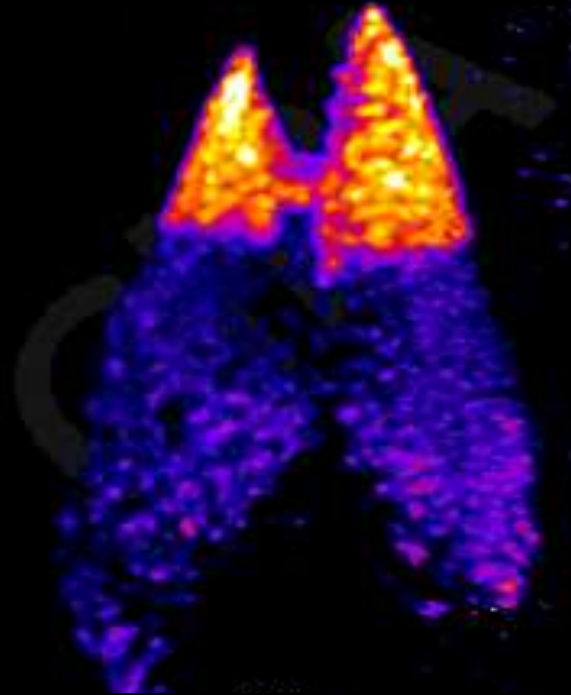


# HEPATOPULMONARY SYNDROME (HPS)

## Pathophysiological and clinical aspects



V. D'Orio  
CHU, Liège

# HEPATOPULMONARY SYNDROME



**Liver diseases**



**Pulmonary vascular**

**insult**

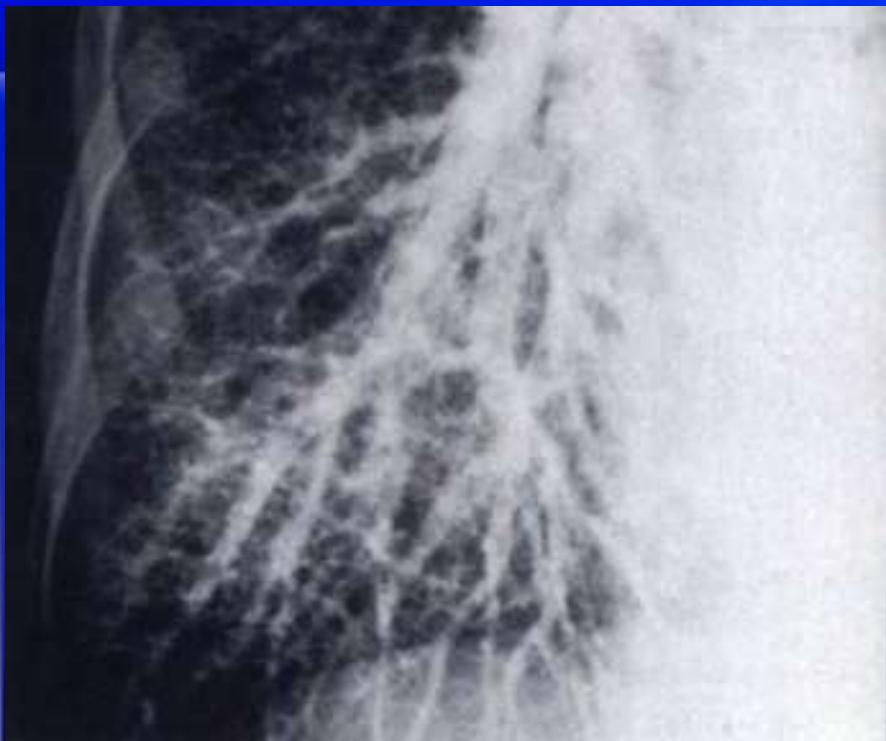


# HEPATOPULMONARY SYNDROME

Variable	Criterion
Oxygenation defect	Partial pressure of oxygen <80 mm Hg or alveolar–arterial oxygen gradient $\geq 15$ mm Hg while breathing ambient air
Pulmonary vascular dilatation	Positive findings on contrast-enhanced echocardiography or abnormal uptake in the brain (>6%) with radioactive lung-perfusion scanning
Liver disease	Portal hypertension (most common) with or without cirrhosis
Degree of severity†	
Mild	Alveolar–arterial oxygen gradient $\geq 15$ mm Hg, partial pressure of oxygen $\geq 80$ mm Hg
Moderate	Alveolar–arterial oxygen gradient $\geq 15$ mm Hg, partial pressure of oxygen $\geq 60$ to <80 mm Hg
Severe	Alveolar–arterial oxygen gradient $\geq 15$ mm Hg, partial pressure of oxygen $\geq 50$ to <60 mm Hg
Very severe	Alveolar–arterial oxygen gradient $\geq 15$ mm Hg, partial pressure of oxygen <50 mm Hg (<300 mm Hg while the patient is breathing 100% oxygen)



# Pulmonary vascular abnormalities



Lower lobe vascular dilatation

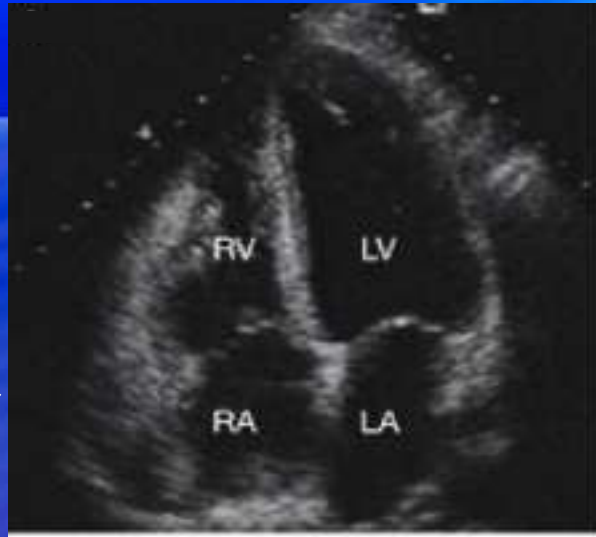


Arteriovenous shunting

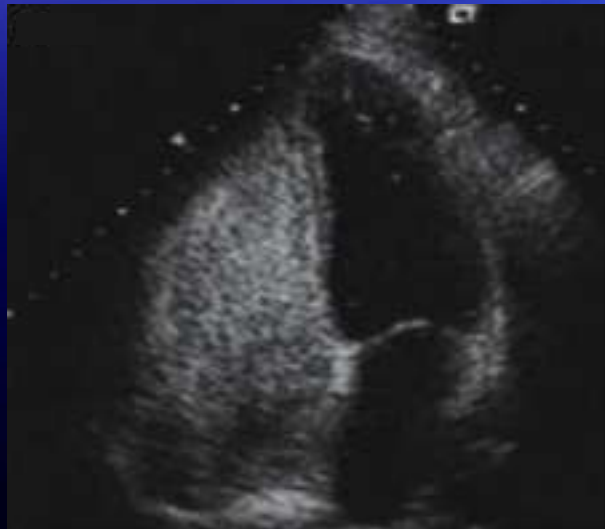


# TT Echocardiography

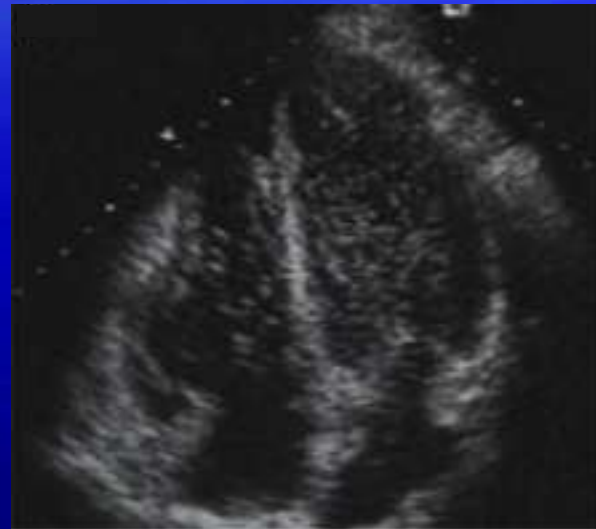
Contrast – enhanced TTE  
by agitated saline



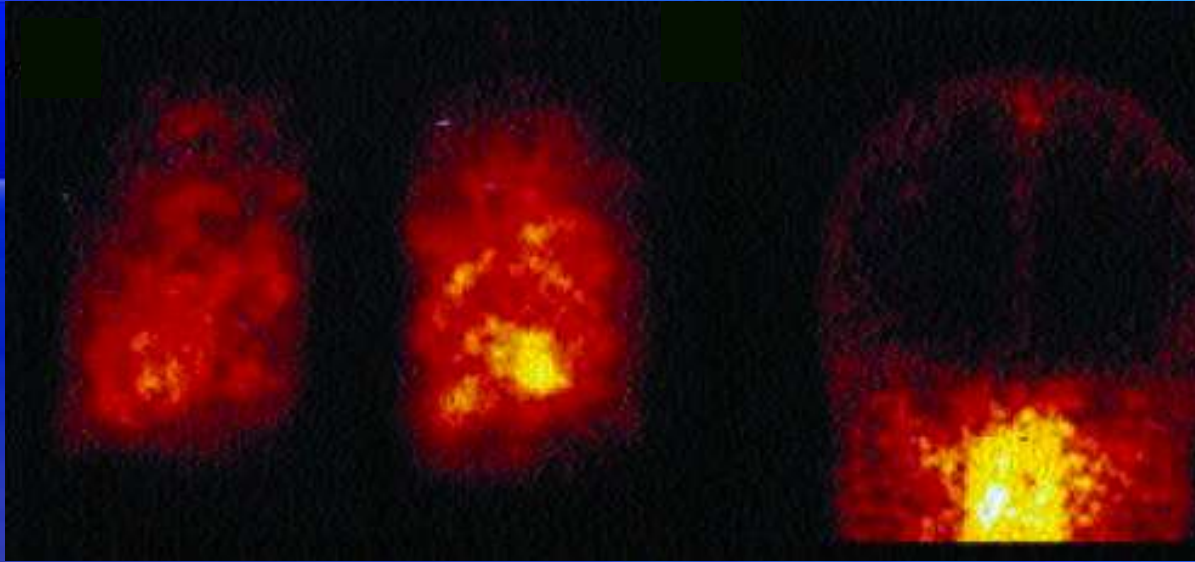
4 chambers apical view



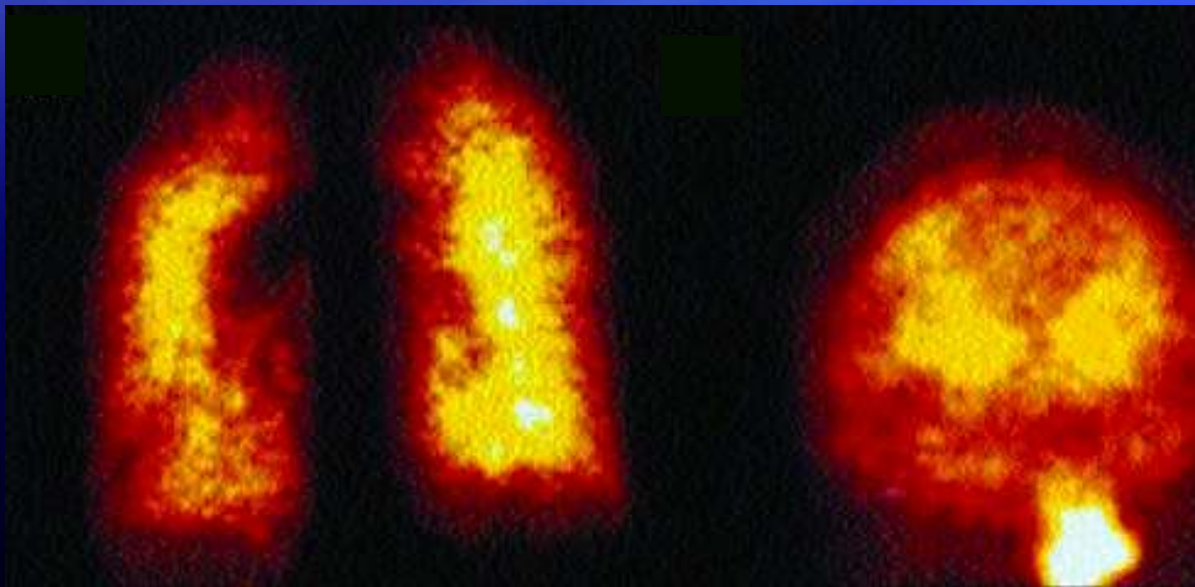
3-6 cardiac  
cycles



# Tc MAA scanning



Normal



HPS



# Tc MAA scanning



**Lung radioactivity (Lr)**

**Body radioactivity (Br)**

**Ratio Br/Lr > 6%**



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# HPS and oxygen defect

## ORTHODEOXIA

### Potential mechanisms

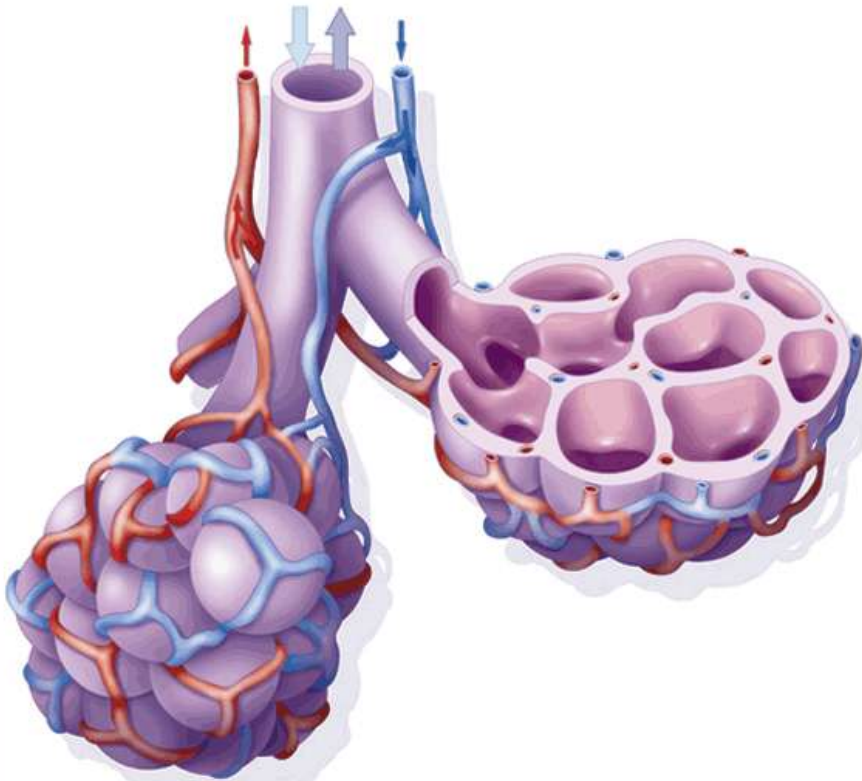
VA/Q mismatch

AV shunting

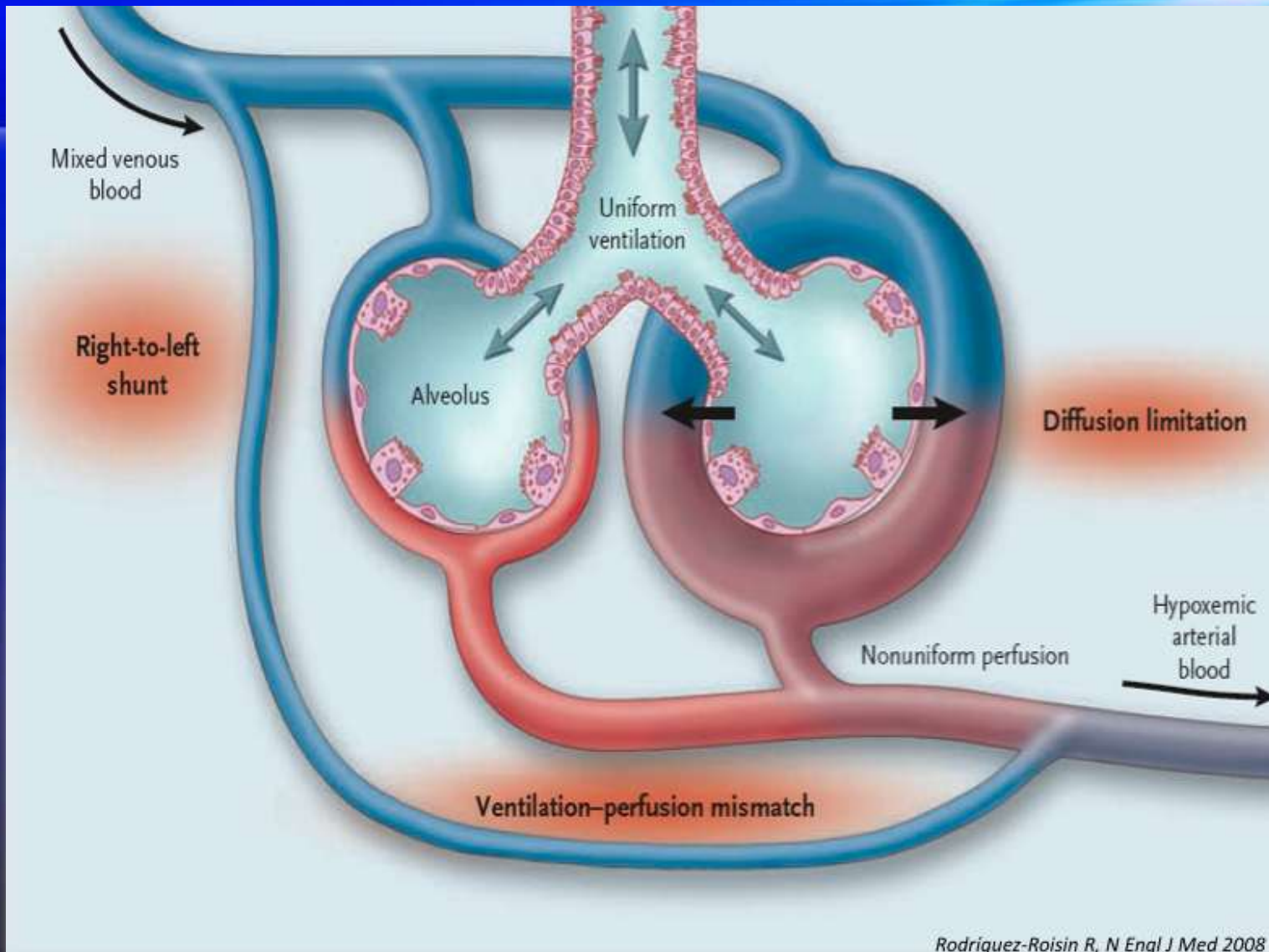
Local alveolar hypoventilation

Hb

$P_{50}$  (2,3 DPG)



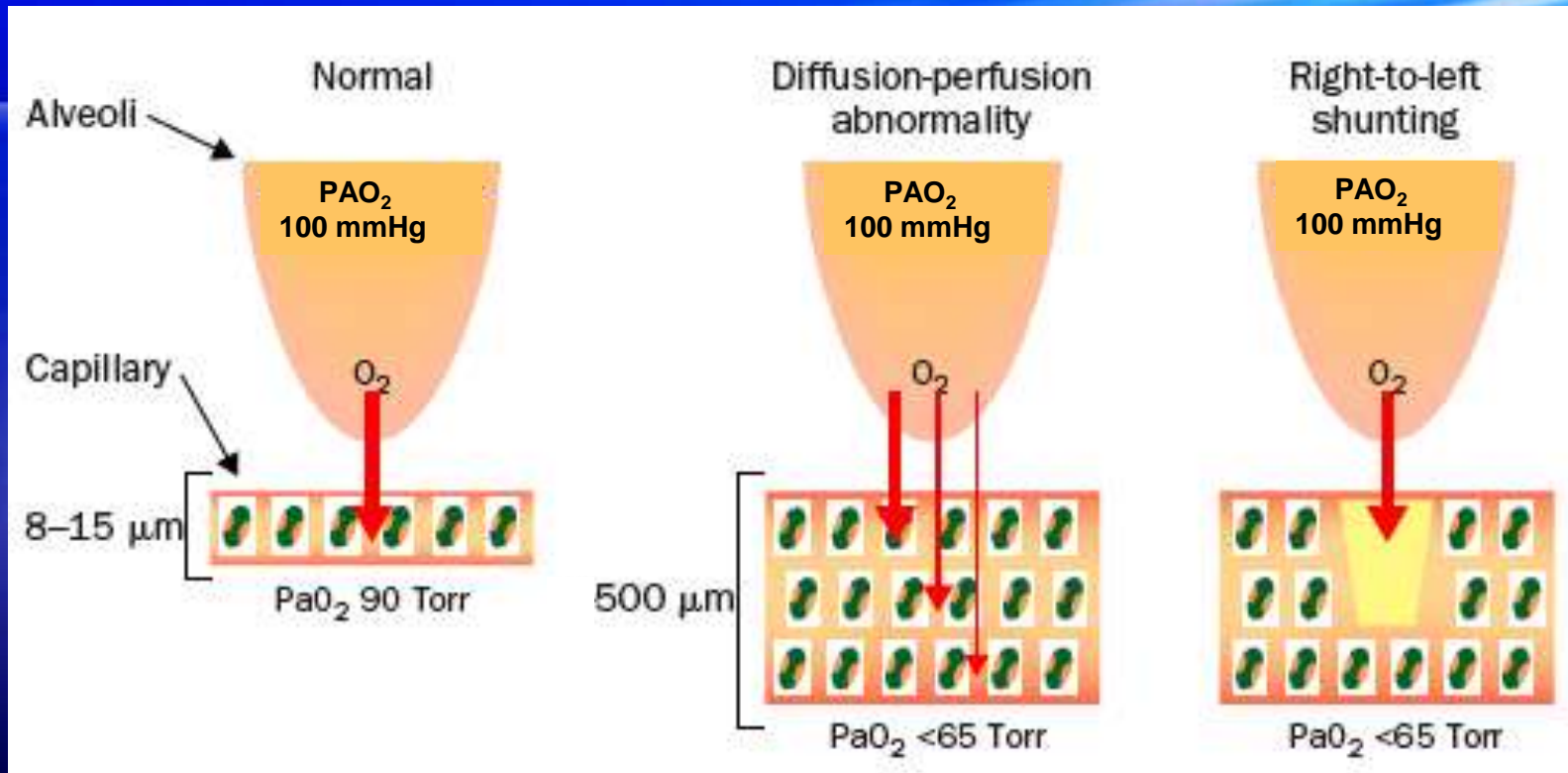
# HPS and oxygen defect



Rodriguez-Roisin R, N Engl J Med 2008



# HPS and oxygen defect



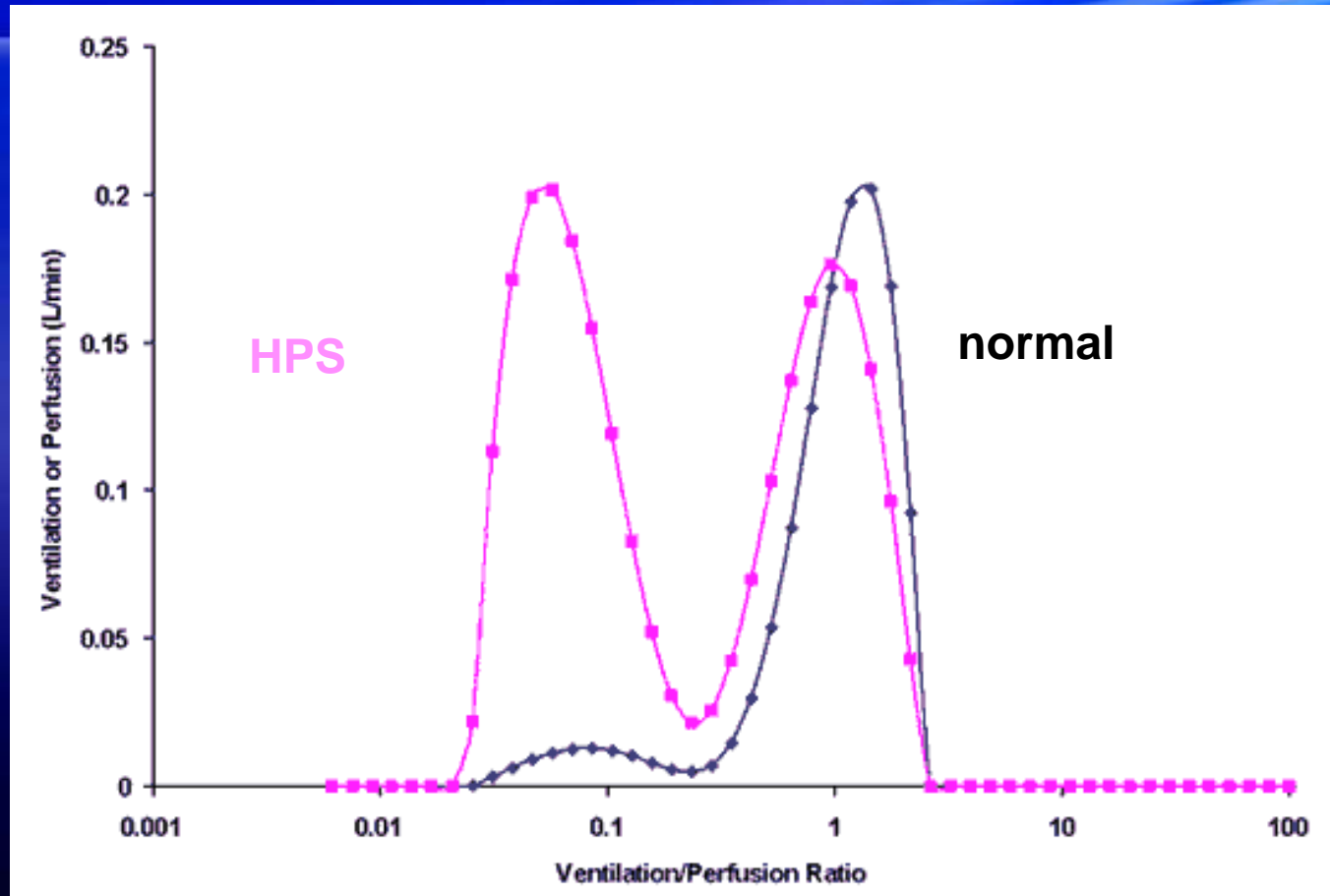
Alveolar-arterial PO<sub>2</sub> gradient : PAO<sub>2</sub> - PaO<sub>2</sub>

Pulmonary shunting :  $( (PAO_2 - PaO_2) \times 0.003 ) / ( (PAO_2 - PaO_2) \times 0.003 + 5 )$

PAO<sub>2</sub> (100 % O<sub>2</sub>) = P<sub>b</sub> - P<sub>H<sub>2</sub>O</sub> - Pa CO<sub>2</sub>



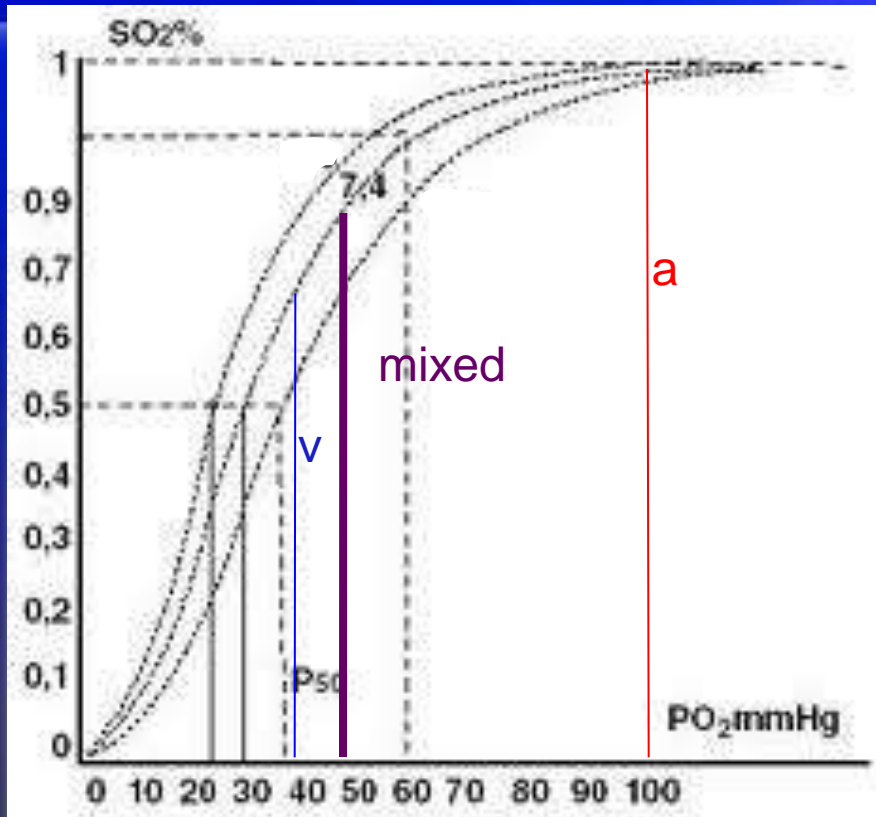
# HPS and ventilation to perfusion mismatch



Multiple inert gases elimination technique



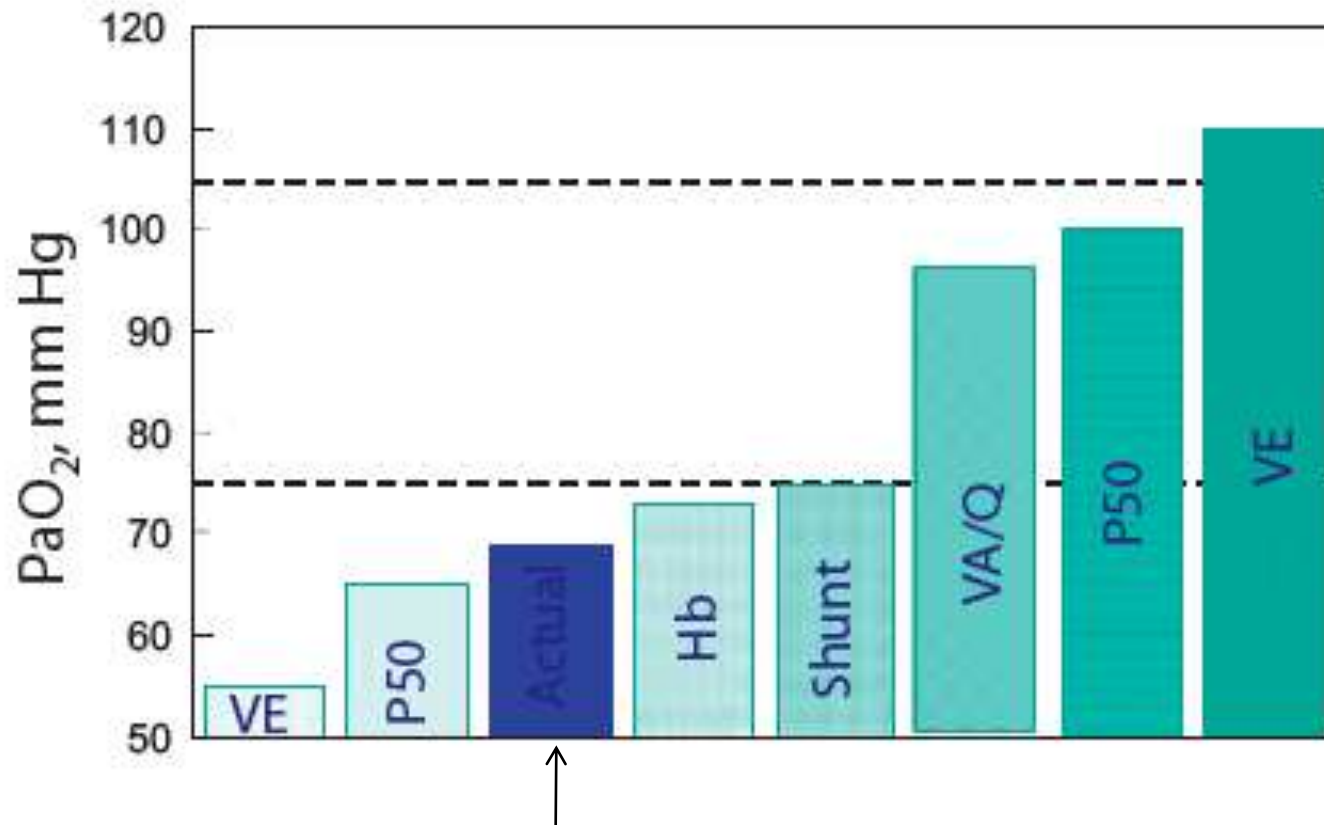
# HPS and oxygen defect



Blood oxygen content ( $C_{O_2}$ )  
$$C_{O_2} = (1.39 \times Hb \times SaO_2) + 0.03 \times PO_2$$



# HPS and oxygen defect



# HEPATOPULMONARY SYNDROME

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# HEPATOPULMONARY SYNDROME



**Liver disease or PH**



**Pulmonary vascular  
insult (remodelling)**

Hepatopulmonary syndrome (vasodilation)

Portopulmonary hypertension (vasoconstriction)



# HEMODYNAMIC CHANGES

## HYPERKINETIC STATE

Increased CO and systemic vasodilation

### Portopulmonary hypertension

Increased PVR

Staging of severity :

Mild :  $25 < \text{mPAP} < 35 \text{ mmHg}$

Moderate :  $35 < \text{mPAP} < 45 \text{ mmHg}$

Severe :  $\text{mPAP} > 45 \text{ mmHg}$

### Hepatopulmonary syndrome

Normal or decreased PVR

Staging of severity :

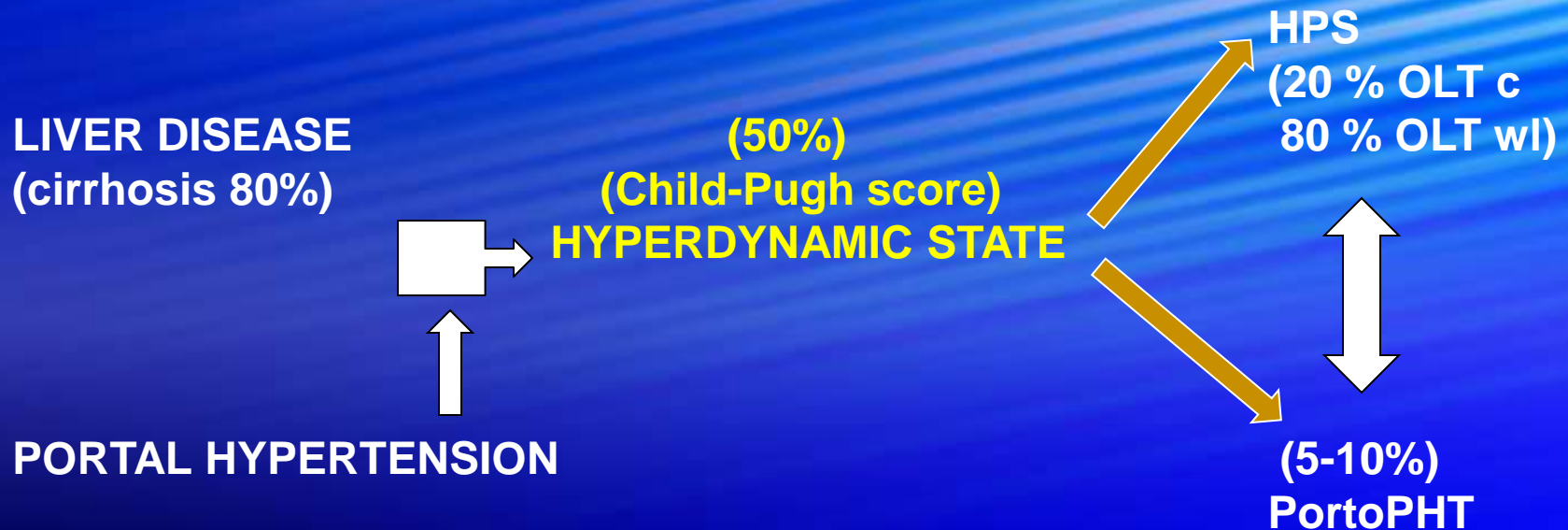
Mild :  $\text{PO}_2 > 80 \text{ mmHg}$

Moderate :  $\text{PO}_2 > 60 \text{ mmHg}$

Severe :  $\text{PO}_2 < 60 \text{ mmHg}$



# PULMONARY VASCULAR CHANGES

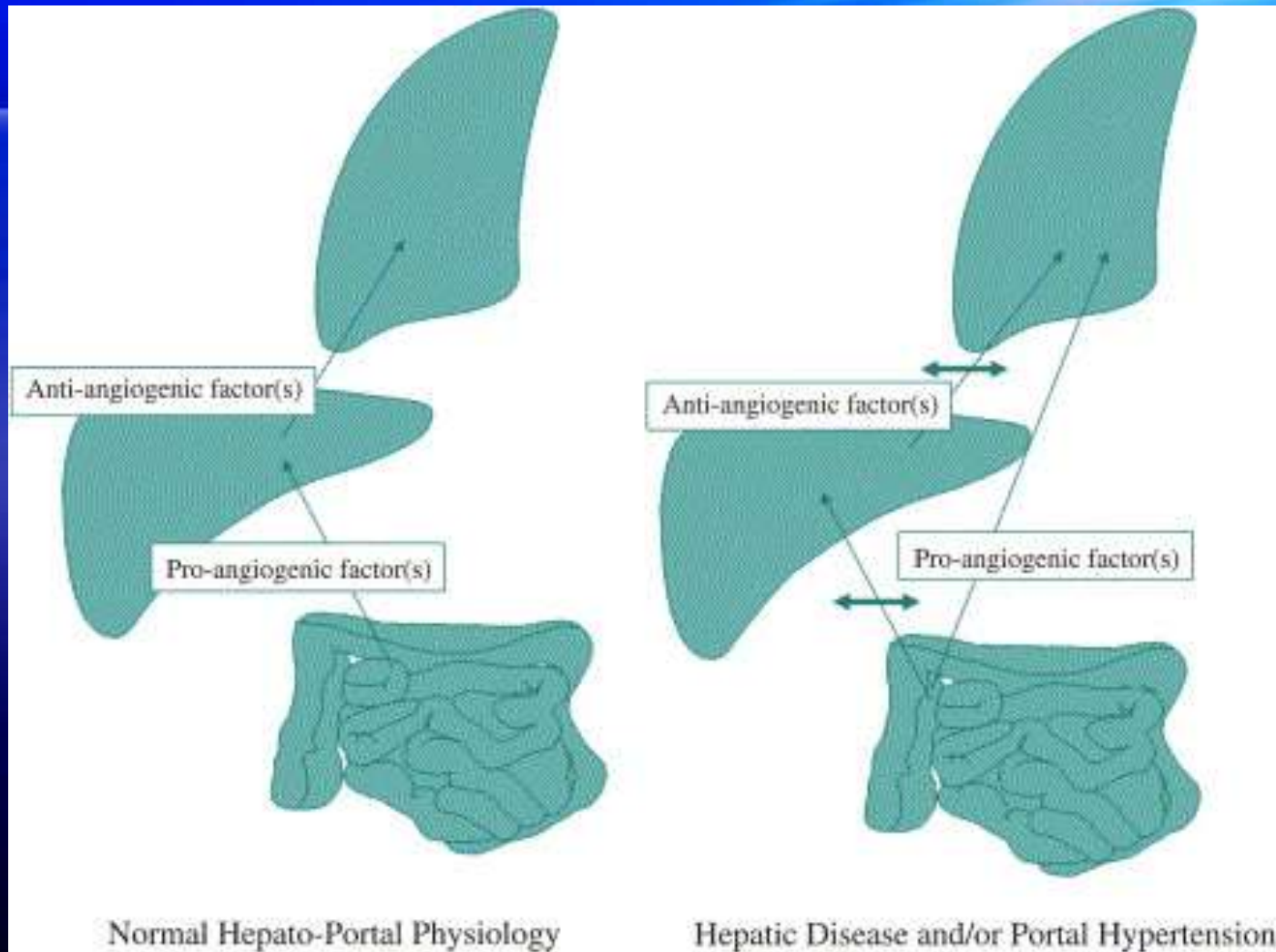


Underlying hypothesis : liver-induced imbalance between

- Angiogenic factors
- Vasoactive mediators



# PULMONARY VASCULAR CHANGES



# PULMONARY VASCULAR CHANGES

## Angiogenic factors

VEGF  
PDGF

HPS?

TGF-B  
ET

PPHT?

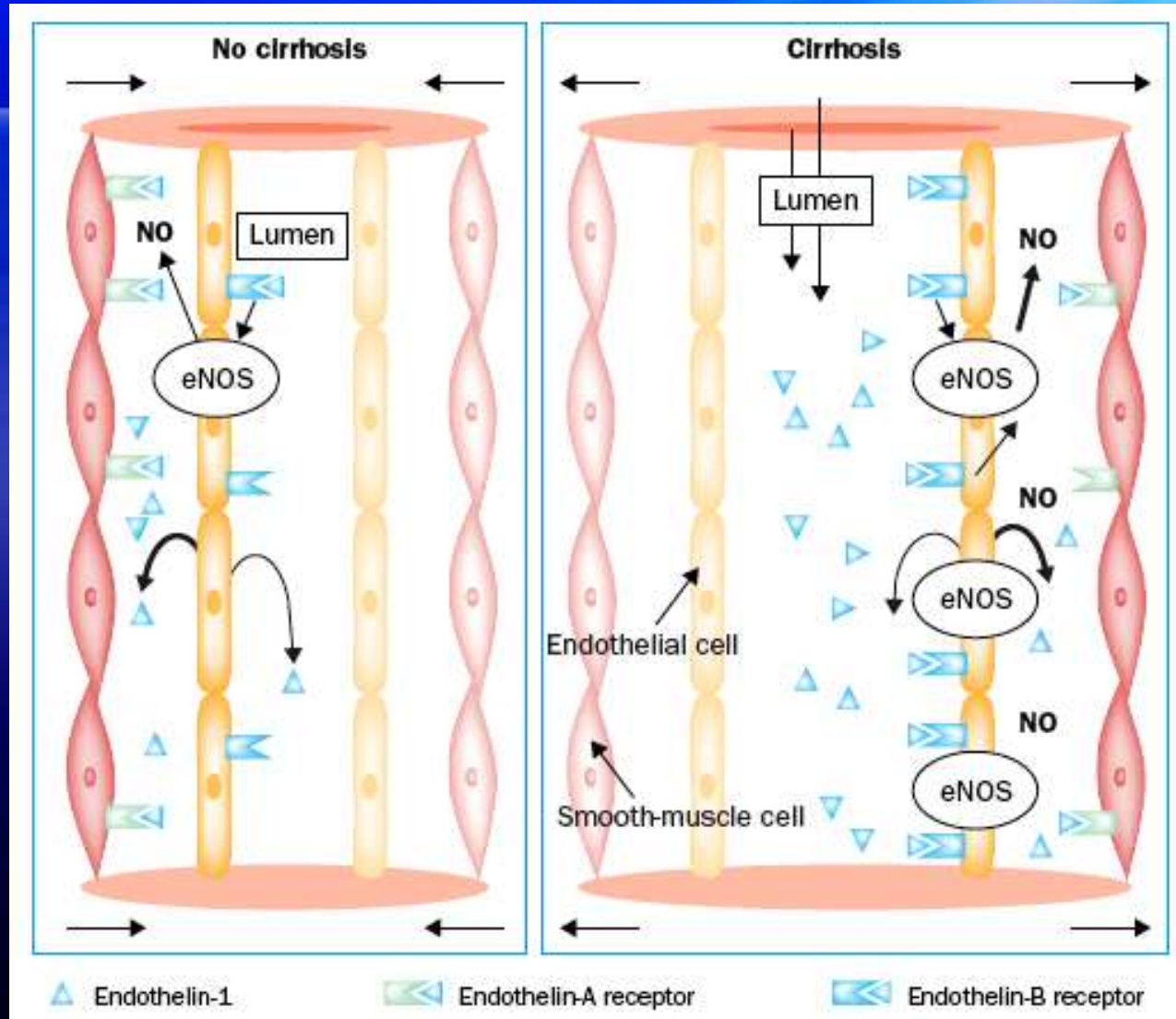
**SWITCH on**

## Anti-angiogenic factors

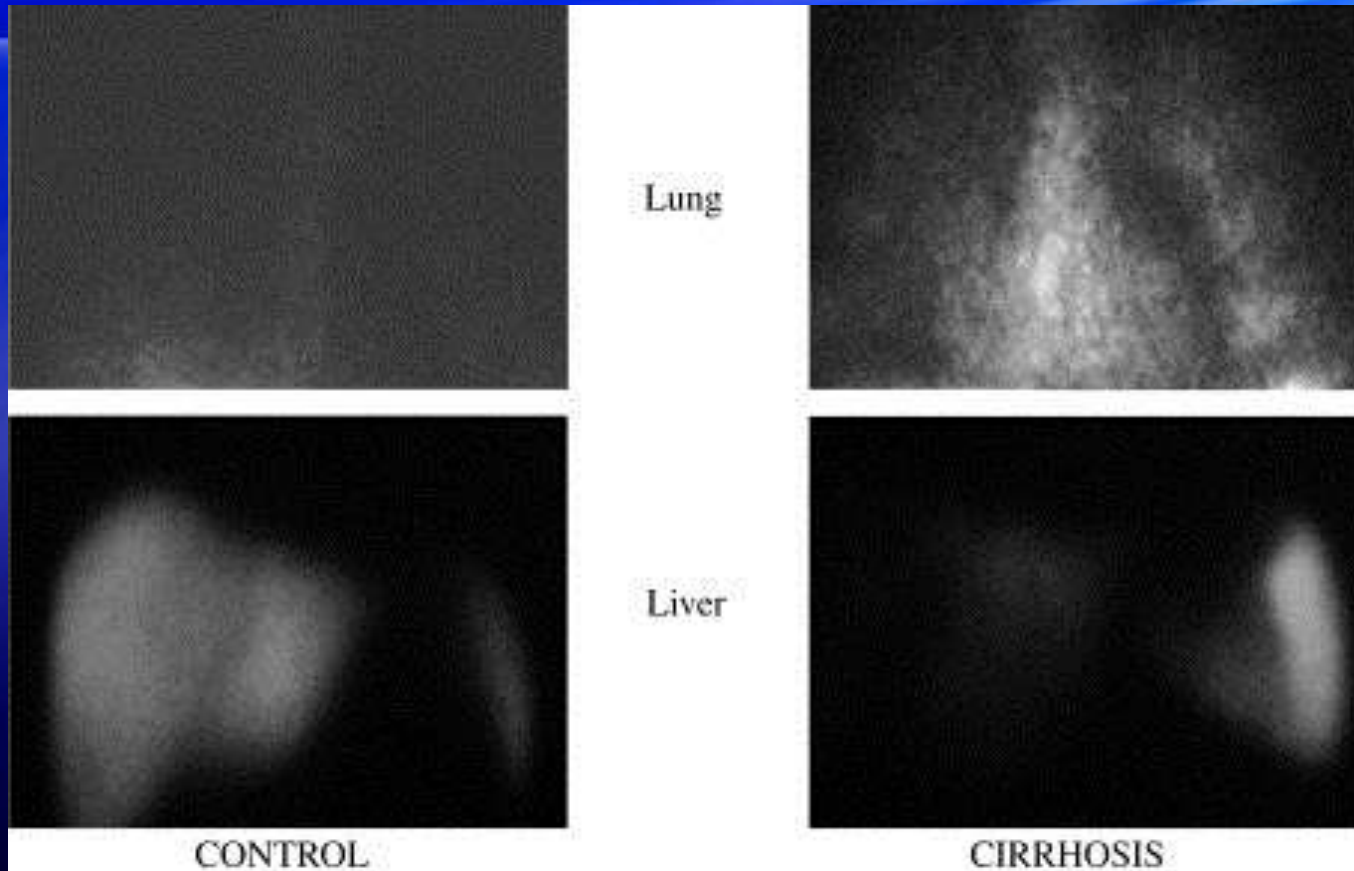
Endostatin  
Angiostatin



# PULMONARY VASCULAR CHANGES



# Hepatic-induced pulmonary inflammatory response



# Hepatic-induced pulmonary inflammatory response

Activated CD68+ macrophages  
in the pulmonary compartment

Increased TGH-B (ALK1-BMP)

Arteriolar proliferation

Elevated PVR

VEGF

Capillary proliferation

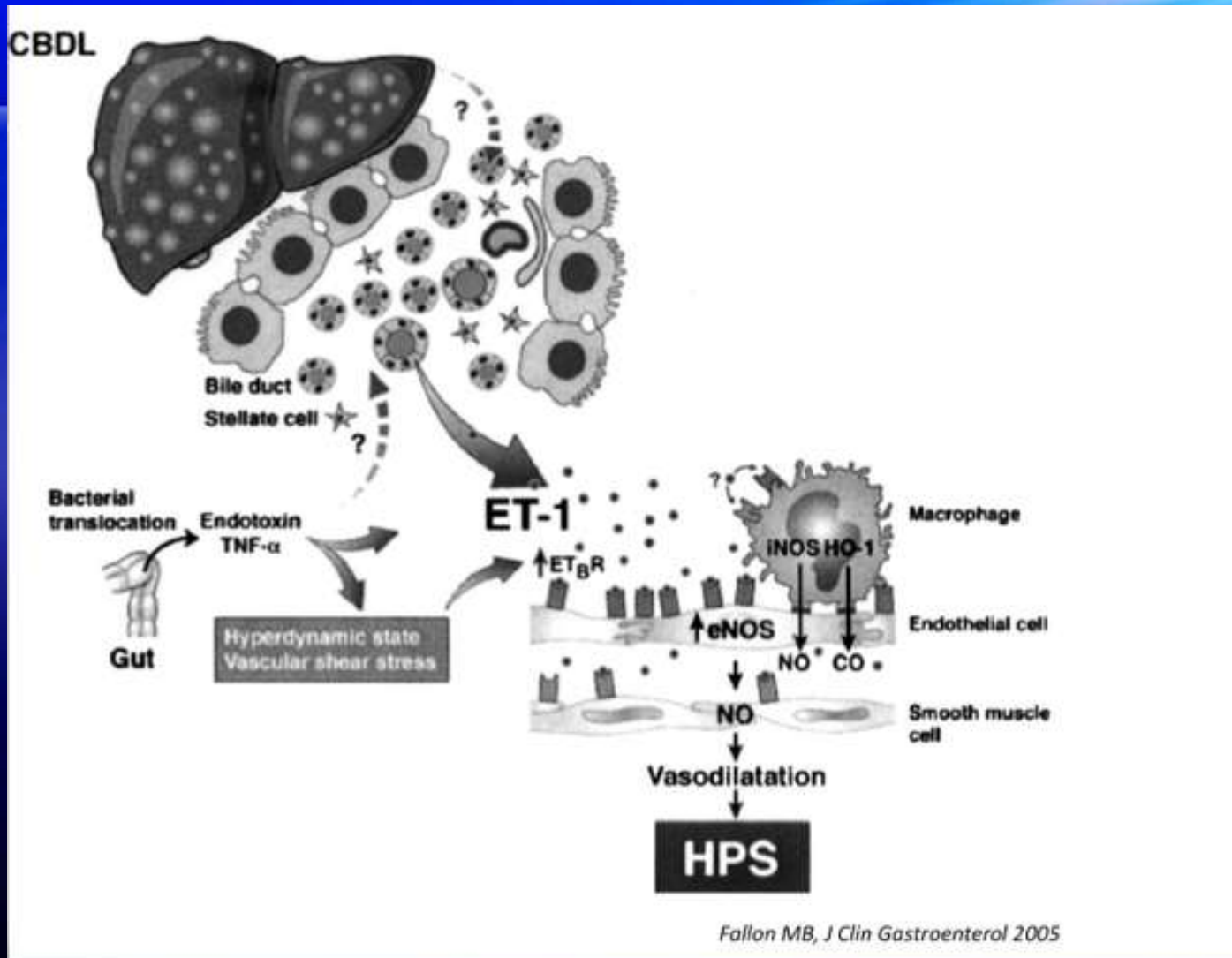
Activation iNOs

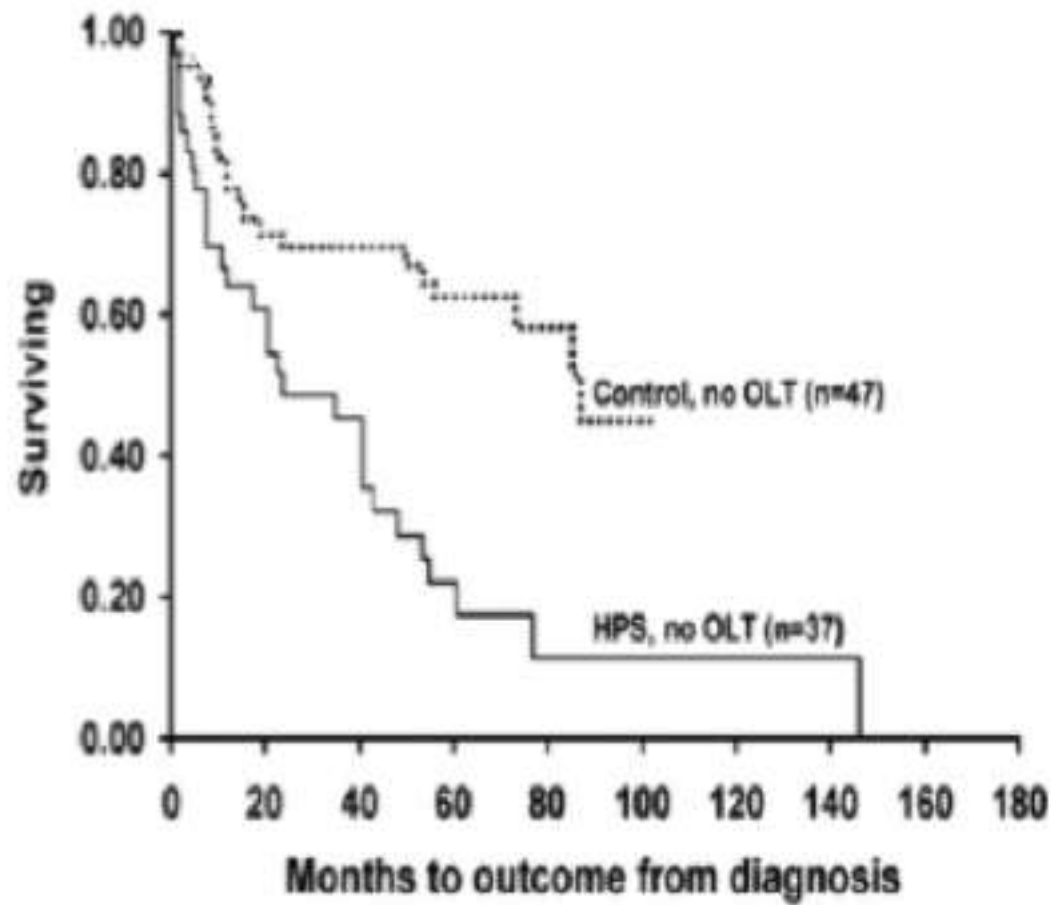
Vasodilation

LOW PVR and High (A-a) gradient

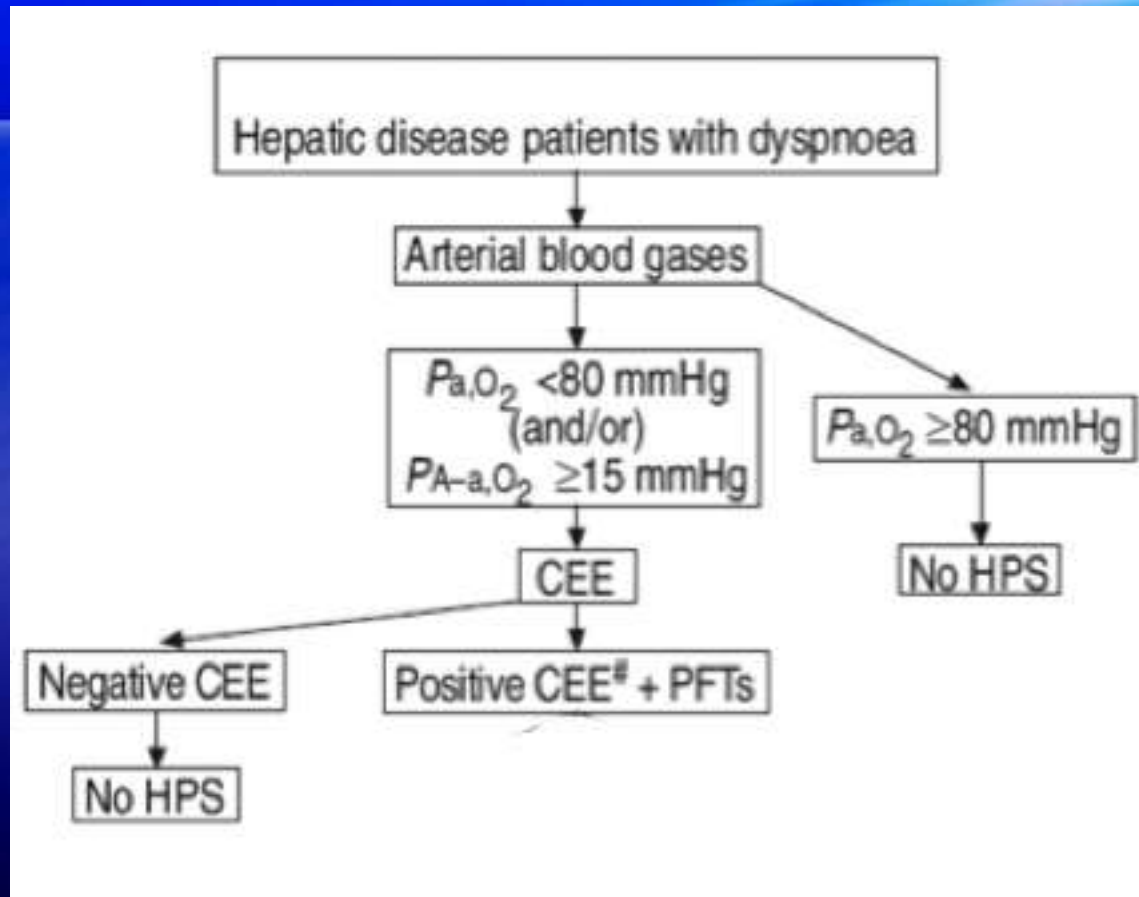


# INFLAMMATORY - INDUCED HPS

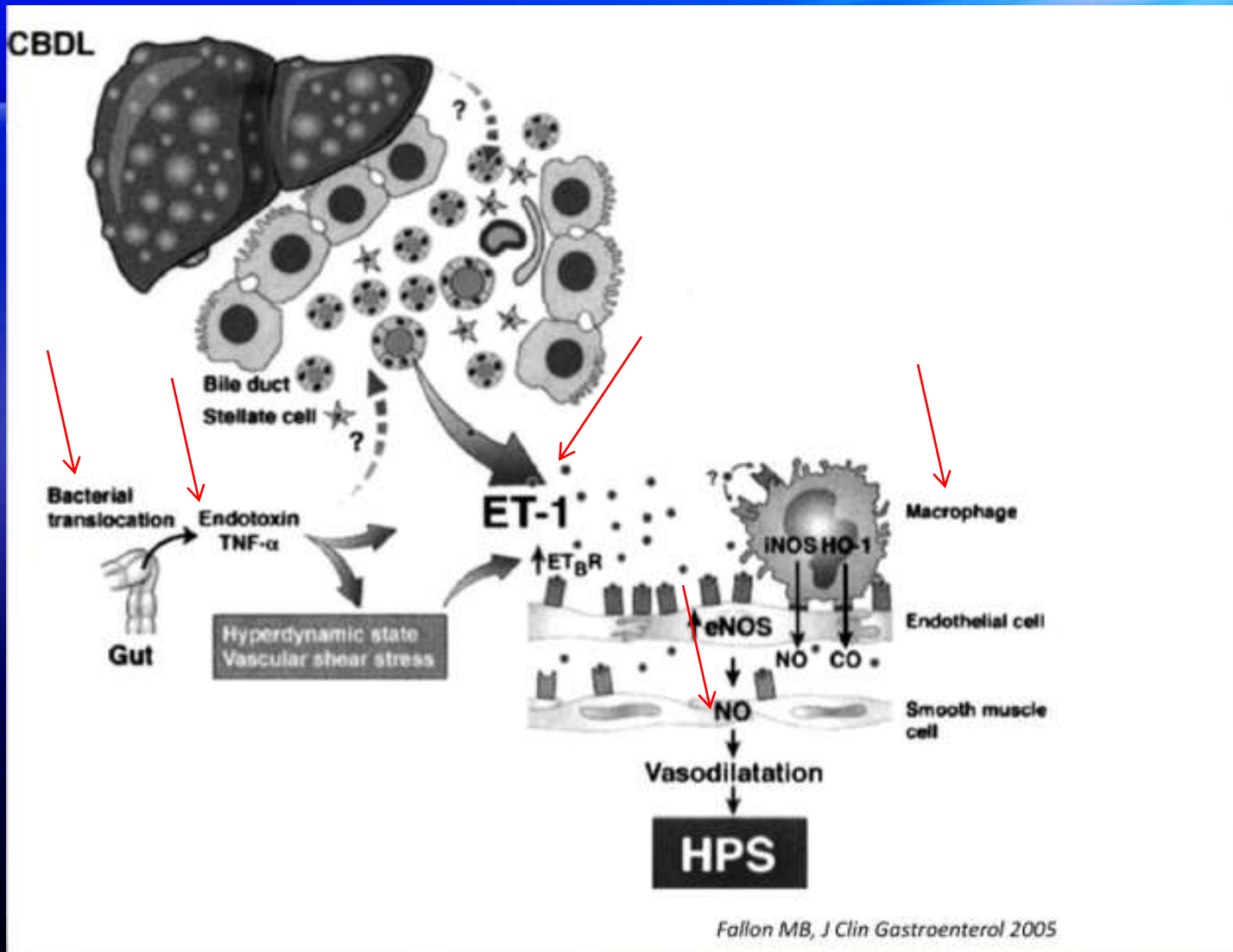


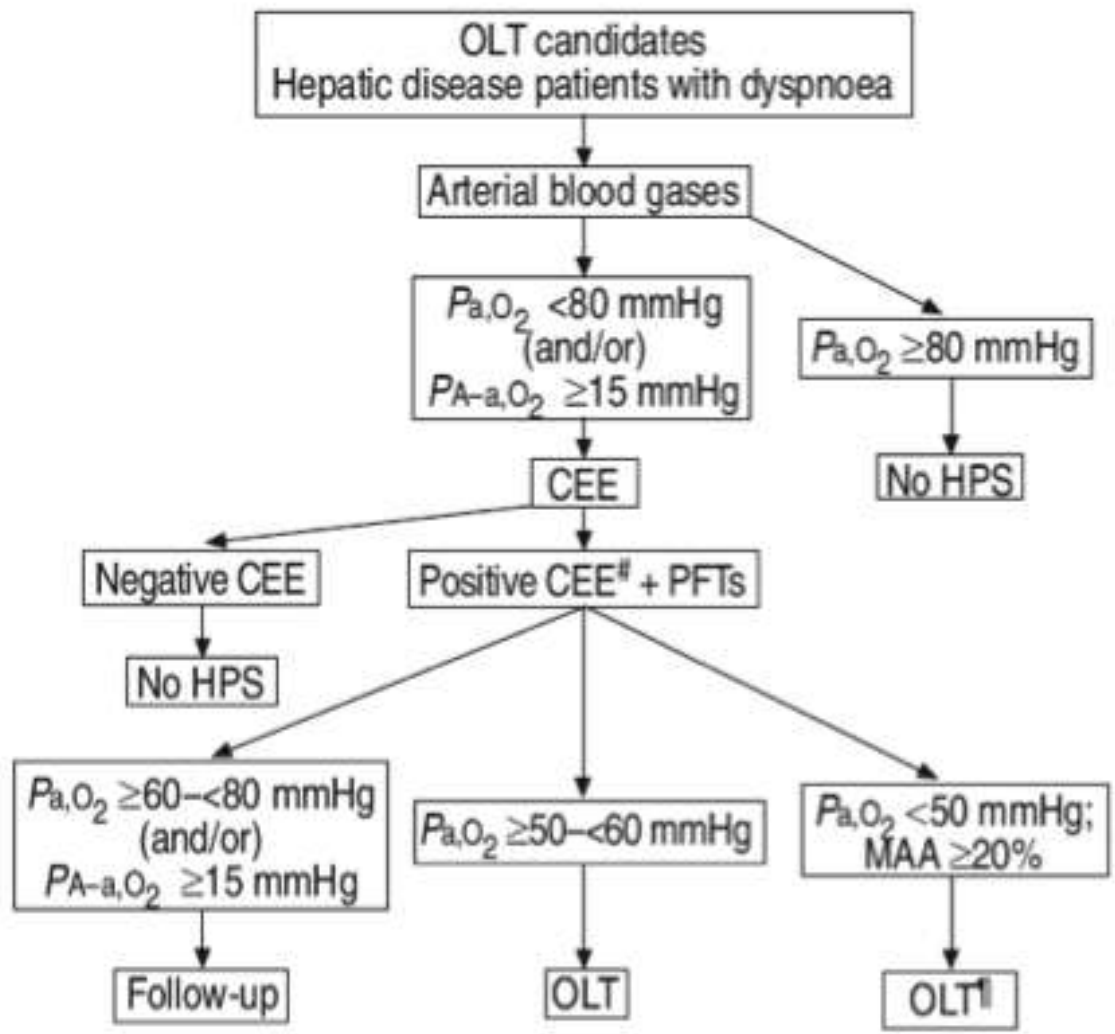


# ALGORITHM DIAGNOSIS



# INFLAMMATORY - INDUCED HPS





# CONCLUSIONS

**HPS is an independent factor of mortality in cirrhosis**

**HPS should be detected in patients suffering from liver diseases and dyspnea**

**CEE is the diagnostic gold standard**

**No clinical evidence for supporting pharmacological therapy**

**OLT remains the only resource with proven efficacy**

