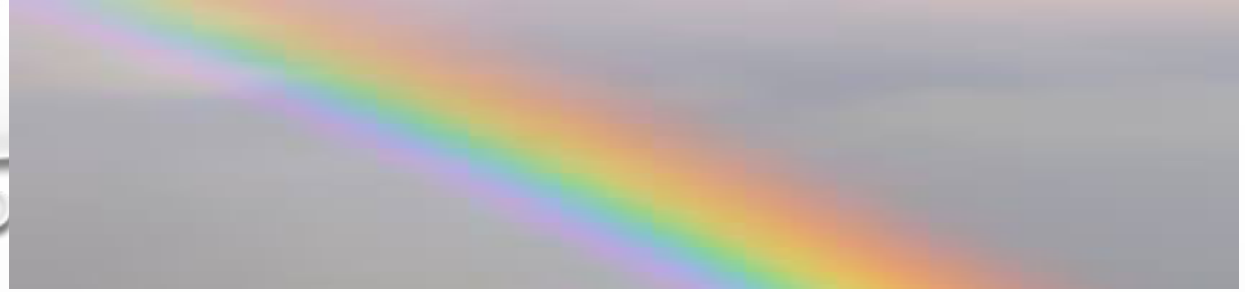
6 months

1 month

ARE PAH-ACHD PATIENTS DIFFERENT ?

ACHD ARE DIFFERENT AND SO ARE THOSE HAVING PAH

WHY?



HETEREOGENEOUS…

prenatal origin of pulmonary vascular diseases, perinatal pulmonary vascular maladaptation/maldevelopment, pulmonary vascular hypoplasia, large variety of CHD (with or without shunt), different surgical/percutaneous approach, different colors

CLASSIFICATION (4 TYPES PH-ACHD)

EISENMENGER SYNDROME
PERSISTENT SYSTEMIC TO PULMONARY SHUNTS
PAH WITH SMALL OR COINCIDENTAL DEFECTS
PAH AFTER DEFECT CLOSURE (FONTAN CIRCULATION)

Brida M, Gatzoulis MA. *Heart* 2018

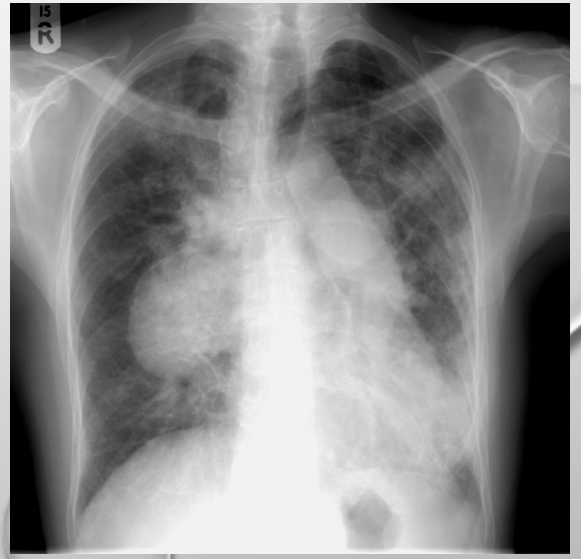
EISENMENGER SYNDROME

- Due to unrestricted systemic-to-pulmonary shunts (atrial, ventricular, arterial)
- Leads to development of PAH and pulmonary vascular disease (PVD)
- Progressive reversal of shunting

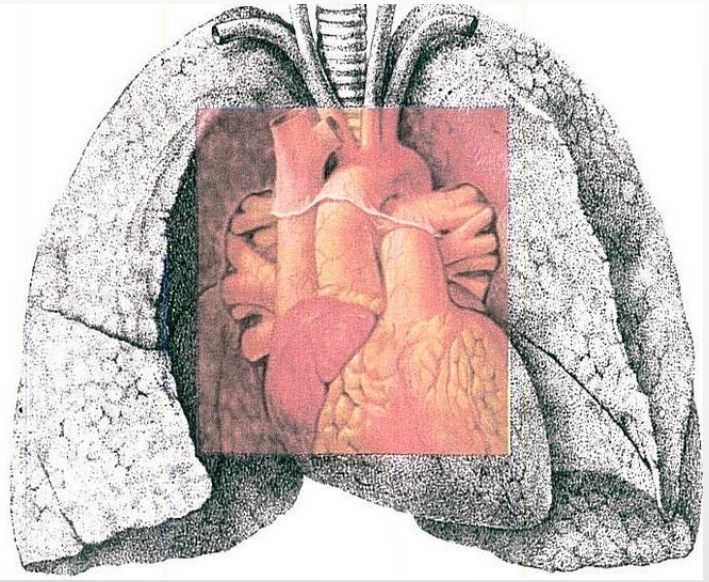
EISENMENGER SYNDROME

- Chronic cyanosis
- Multisystem involvement

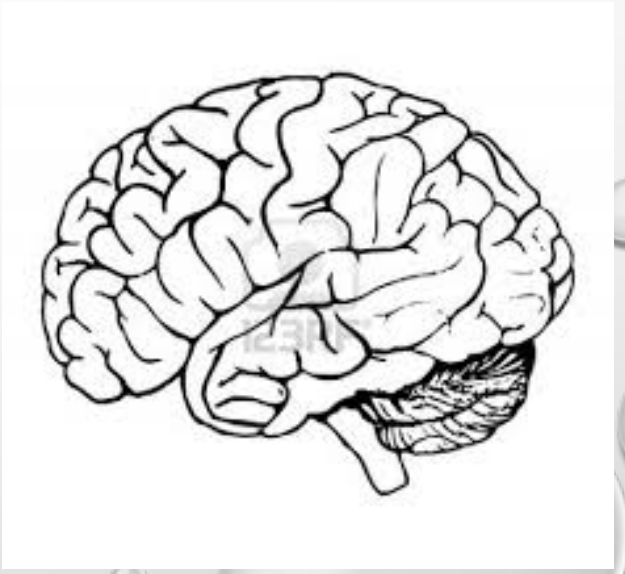
Defect closure is contraindicated: the defect functions as a 'relief valve'



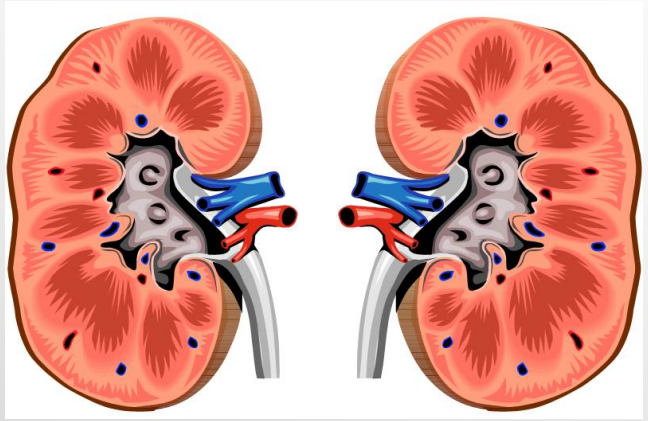
EISENMENGER SYNDROME
HEART, LUNGS, BRAIN



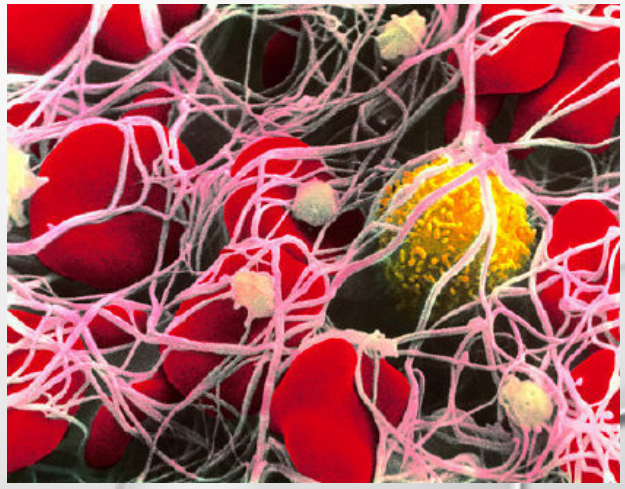
- Chest pain
- Coronorary compression
- Pulmonary embolism
- Haemoptysis
- Cerebral event
- Cerebral abscess (4%)



EISENMENGER SYNDROME
KIDNEY, HAEMATOPOIETIC SYSTEM



- Diminished renal flow
- > urea > uric acid
- Nephrotic syndrome
- Secondary erythrocytosis
  Thrombocytopenia
- Coagulation abnormalities



EISENMENGER SYNDROME

Untreated patients have a poor survival with 10-year mortality rates ranging between 30% and 40%

TREATMENT:

- General measures: contraceptive methods, psychosocial support, active lifestyle, endocarditis prophylaxis, immunisation (influenza and pneumococcal infections)
- Supportive therapy
- PAH–DTT (disease-targeting therapy)
- Heart and lung transplantation, or lung trans- plantation with repair of the underlying cardiac defect

EISENMENGER SYNDROME

SUPPORTIVE THERAPY

- Iron deficiency anaemia (transferrin saturation <20%) is associated with worse outcome. Iron supplementation. NO venesection
- Oxygen supplementation ?? (has not been shown to have a positive effect on exercise capacity nor on survival)
- Oral anticoagulants remain controversial (high prevalence of pulmonary arterial thrombosis in situ, arrhythmia and stroke but also pulmonary haemorrhage and haemoptysis

EISENMENGER SYNDROME

Cardiac catheterisation (PVR and AVT): YES
NO CCB if positive AVT : significant peripheral vasodilation, increased right-to- left shunting (hypoxia), syncope and sudden cardiac death

PAH–DTT in ES:

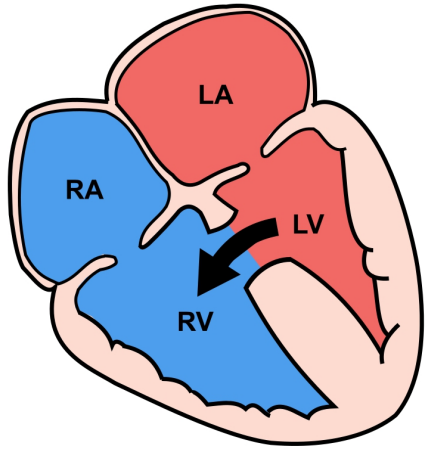
- endothelin-1 receptor antagonists (ERAs), BREATHE-5, MAESTRO
- phosphodiesterase type-5 inhibitors (PDE-5i)
- guanylate cyclase inhibitors
- prostanoids

EISENMENGER SYNDROME

VARIABLES

Better Prognosis	Determinants of Prognosis	Worse Prognosis
Post-tricuspid shunt	Level of shunt [8]	Pre-tricuspid shunt
Simple defect (i.e. VSD, PDA)	Complexity of CHD [11]	Complex defect (i.e. single ventricle)
Mild Resting O_2 saturations 85-90%	Cyanosis [8, 10]	Moderate / severe Resting O_2 saturations <85%
Transferrin saturation of >20%	Iron deficiency anaemia [18]	Transferrin saturation of <20%
I, II	NYHA functional class [12]	II, IV
Slow	Rate of symptoms progression	Rapid
No	Right ventricle failure	Guarded prognosis
Longer (> 400 m)	6 minute walk distance [10]	Shorter (< 300 m)
BNP plasma levels <13.9 pmol/L Normal CRP levels	Biomarkers (BNP, CRP) [13, 14]	BNP plasma levels > 30 pmol/L CRP levels >10 mg/L
TAPSE ≥ 1.5 cm RA area < 25 cm^2 RA/LA < 1.5 No pericardial effusion	Echocardiographic markers [8, 15]	TAPSE < 1.5 cm RA area ≥ 25 cm^2 RA/LA ≥ 1.5 Pericardial effusion
RAP < 8 mmHg and CI ≥2.5 L/min/m^2	Baseline haemodynamics	RAP > 15 mmHg and CI ≤ 2.0 L/min/m^2
Decrease in PVRi ≥ 25%	Acute vasoreactivity testing [16]	No changes or decrease in PVRi ≤ 25%

- Level of shunt
- Complexity of CHD
- Cyanosis
- Iron deficiency anaemia
- NYHA and rate of symptoms progression
- RV failure
- 6 min walk distance
- Biomarkers
- ECHO
- Hemodynamics and AVR

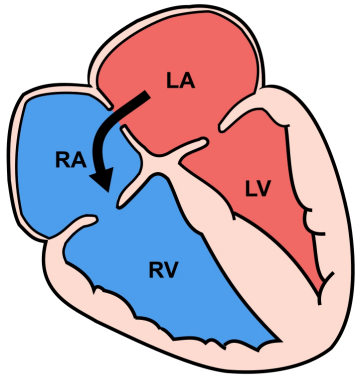


PERSISTENT SYSTEMIC TO PULMONARY SHUNTS

- Shunt closure may be beneficial? : Severity of PAH and PVR
- Age is not a good predictor of irreversibilityof PAH

Defect closure should not be based on feasibility but on long-term benefits

Hosseinpour AR Congenital Heart Disease. 2017



PERSISTENT SYSTEMIC TO PULMONARY SHUNTS

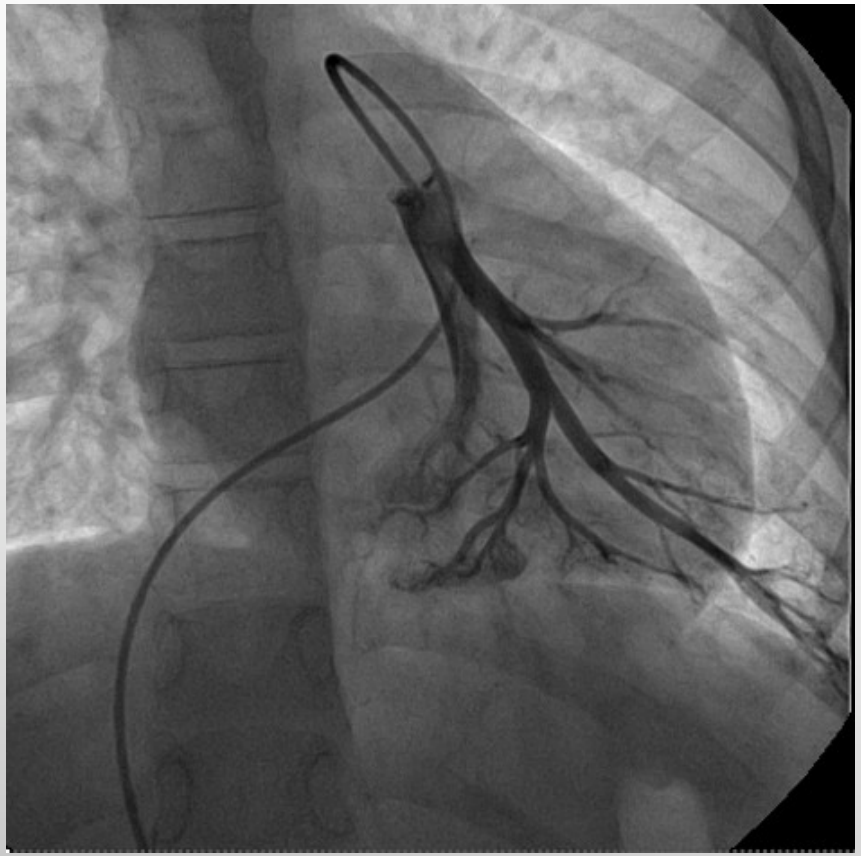
Closure NO: PVR index >8 WU m2

Closure YES: PVR index <4 WU m2

Grey zone: PAH–DTT , fenestrated closure

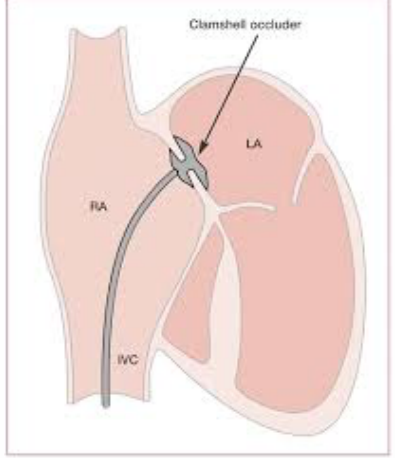
PATIENT MUST CONTINUE PAH–DTT medication. Repeat cardiac catheterisation 6-12 months after closure

PAH WITH SMALL OR COINCIDENTAL DEFECTS



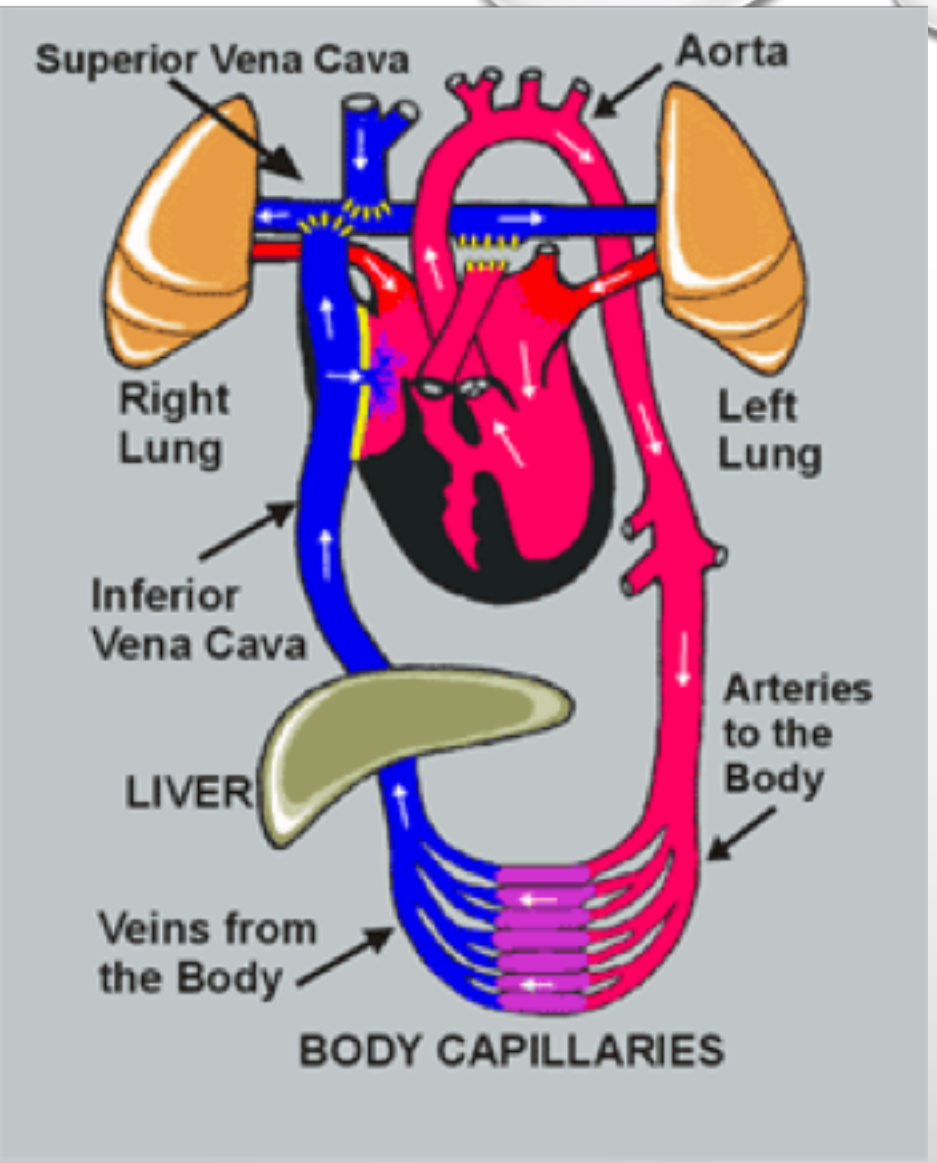
- Not considered primarily responsible for PAH and may be beneficial
- Pathophysiology and clinical phenotype similar to idiopathic PAH
- Treatment: PAH–DTT, anticoagulation?

the defect should not be closed (relief valve)



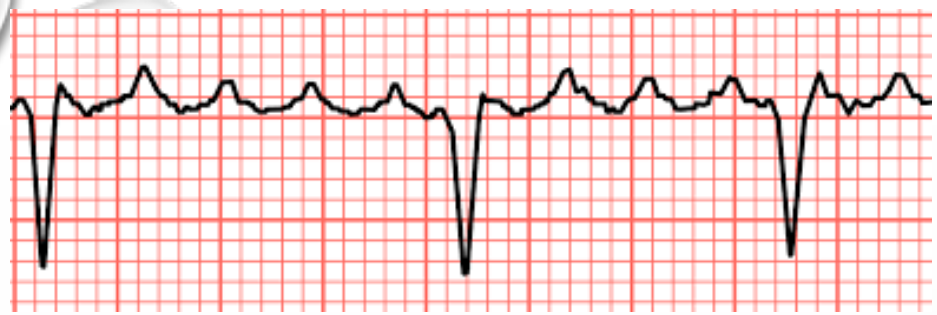
PAH AFTER DEFECT CLOSURE

- Presenting with PAH often many years after defect closure
- Late diagnosis and closure ? Genetic? other predisposition to PAH?
- Incidence of PAH: from 2.1% after closure > 15% 50 years later
- 10-year survival worse in patients who developed PAH after closure
- Treatment: DTT



FONTAN CIRCULATION

- Fontan patients with elevated PVR (but no PAH, as conventionally defined) might benefit from PAH–DTT.
- The consensus on selection criteria from the Fontan cohort that might benefit from DTT has not yet been reached
- Recommendations for general PAH–DTT cannot be made before more data become available



ARRHYTHMIA IS A STRONG PREDICTOR OF DEATH (EVEN AFTER ADJUSTING FOR DEMOGRAPHIC AND CLINICAL VARIABLES)

- Related to the myocardial substrate in conjunction with longstanding pressure/volume overload, cyanosis, surgical scars
- Affect 1 in 6 patients at 5 years FU
- The onset of arrhythmia should be perceived as a marker of progression of the disease

Drakopoulou M Heart 2018

YES

PAH-ACHD PATIENTS ARE DIFFERENT

ACCURACY, DEDICATION, CARE….

TEAM WORK