

# WHO classification of pulmonary hypertension Evian 1998, revised Venice 2003

Based on clinical evolution, histopathology, and response to therapy

1. Pulmonary arterial hypertension (PAH)
  - idiopathic (IPAH, formerly PPH), sporadic or congenital
  - PAH associated with intake of anorexigens, HIV, liver cirrhosis, connective tissue disease, **congenital left- to-right shunts**, PVOD
2. Pulmonary hypertension associated with LHF
3. Pulmonary hypertension associated with hypoxia and/or chronic lung disease or hypoventilation
4. Acute or chronic thromboembolic pulmonary hypertension
5. Miscellaneous (sarcoidosis, schistosomiasis, etc)

# Congenital cardiac shunt-induced PAH: understanding the effects of shunt flow on Ppa – and shunt direction

Review of studies on pulmonary hemodynamics in a total of 91 normal subjects

## Mean slope of Ppa-Q:

1.0 mmHg - L/min in young subjects

2.5 mmHg - L/min in old subjects

## Mean slope of Ppa-Pla:

1 mmHg - 1 mmHg

*From Reeves et al.. In: Pulmonary Vascular Physiology and Pathphysiology. Lung Biology in Health and Disease, Vol 38, Ed Weir and Reeves, Marcel Dekker 1989; chap 4, pp 107-133*

## Example: left-to-right shunt-induced pulmonary hypertension

- Application for reimbursement of specific therapy for CHD-PAH: patient 67 yr with dyspnea and fatigue, pulmonary hypertension and ASD (echo)
- Cath:  $Q_p/Q_s = 3.2$ ,  $Q_s = 5$  L/min, Ppa 80/15, mean 40 mmHg, Ppao 11 mmHg, Pra 10 mmHg, SaO<sub>2</sub> 95 %
- With a normal pulmonary blood flow, Ppa/Q slope 2.5 mmHg/L/min, Ppa with be at 15 mmHg
- Indication for shunt closure, not medical therapy!

# The Eisenmenger syndrome

Syndrome of pulmonary hypertension initially caused by a cardiac left-to-right shunt of any cause, eventually leading to right heart failure and increased pressures causing shunt reversal, cyanosis, polycythemia and digital clubbing

- *Eisenmenger V. Die angeborene Defect der Kammerscheidewand des Herzen. Z Klin Med Suppl 1897; 32: 1-28*
- *Wood P. The Eisenmenger syndrome or pulmonary hypertension with reversal of shunt (The Croonian Lectures). Br Med J 1958; 2: 701-9, 755-62*

## How frequent is the Eisenmenger syndrome?

- Incidence in proportion to left-to-right shunt flow, pressure, duration and individual susceptibility  
*Hoffman et al, Circulation 1981; 64: 873-77*
- 5 % of congenital heart diseases (recent ESC registry), depends on access to corrective surgery
- Late complication of ASD
- 10 % of VSD > 2 yr
- 50 % of large VSD

# WHO classification of systemic-to-pulmonary shunts - Venice 2003

## 1. Type

- Simple: ASD, VSD, PDA, anomalous venous return
- Combined: describe
- Complex: truncus arteriosus, single ventricle, AV septal defects

2. Dimensions: small (ASD < 2, VSD < 1 cm) or large

3. Associated cardiac abnormalities

4. Correction status: non, partially or totally corrected

# Treatment of CHD-PAH

- CHD-PAH in treprostinil, beraprost and sitaxsentan RCT trials, a posteriori subgroup analysis unconvincing
- Case series suggesting prostacyclin and bosentan efficacious, with sustained improvement in functional class, increase in 6MWD around 50 m, and improved SaO<sub>2</sub> in Eisenmengers
- RCT: BREATHE-5 under way

# Biology: angiopoietin-1 / BMPR2 signalling part of inflammation-angiogenesis-related remodelling

BMPR2 mutation

VEGF, A-II, MCP1, ET-1  
Angiopoietin-1

Tie2

BMPR2 receptor

5HT, ET-1

- ↓ Smad signalling

Unrestricted PVSMC proliferation  
Pulmonary arterial hypertension

