Pulmonary vascular complications of hepatic disease

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LUNG

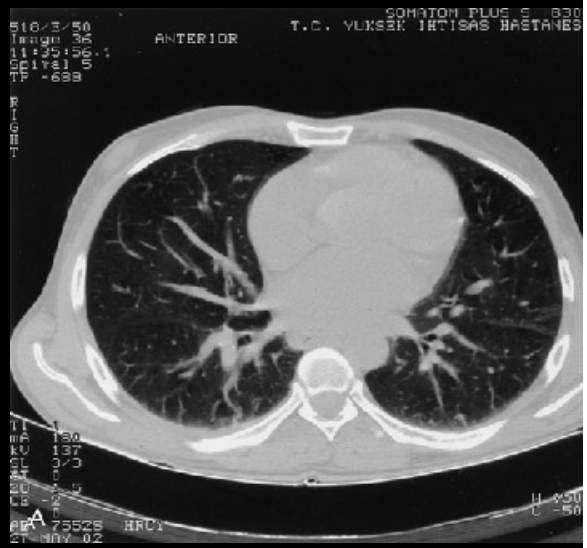
GUT AND PORTAL SYSTEM

Pulmonary vascular complications of hepatic disease

- Hepatopulmonary syndrome (HPS)
- Portopulmonary hypertension (PPH)

HEPATOPULMONARY SYNDROME

Definition



- **Defect in arterial oxygenation**
  - **Hypoxemia :**
    - **PaO2 < 80mmHg on room air**
    - **Alveolo-arterial oxygen gradient >15 mmHg**
- **Intrapulmonary vascular dilatation**
- **Liver Disease or portal hypertension**

Prevalence in adults

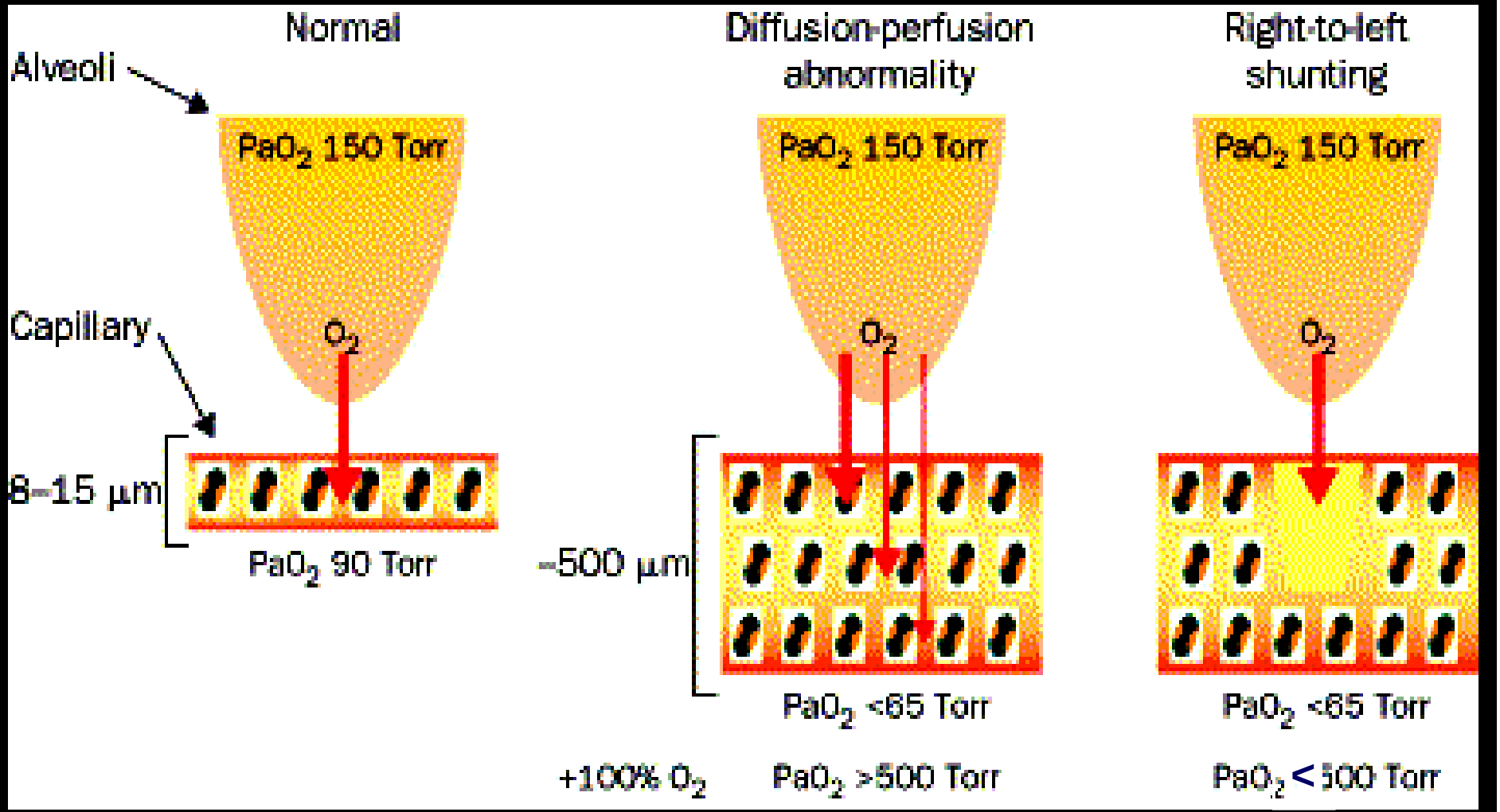
- Cirrhosis : 4 - 80 % (20%)
- Budd Chiari Syndrome : 28%
- Chronic viral hepatitis (w/wo cirrhosis) : 10%
- Portal Vein Obstruction : 2%

Pathophysiology of hypoxemia

Intrapulmonary capillary dilatation
Increased pulmonary blood flow

- Diffusion-perfusion disturbance
- Right-to-left shunting

Pathophysiology of hypoxaemia



Pathophysiology of Intrapulmonary vascular dilatation

- Decrease in vascular tone
- Imbalance in favour of endogenous vasodilatators over vasoconstrictive factors
  - Increased systemic and intrapulmonary production of Nitric oxide (NO)

HPS

NO

Animal model

Rat ; CBD ligation (biliary cirrhosis + HPS)

↓

↑Circulating and exhaled NO levels

↑ Circulating Endothelin-1

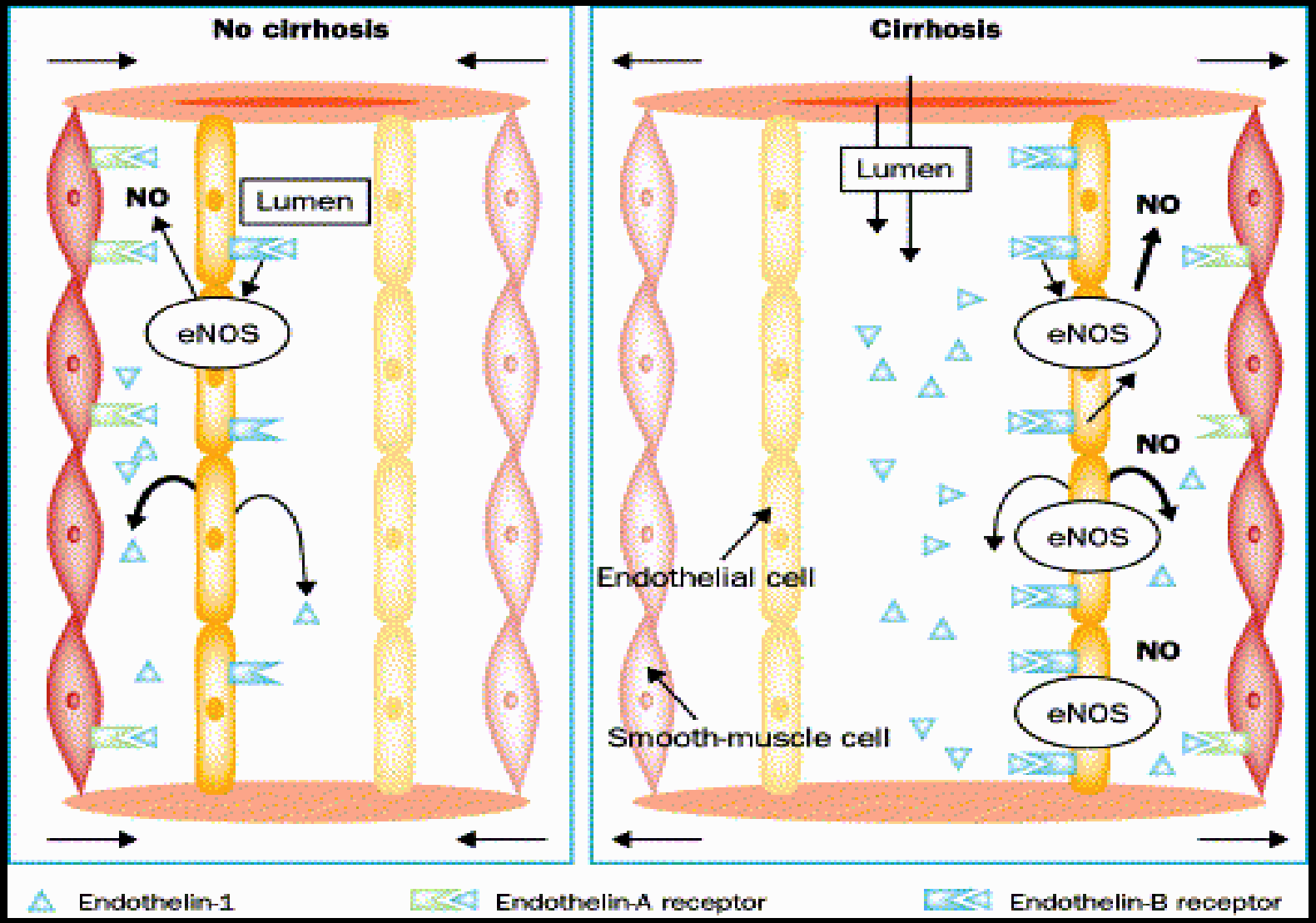
Overexpression of pulmonary endothelial Endothelin B receptors

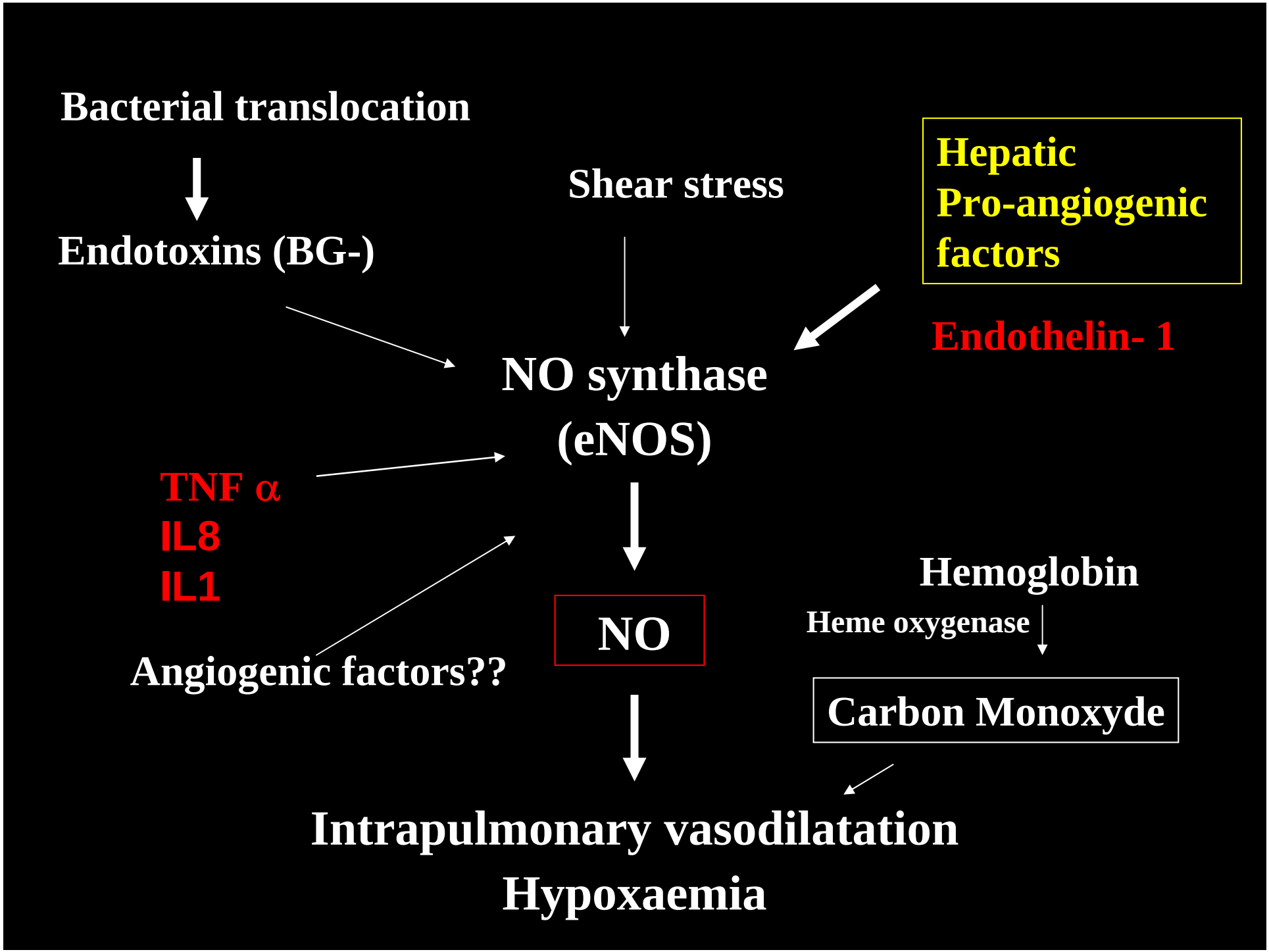
Correlated with A-a O2 gradient and the increase in NOS activity

HPS reversibility if inhibition of NOS

Cirrhosis

Role of Endothelin- 1

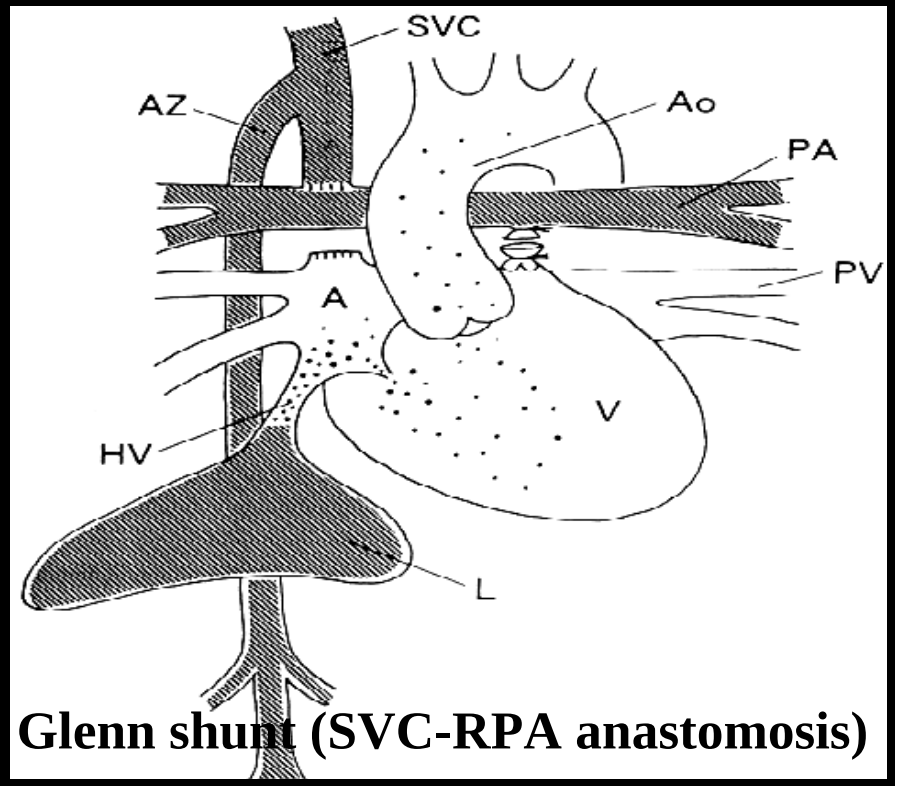



Bacterial translocation
Endotoxins (BG-)
Shear stress
Hepatic
Pro-angiogenic
factors
Endothelin- 1
NO synthase
(eNOS)
TNF α
IL8
IL1
Angiogenic factors??
NO
Hemoglobin
Heme oxygenase
Carbon Monoxyde
Intrapulmonary vasodilatation
Hypoxaemia

Intrapulmonary vascular dilatation and arteriovenous malformations

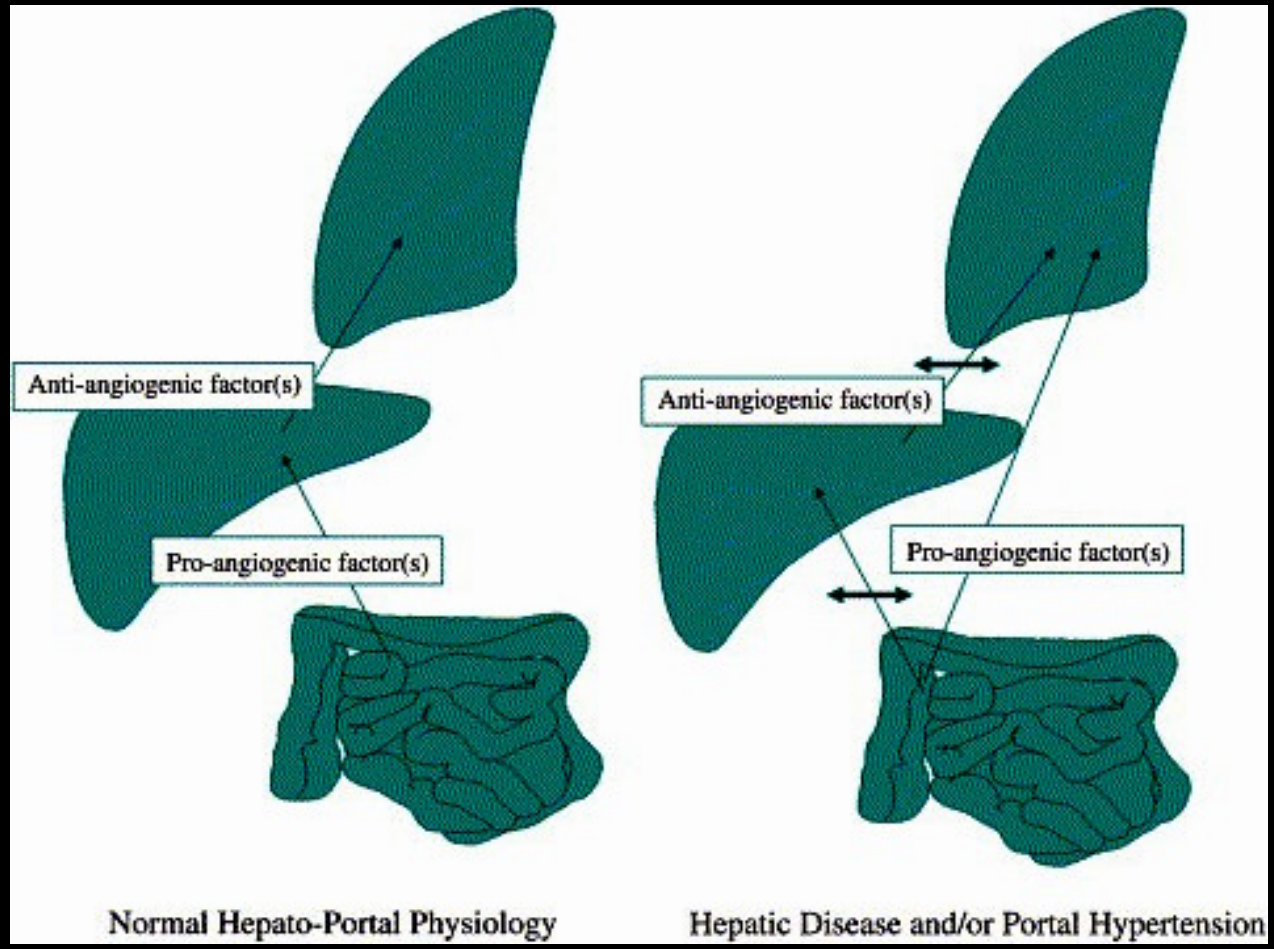
- **Role of anti-angiogenic factors**
  - **When lungs are deprived of hepatic venous flow**

- **Role of pro angiogenic factors**
  - **When the liver is deprived of portal venous flow:**
    - -Porto caval congenital fistulas
    - -Porto caval surgical shunts



Glenn shunt (SVC-RPA anastomosis)

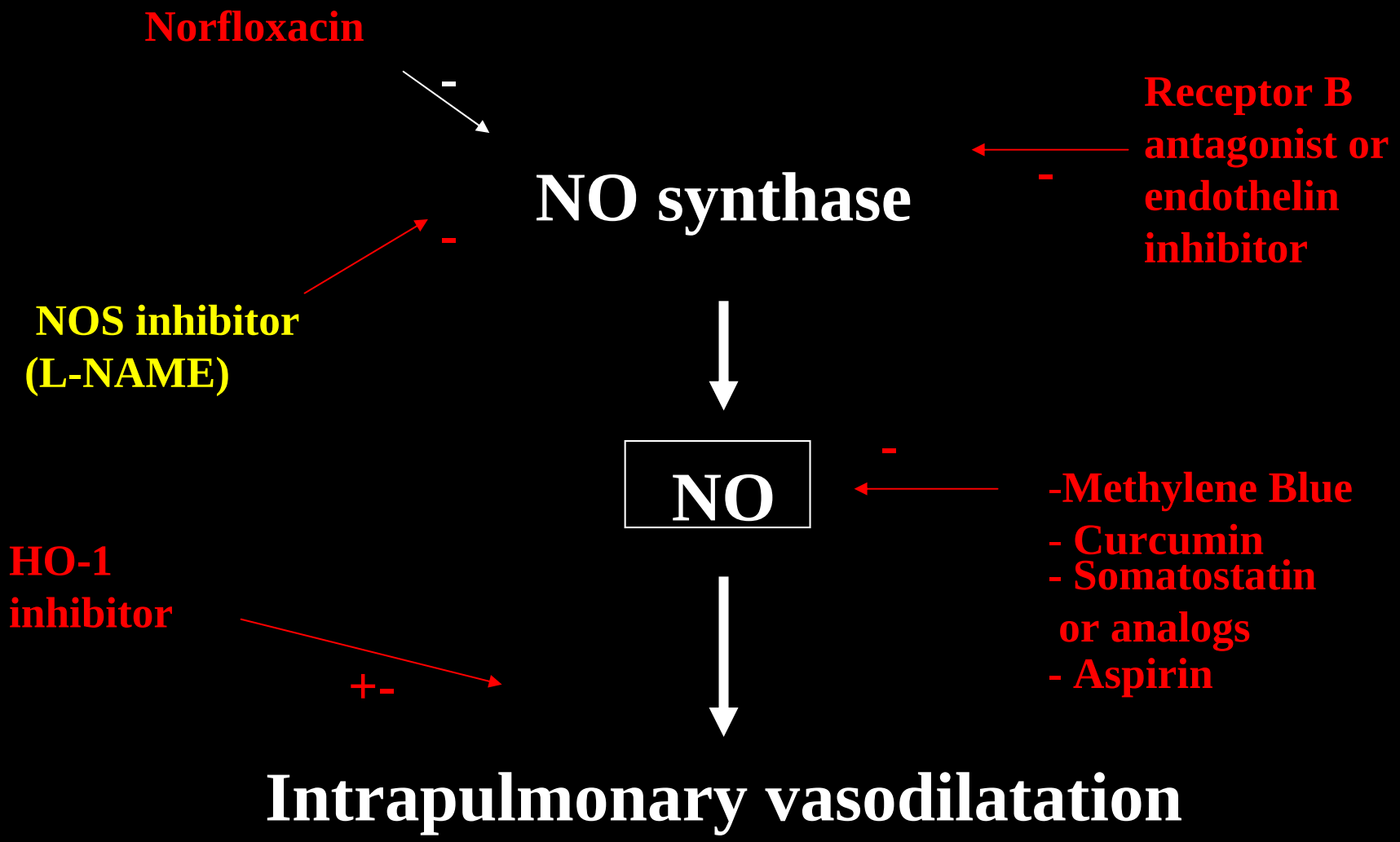
In summary…



From Hervé P et al. Best Practice and Research Clinical Gastroenterology, 2007

HPS is reversible

Medical therapies in patients with cirrhosis



Surgical Treatment

- **HPS Reversal :**
  - Mesenterico-left portal vein bypass (extrahepatic portal vein obstruction)
  - Cavoplasty (Budd-Chiari syndrome)
  - Ligation or occlusion (congenital porto-caval fistulae)
  - Liver transplantation in patients with cirrhosis

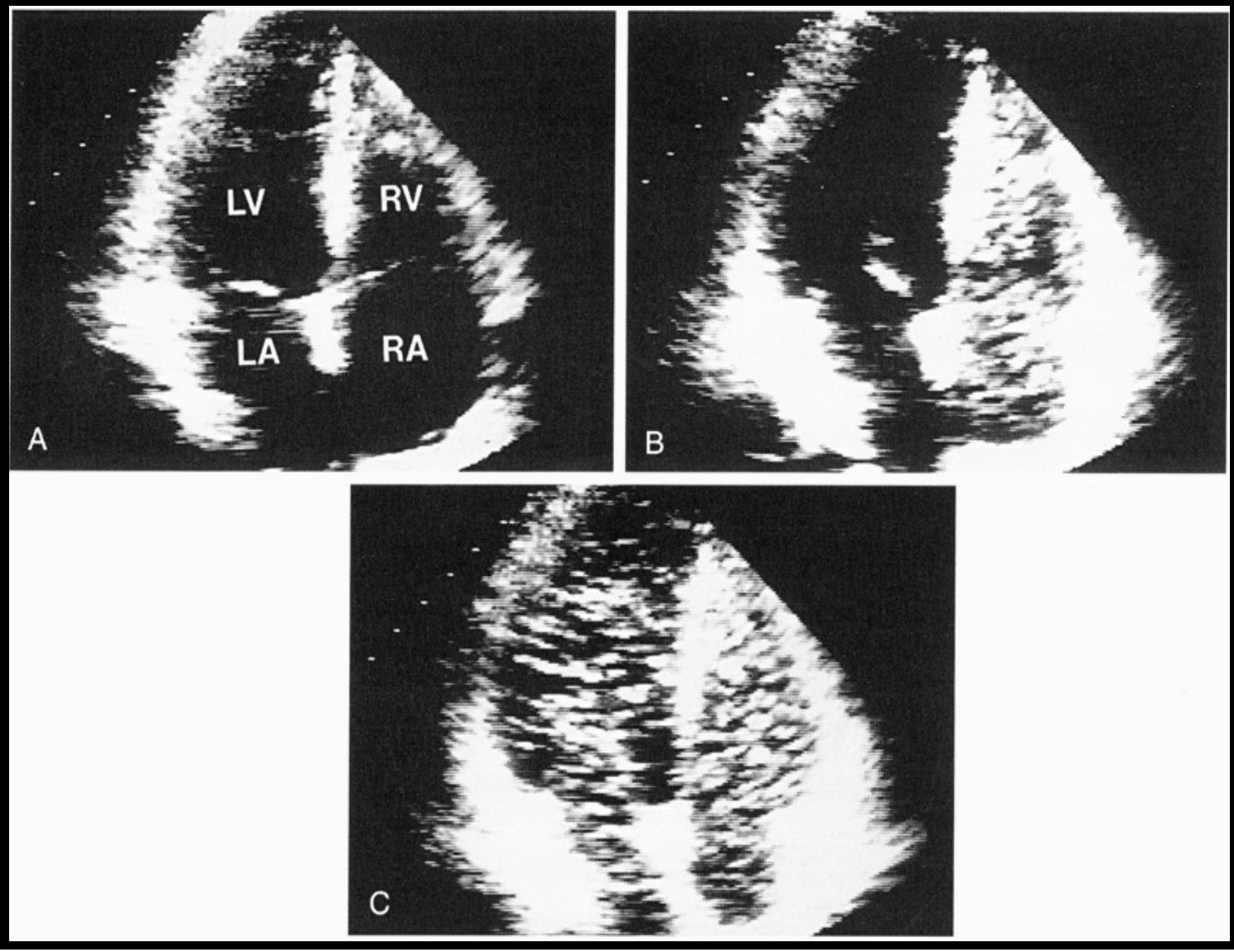
Reversal dependant on the severity of hypoxemia

HEPATOPULMONARY SYNDROME

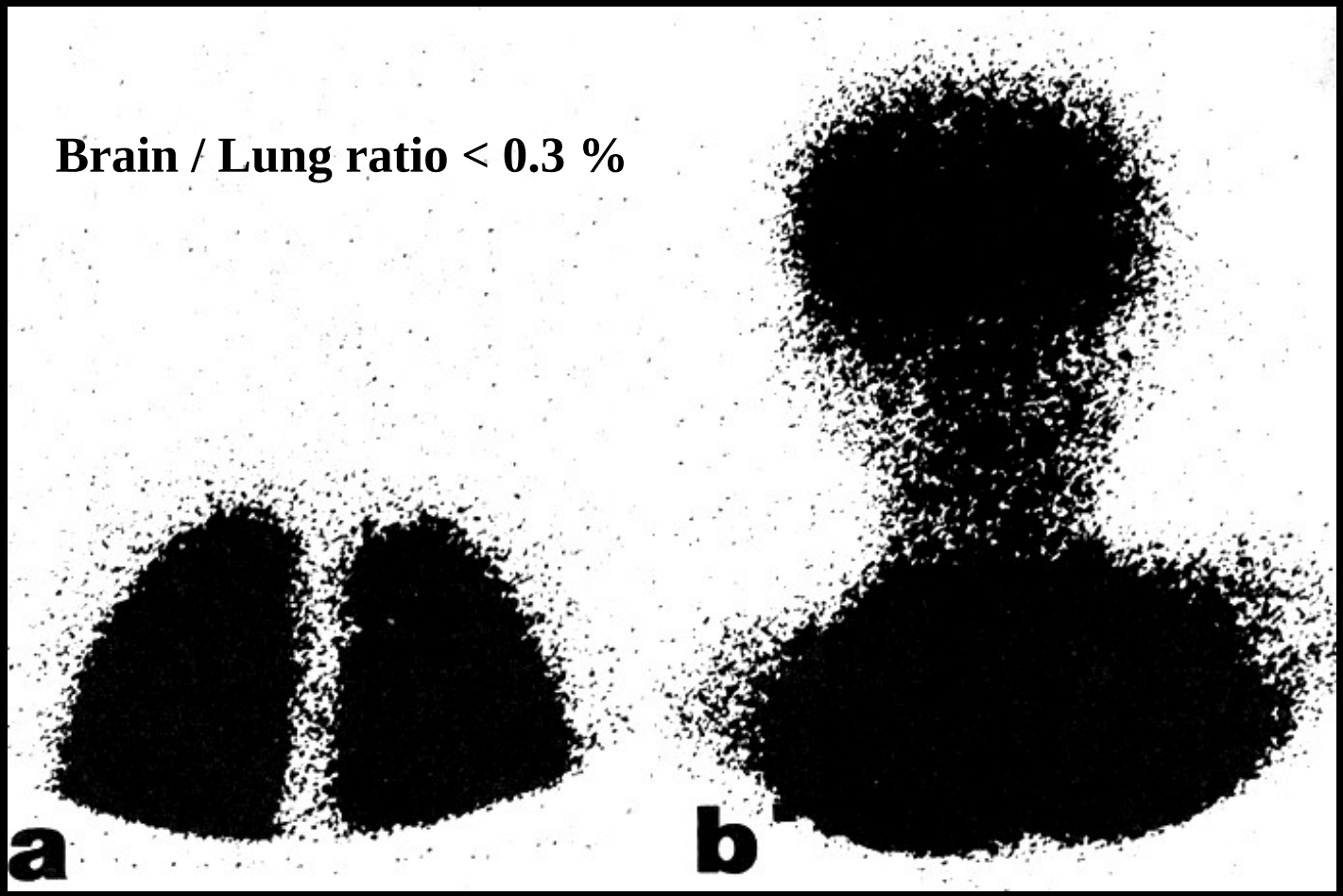
Early Screening

- **Exercise dyspnea**
- **Orthodeoxia :**
  - **Oxygen saturation in supine and upright position**
  - **> 5% decreased of SaO2 in upright position**
- **Intrapulmonary shunting**
  - **Contrast enhanced echocardiography (sensibility > specificity)**
  - **Macroaggregated albumin scan**

Contrast-enhanced echocardiography with IV injection of agitated saline solution



Radiolabelled (99technecium) macroaggregated albumin scan



Hepatopulmonary Syndrome

Prevalence in children (Bicêtre)

Abnormal shunt index at MAA scan

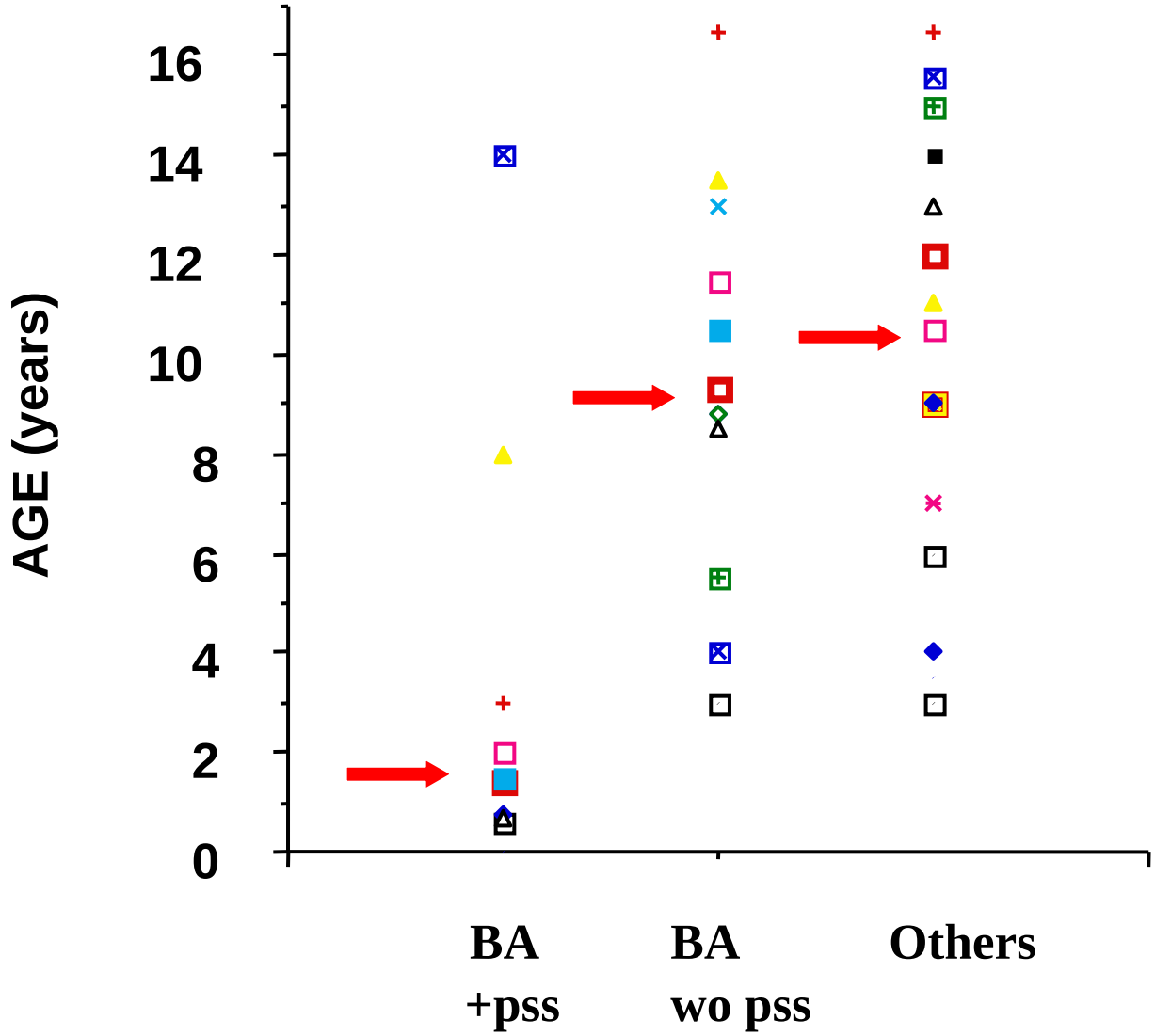
18%

(of 309 children)

Hypoxemia :

- **BA : 1.2%**
- **+ PSS : 20%**
- **Other causes of cirrhosis : 2%**
- **Hepatoportal Sclerosis : 13%**
- **Congenital hepatic fibrosis: 1.5%**
- **Extrahepatic PVO : 0.5%**
- **Portocaval fistulae : 2 / 8**

Age at diagnosis (n=42 children)



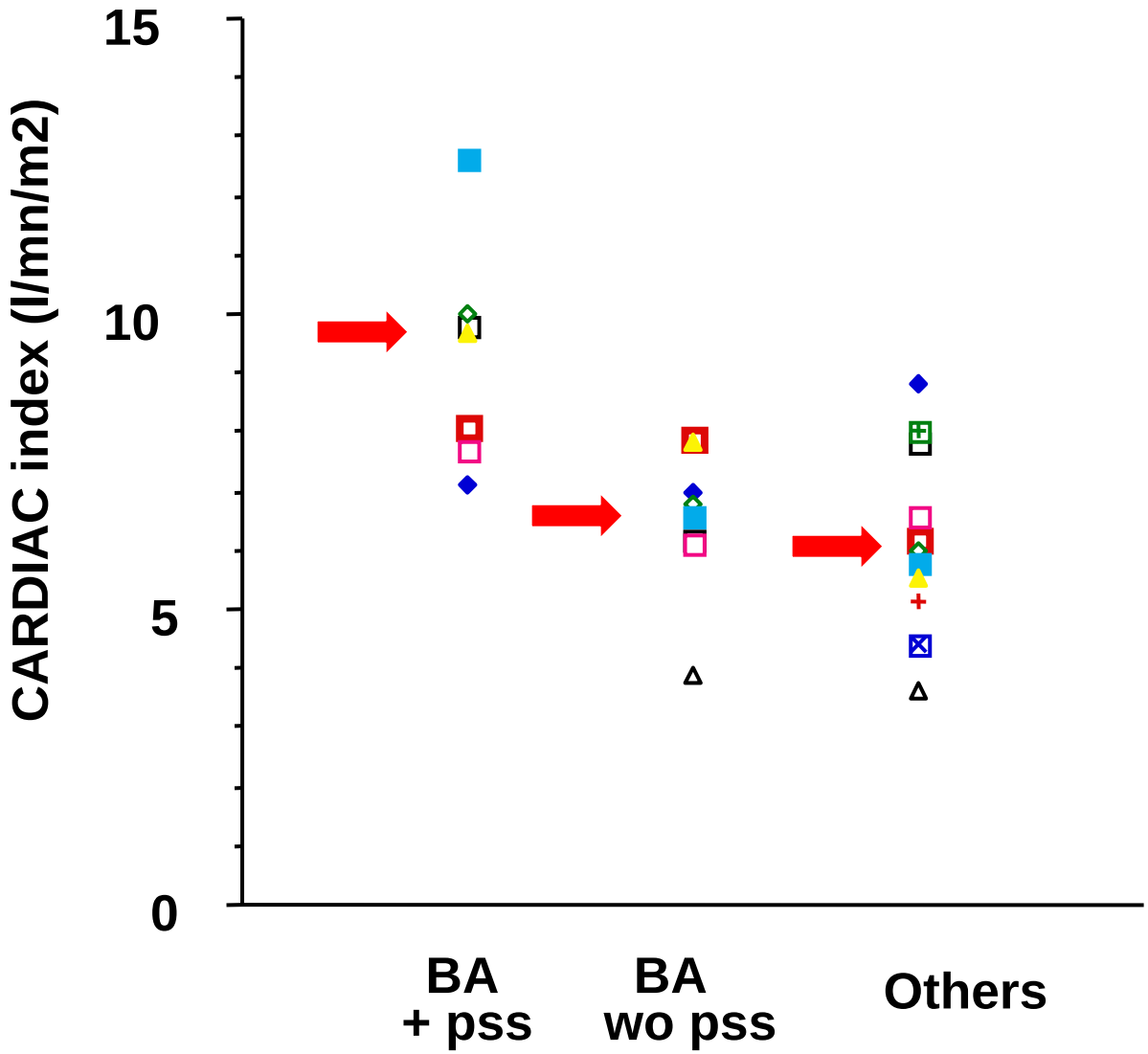
Initial symptoms (34/42 children)

Age : 1.5 - 18 y

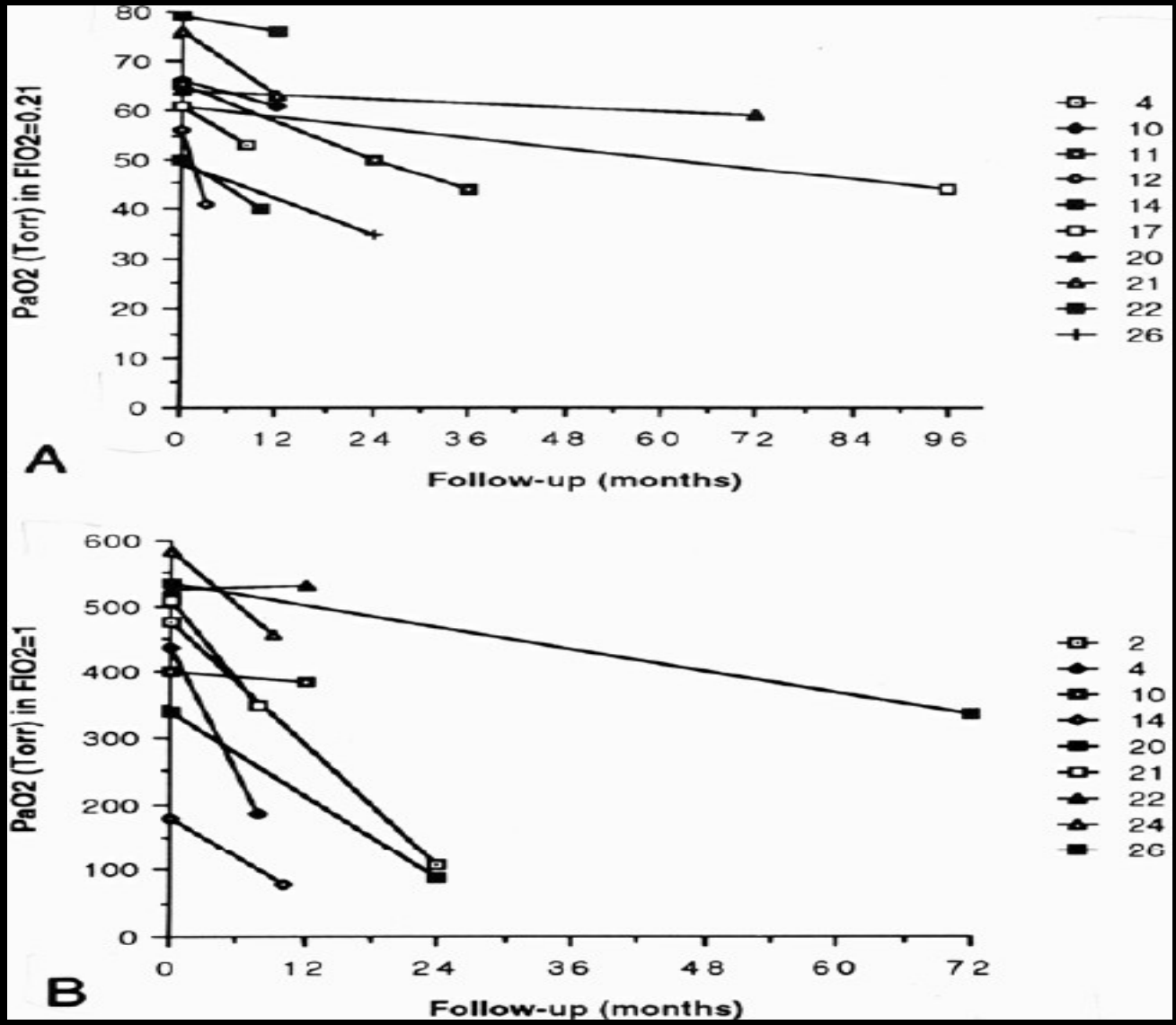
- **Dyspnea during exercise** **24 pts**
- **Cyanosis** **19 pts**

Arterial blood gas N=42	**PaO2 mmHg (moy)**
Room Air	**42-70 (59)**
100% O2	**167-585 (363)**

Cardiac index in 24 children



Outcome


PaO2 (Torr) in FIO2=0.21
80
70
60
50
40
30
20
10
0
0 12 24 36 48 60 72 84 96
Follow-up (months)
A
4
10
11
12
14
17
20
21
22
26
PaO2 (Torr) in FIO2=1
600
500
400
300
200
100
0
0 12 24 36 48 60 72
Follow-up (months)
B
2
4
10
14
20
21
22
24
26

Surgical treatment (other than OLT)

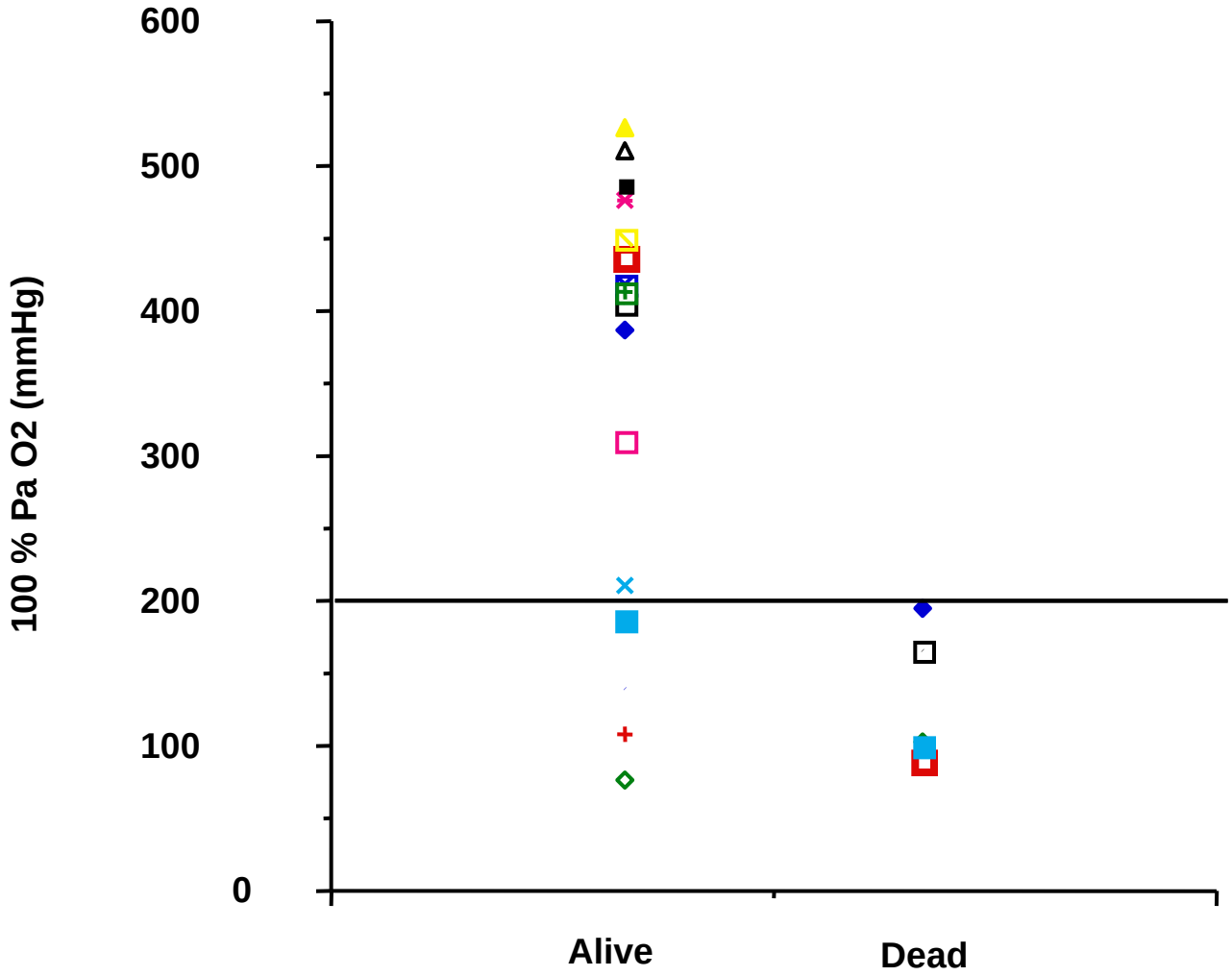
	N	Success
Ligation of portocaval fistulae	2	2
Mesenterico-left PV bypass	1	1

Liver transplantation (25 children)

- **Survival : 20 / 25 (80%)**
- **Follow-up post-OLT : 3 m-12 y (m: 7 y)**
- **Reversal of HPS : 100% (28 -210 days)**
- **No cardiac nor pulmonary complications**

Prognostic factor

PaO2 on 100% O2



HEPATOPULMONARY SYNDROME

Conclusion

- **Regular screening : cirrhosis/PHT / PSS**
- **If PAaO2 >15 mmHg and/or PaO2 60–80 mmHg, OLT can be considered.**
- **• If hypoxaemia is severe (PaO2 50–60 mmHg), consideration of OLT is vital.**
- **• If the hypoxaemia is very severe or extreme (PaO2 <50 mmHg), OLT needs to be considered on an individual basis.**