



Course n°: 2. Cardiovascular system

Date: *(18-20 of September 2013)*

Language: Romanian

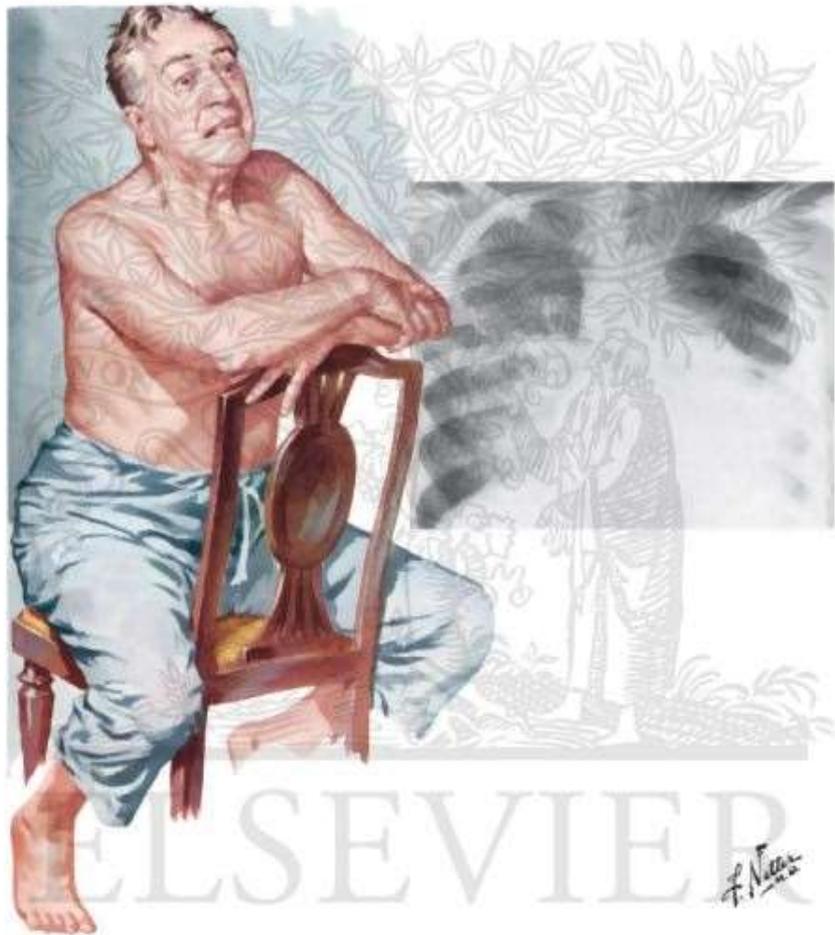
City: Târgu Mures

Country: Romania

Speaker: Adrian BELÎL, PhD (Republic of Moldova)

# Volume replacement in patients with acute pulmonary edema

## Un caz clinic tipic de...



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- Pacient de 70 de ani
- DZ tip II, HTAE si ICC NYHA III
- Prezinta, cu debut acut:
  - Senzatie de sufocare;
  - Respiratie suieratoare;
  - Anxietate;
  - Tuse cu sputa spumoasa
  - Transpirație excesivă
  - Piele palidă
  - Dureri în piept
  - Palpitații
  - Presiune arteriala scazuta

## Rx Th la pacientul dat ar putea arata astfel:



Edem pulmonar acut la un pacient cu IMA anterior.

- Infiltrate alveolare
- Redistribuire vasculara
- Hiluri pulmonare “sterse”

<http://emedicine.medscape.com>

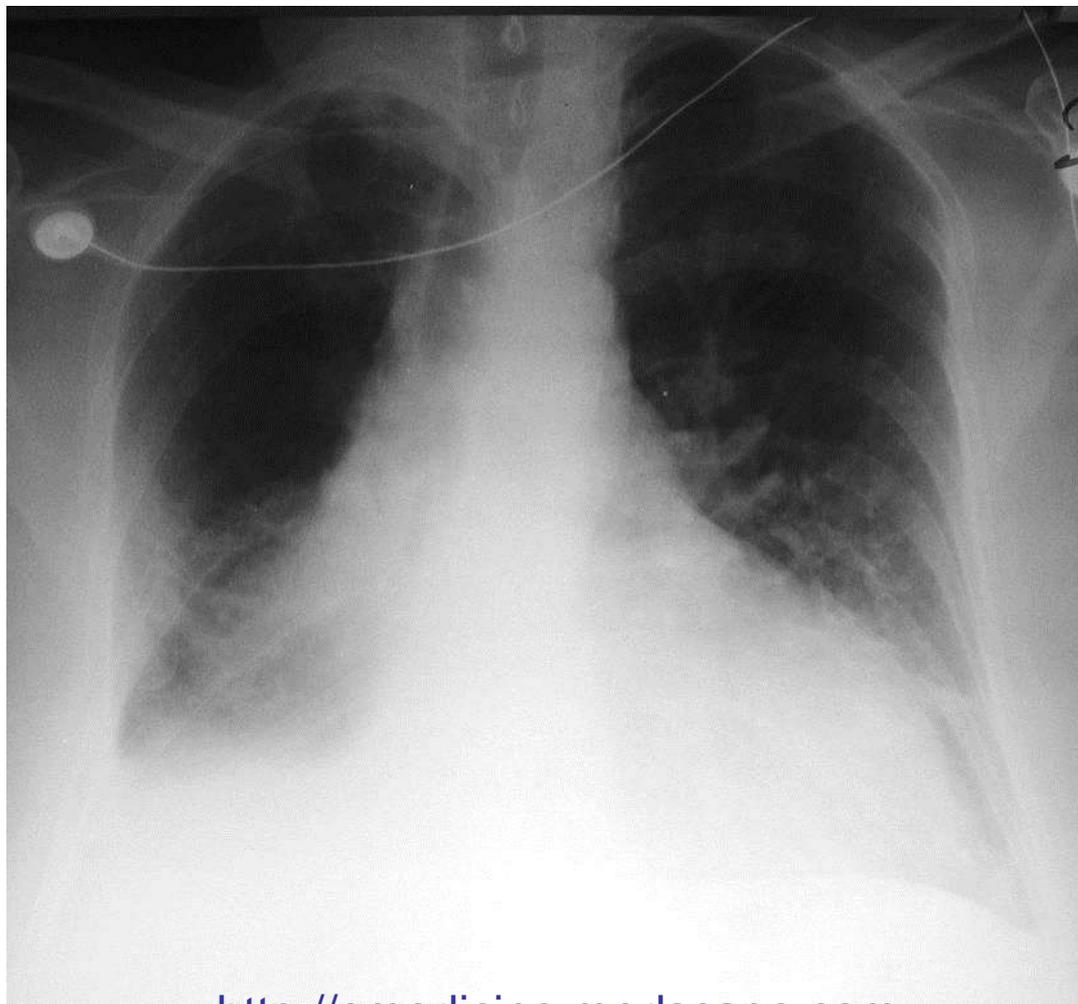
## Rx Th la pacientul dat ar putea arata astfel:

EPA la un pacient cu cardiomiopatie ischemica

- Lobii superiori:  
liniile Kerley A
- Lobii inferiori:  
liniile Kerley B  
(1 mm latime, 1 cm lungime)

<http://emedicine.medscape.com>

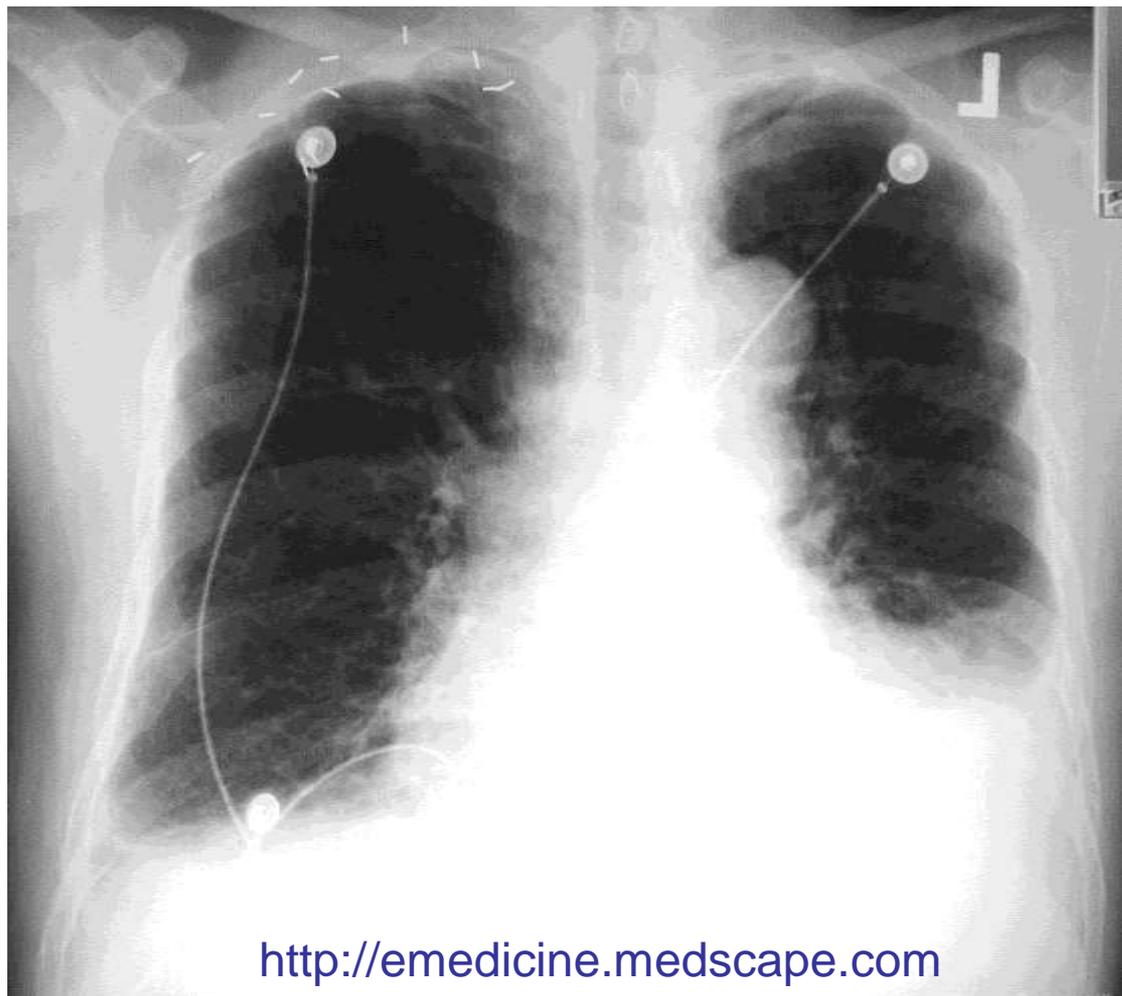
## Rx Th la pacientul dat ar putea arata astfel:



<http://emedicine.medscape.com>

Cardiomegalie,  
efuziuni pleurale  
bilaterale, opacitate  
alveolara la un  
pacient cu EPA

## Rx Th la pacientul dat ar putea arata astfel:



<http://emedicine.medscape.com>

Edem pulmonar  
interstitial,  
cardiomegalie si  
efuziune pleurala pe  
stanga (debut de  
EPA)

## Rx Th la pacientul dat ar putea arata astfel:

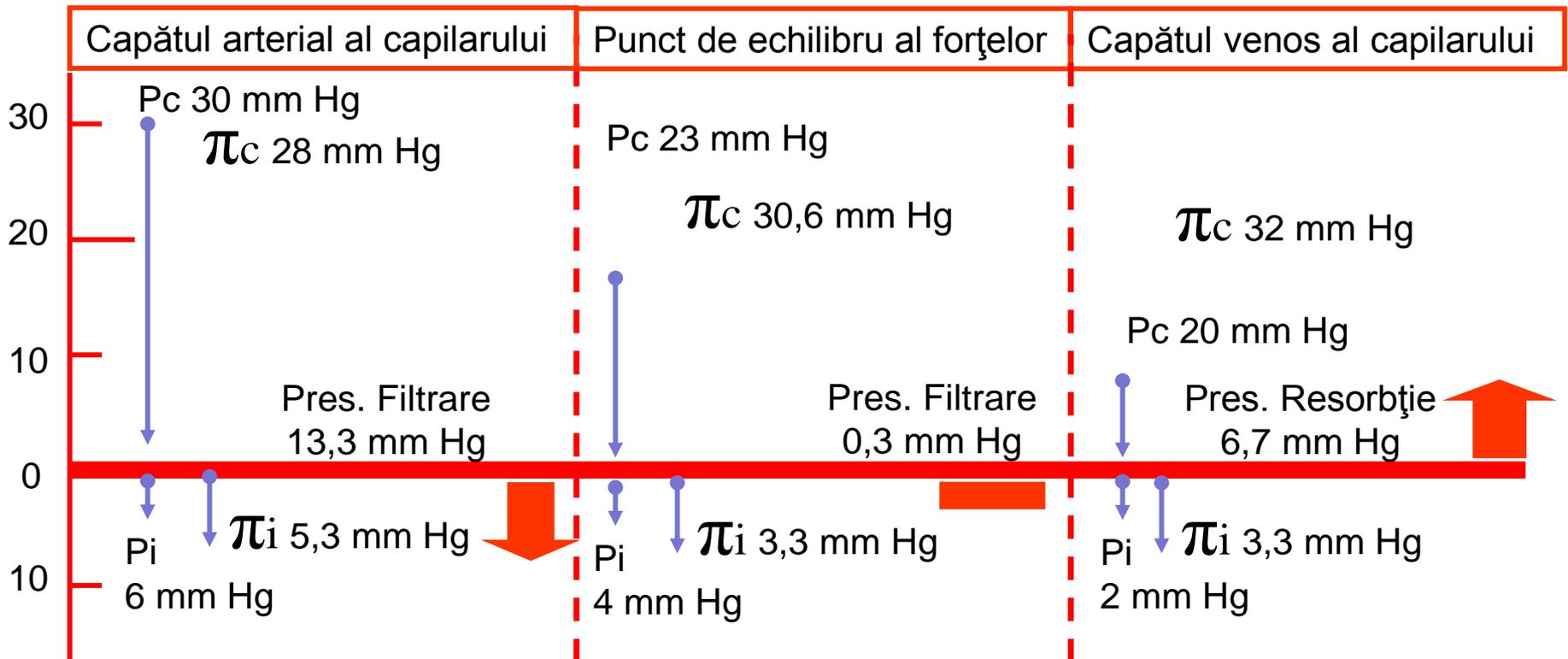


Edem pulmonar  
interstitial cu  
efuziune pleurala

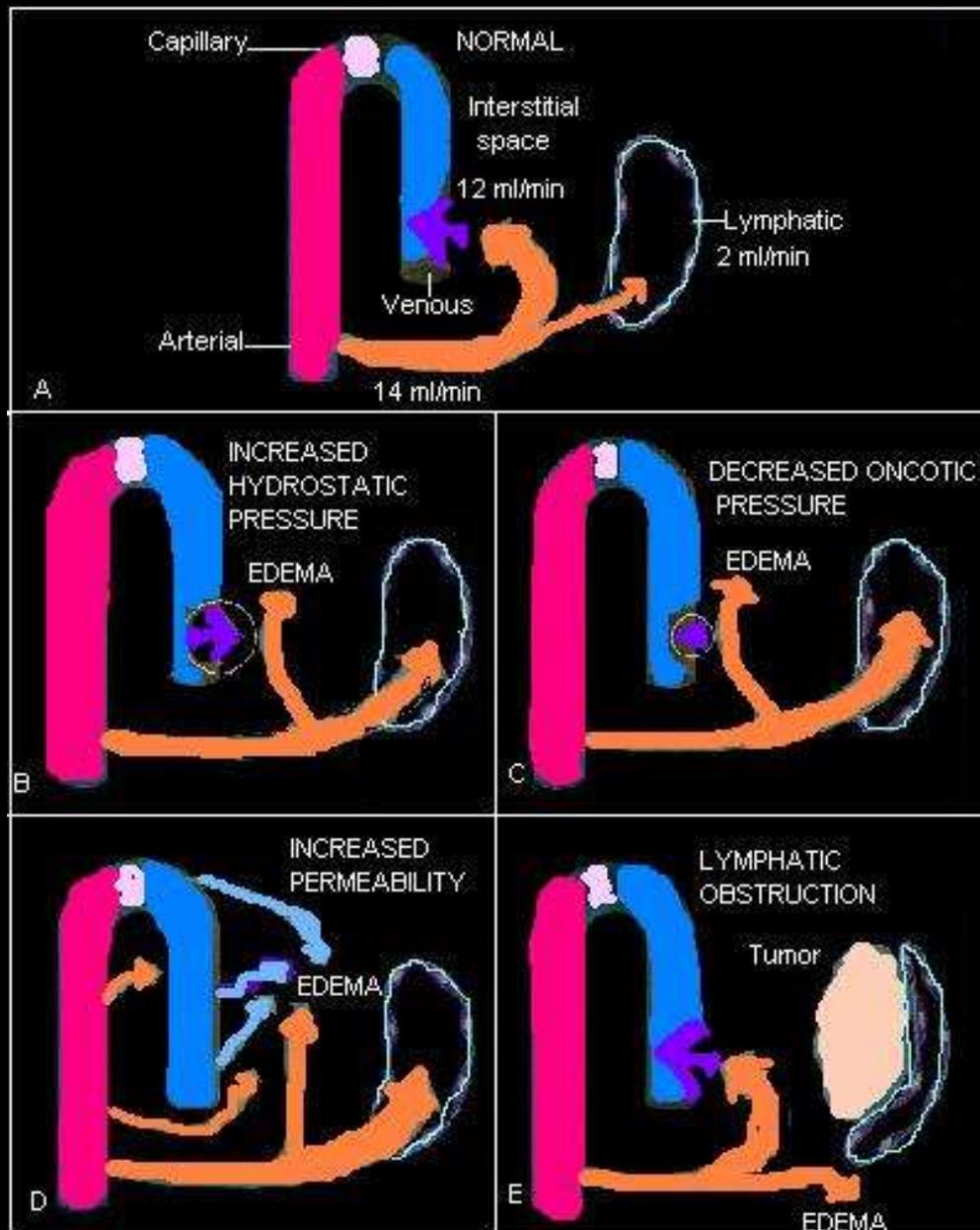
<http://emedicine.medscape.com>

## Echilibrul Starling - Pappenheimer - Staverman

$$Q = Kf \times [(Pc - Pi) - \sigma (\pi_c - \pi_i)]$$

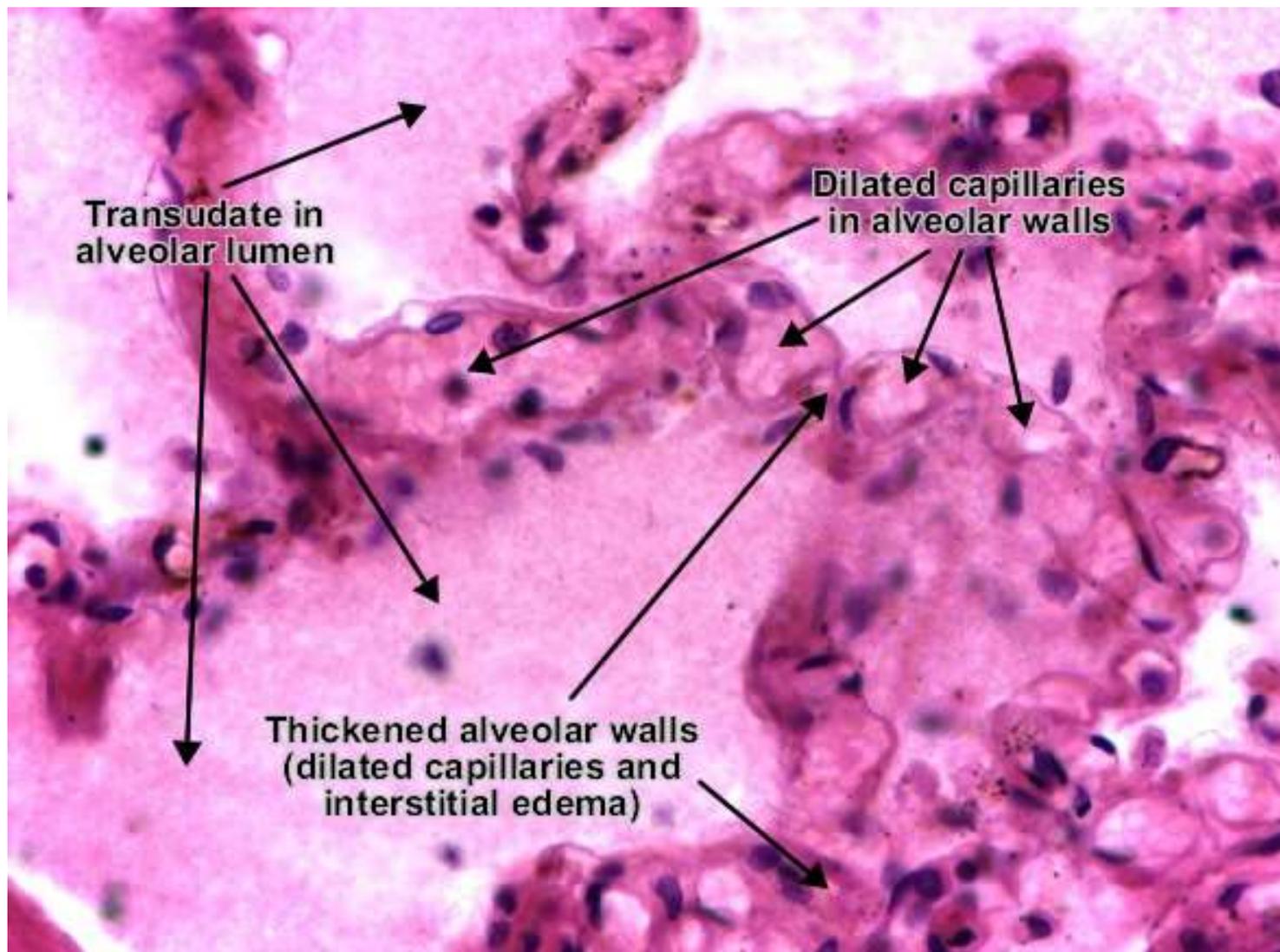


## Mecanismele edemului pulmonar acut (2)



- Întoarcere venoasa excesiva ( $\uparrow$  presarcina)
  - RVS  $\uparrow$  (postsarcina  $\uparrow$ )
  - Disfunctia VS
    - disfunctie sistolica
    - disfunctie diastolica
    - insuficienta contractila
  - Dereglari de ritm si frecventa
- !** VD continua sa pompeze, în timp ce VS e în disfunctie

## Mecanisme edemului pulmonar acut (3)



- O<sub>2</sub>
- VNI/VPA + PEEP

↑ contractilitatii →

Dopamina  
Dobutamina  
Milrinona  
Norepinefrina

NTG  
Furosemd  
Morfina

Nitroprusiatul  
Hidralazina  
NTG

↓ presarcinii

↓ postsarcinii

## Reducerea presarcinii: morfina

## Avantaje

- Histaminoeliberarea reduce presarcina
- Anxioliza scade catecolaminele circulante
- Reduce postsarcina

## Dezavantaje

- Nu e demonstrat efectul de reducere a presarcinii
- Poate deprima respiratia
- Rush/urticarie
- Greață/voma
- Efect cardiodepresor
- Reduce presiunea venoasa, insa acest fapt nu coreleaza cu presarcina (PICP)
- Crește presiunea de umplere cardiaca si reduce DC

Timmis, et al (Br Med J, 1980)  
Vismara, et al (Circulation, 1976)

## Reducerea presarcinii: morfina

### Dezavantaje

- 38% dintre pacienti: deteriorare subiectiva dupa morfina
- 46% dintre pacienti: deteriorare obiectiva dupa morfina
- Nicio deteriorare a starii dupa NTG fara morfina  
Hoffman et al., (Chest, 1987)
- Riscul de IOT dupa morfina: OR=5  
Sachetti, et al. (Am J Emerg Med, 1999)
- Mortalitatea dupa morfina: OR=4,84  
Peacock, et al. (Emerg Med. J., 2008)

# Benzodiazepine în loc de morfina

## Reducerea presarcinii: furosemidul

## Avantaje (?)

## Dezavantaje

- În EPA: RFG ~20% din N
- Efect diuretic peste 30-120 min
- Venodilatatie în 5-10 min, inasa nu coreleaza cu ↓PICP (presarcina VS)
- Eficient doar la cei cu diureza pastrata
- ↓DC cu 17% în primele 90 min (normalizare dupa diureza)
- ↑ PAS, PAD si AV in primele 30 min (normalizare dupa diureza)
- Activeaza sistemul RAA (↑↑ renina, NE, arginin-vasopresina);
- Creste tranzitor (~15 min) PICP (nu si la premedicarea cu NTG si IEC)

Kiely et al. (Circulation, 1973); Ikram, et al. (Clin Sci, 1980); Pickkers, et al. (Circulation, 1997); Nelson, et al (Eur Heart J, 1983); Francis, et al (Ann Intern Med, 1985)

## Reducerea presarcinii: nitroglicerina

## Avantaje

- Reducere rapida si semnificativa a presarcinii;
- Reduce RVS in doze  $\geq$  moderate
- $\uparrow \leftrightarrow$  DC si FEVS
- T1/2 scurt
- Multiple forme de administrare
- Sublingual ~ intravenos

## Dezavantaje

- ! Hipotensiune
- ! insuf. mitrala acuta
- ! stenoza Ao
- ! HTP
- ! Viagra

## Suportul inotrop (+): dopamina, dobutamina

## Avantaje

- ↑↑ DC

## Dezavantaje

- ↑ RMO<sub>2</sub>, AV, ischemia
- Aritmogene la doze mari
- Catecolaminemia pacientului dezvoltă rapid toleranță față de D.

## Suportul inotrop (+): iPDE – milrinona

## Avantaje

- Independente de adrenoreceptori
- Independente de catecolaminemie
- Nu dezvoltă toleranță
- Nu afectează RMO<sub>2</sub>
- ↑ DC: milrinona ≥ Dopa, Dobut.
- ↓ PICP: milrinona ≥ Dopa, Dobut.

## Dezavantaje

- Amrinona - proscrisă
- Nu reduce mortalitatea
- Cost înalt
- Ocazional - aritmii

## Paradoxul nr. 1 – secretia AVP

- Scaderea osmolaritatii plasmatice cu 1-2% suprima secretia AVP
- Hipervolemia: suprima secretia AVP

Dar, în cazul insuficientei cardiace

- Stimularea secretiei AVP, produsa de hipovolemia arteriala este mai puternica decât inhibitia secretiei AVP, produsa de hiposodemie si/sau hipervolemia venoasa

**Hipervolemie venoasa**

**Hipovolemie arteriala**

## Rezolvarea paradoxului 1: derivatii ANP

### Nesiritida (B-ANP recombinat)

- ↓↓ PFCP si RVS
- ↑↑ natriureza si DC
- ↔ AV
- Ameliorare timp de 1 ora

Mills, et al (J Am Coll Cardiol, 1999)

Colucci, et al (N Engl J Med, 2000)

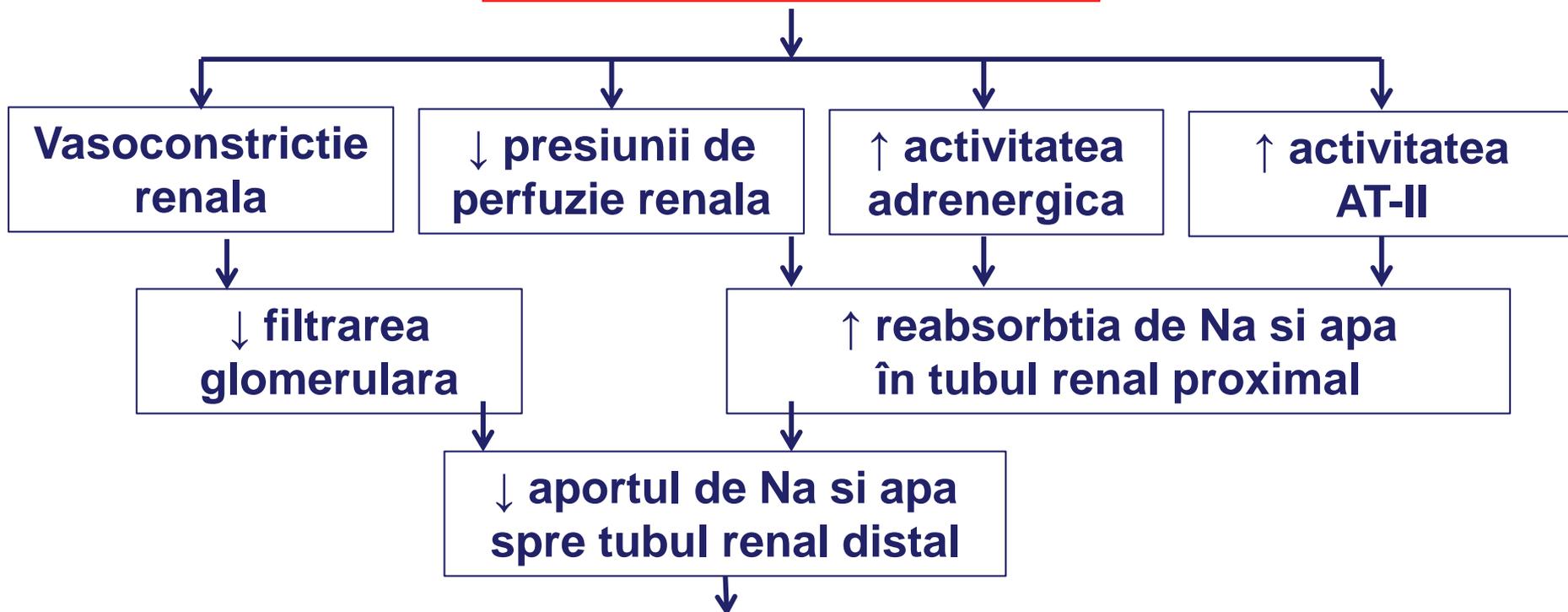
### Dezavantaje

- Studii sponsorizate de producator
- Cost: 40 x NTG (~456\$/fiola)
- Creste durata de spitalizare cu 2 zile, dar... scade readmisia in spital a supravietuitorilor
- Suspectata cresterea mortalitatii (19% N vs 13 NTG la 90 zile)

Sackner-Bernstein, et al. (Circulation, 2005)  
VMAC trial (JAMA, 2002)

Paradoxul nr. 2 – efectul « aldosterone escape »

**Hipovolemia arteriala**



**«scaparea» de sub actiunea aldosteronului si rezistenta fata de peptidele natriuretice**

## Avantaje

- Reduc activitatea SRAA
- ↓ Catecolaminele si postsarcina
- Amelioreaza relaxarea VS
- Aplicabil in acutizarea ICC
- ↓ PICP in  $\leq 10$  min 25 mg captopril
- ↔ PAM si AV
- ↑↑↑ RFG si diureza

Barnett, et al (Curr Ther Res, 1991)

Langes, et al (Curr Ther Res, 1993)

Variante, et al (Clin Cardiol, 1993)

## Avantaje

- Odds IOT = 0,28
- ↔ hipotensiunea
- ↔ necesitatea vasopresorilor
- ↓↓↓ durata UTI (29 vs. 78 ore)
- Sinergic cu NTG
- Alternativa NTG

Sacchetti, et al (Am J Emerg Med, 1999)

Southall, et al (Acad Emerg Med, 2004)

**Conceptul «miscarii lichidelor» (« liquid shifting »):**

- reducerea hipervolemiei venoase
- compensarea hipovolemiei arteriale

## Cum ramane cu perfuzarea i.v. de lichide în cazul EPA /IC ?

- 50% dintre pacientii cu EPA nu sunt încarcati cu lichide;
- Mai curând – disfunctie vasculara
- Diureticele – deseori inutile (insa, sunt supra-utilizate)

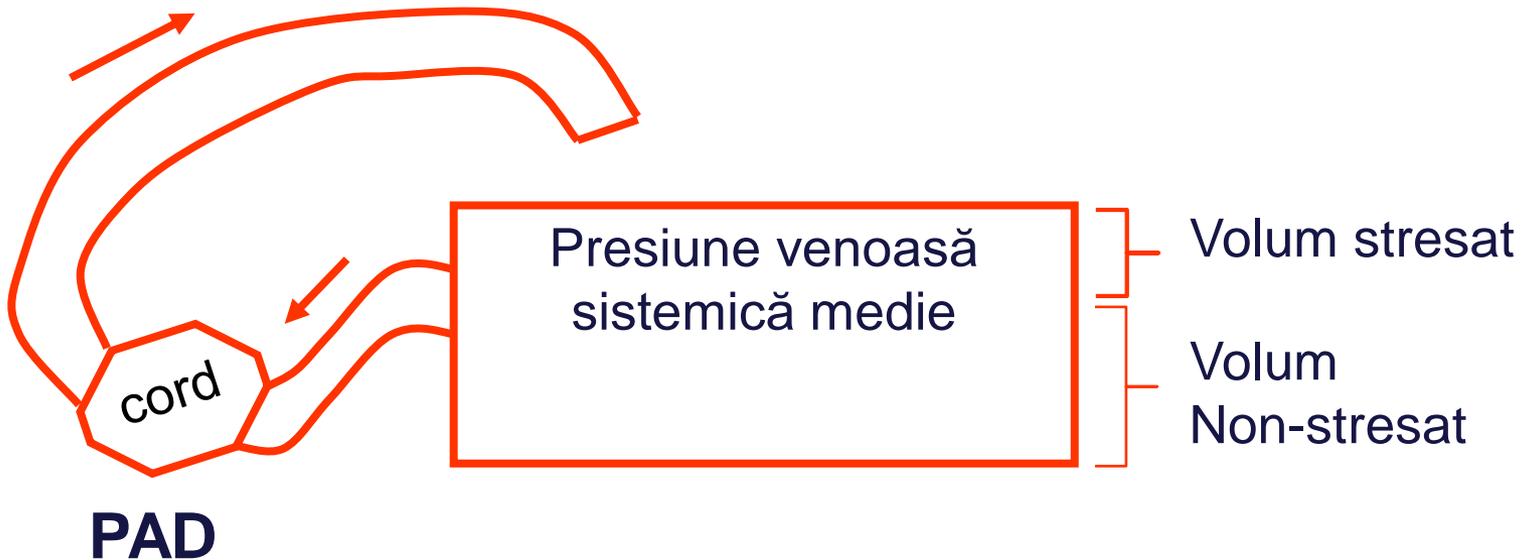
Cotter, et al. (Am Hearth J, 2008) and Collins et al. (Am Emerg Med, 2008)

# Relația dintre volemie și performanța cardiacă

## Modelul Magder

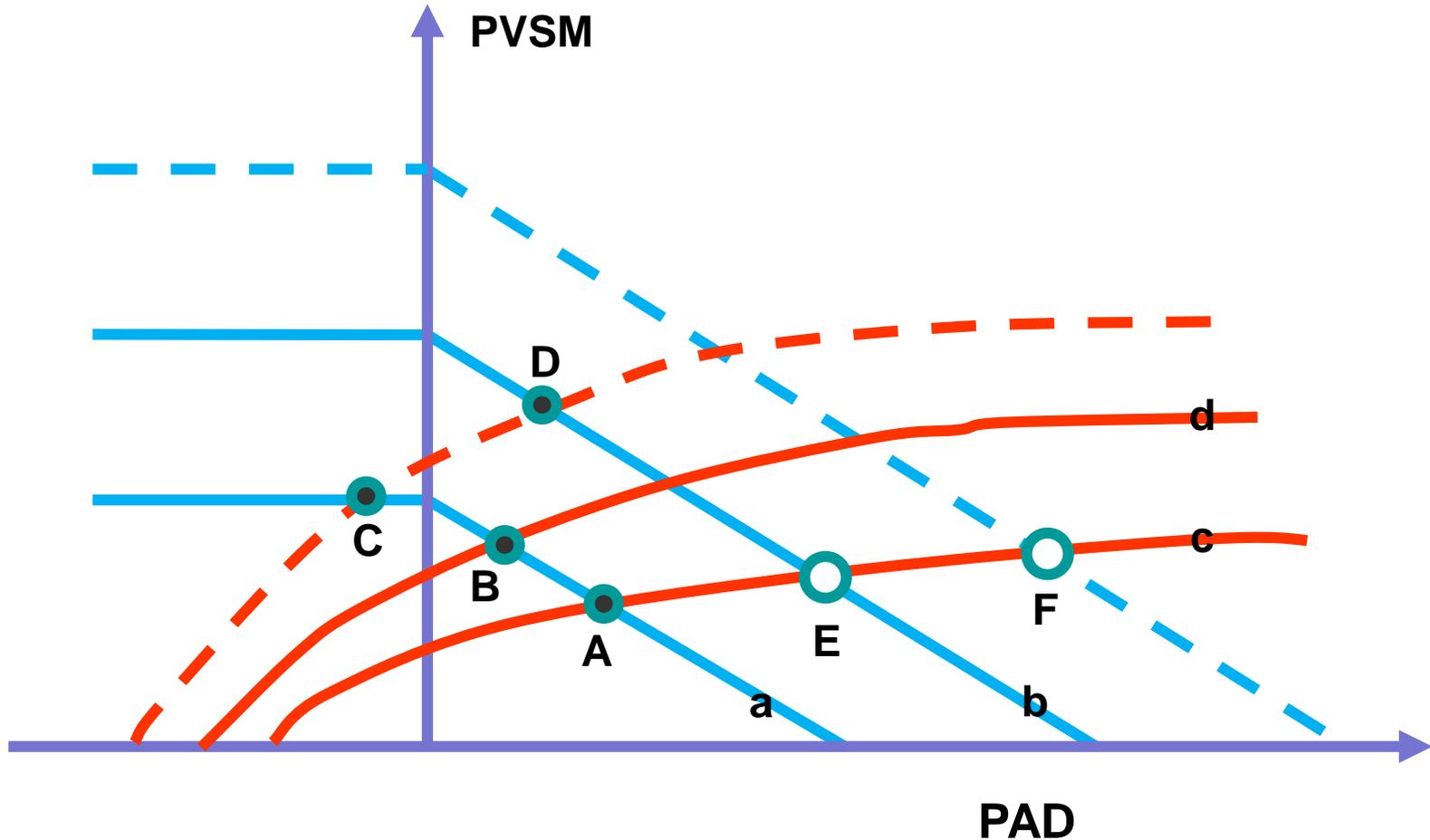
Presiunea transmurală = 0

Presiunea transmurală > 0

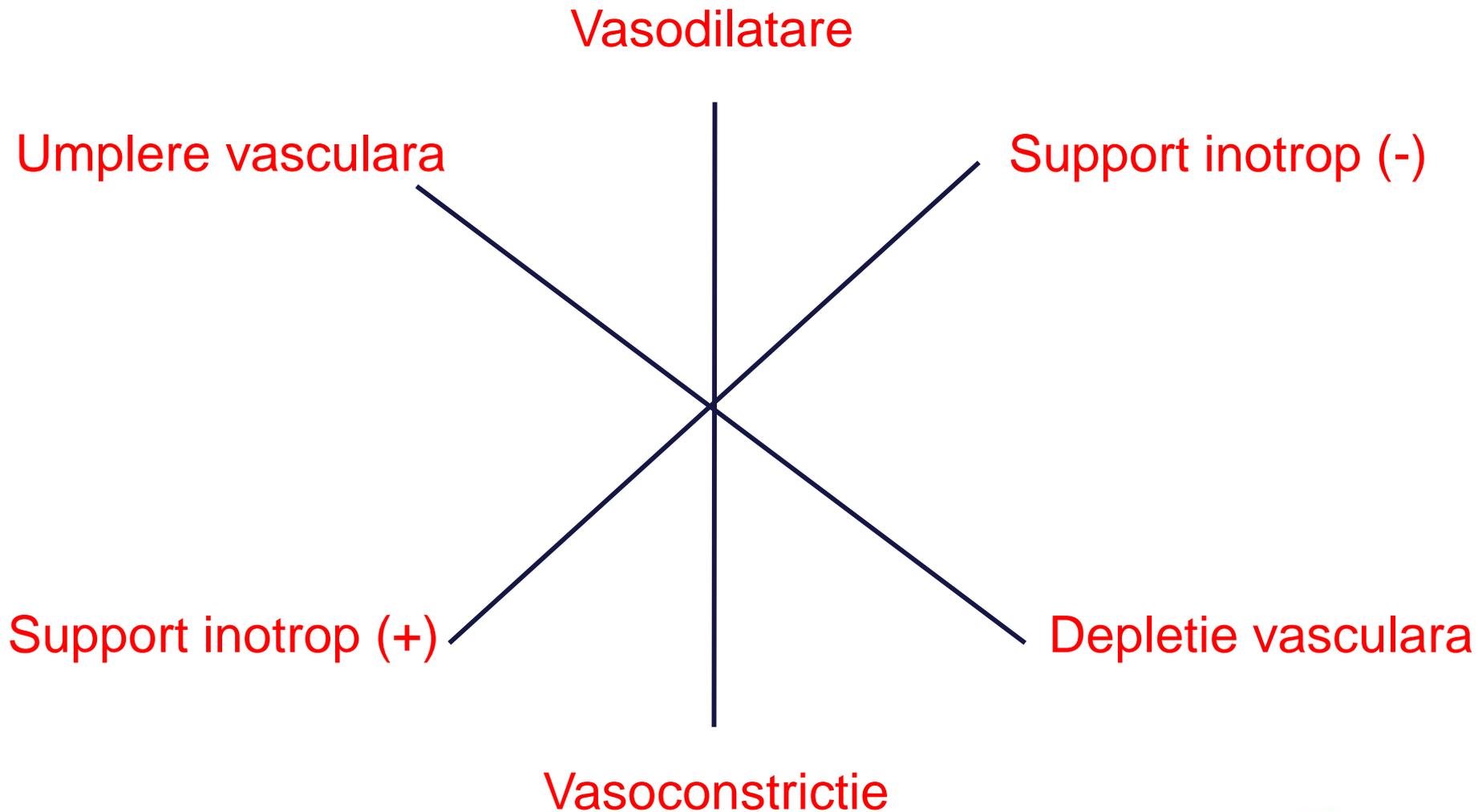


# Relația dintre volemie și performanța cardiacă

## Modelul Guyton: relația retur venos - PAD - DC

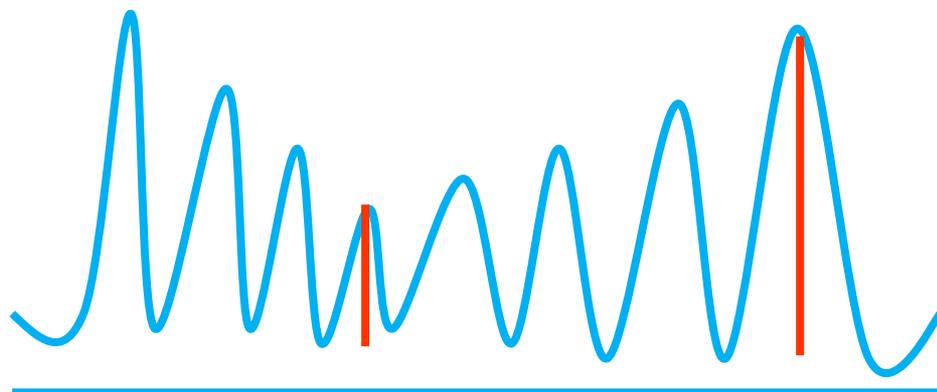
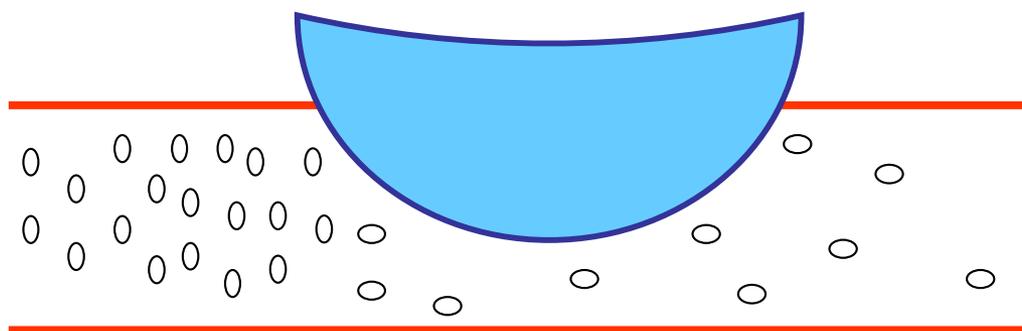


1. **Este presarcina actuală optimală, iar administrarea i.v. de volum va conduce la creșterea DC sau nu ?**
2. **Frecvența și ritmul cardiac sunt în limite fiziologice?**
3. **Care stare a RVS – vasoconstricție, vasodilatate sau tonus normal vor contribui la optimizarea (creșterea) debitului cardiac?**
4. **Este oare balanța de oxigen ( $DO_2$ - $VO_2$ ) echilibrată?**
5. **Care este starea contractilității miocardice ?**



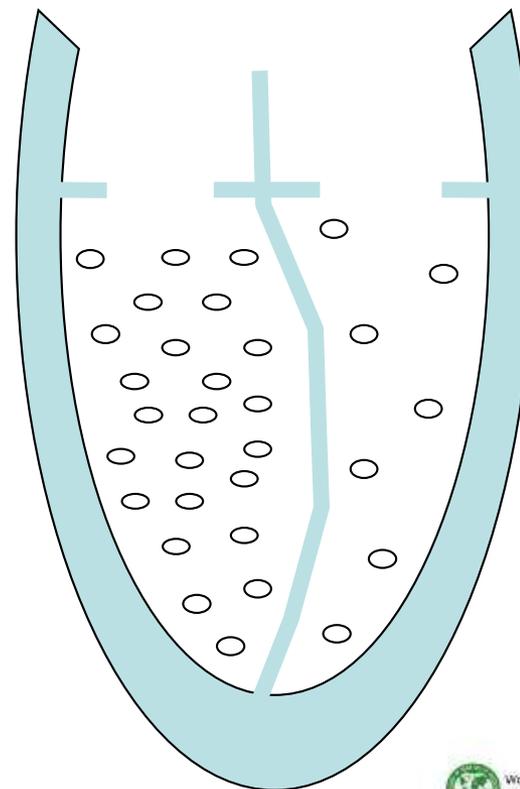
# Relația dintre volemie și performanța cardiacă

## Volemia și interferența cord-pulmon



1 ciclu respirator

$\Delta PP \geq 13\%$

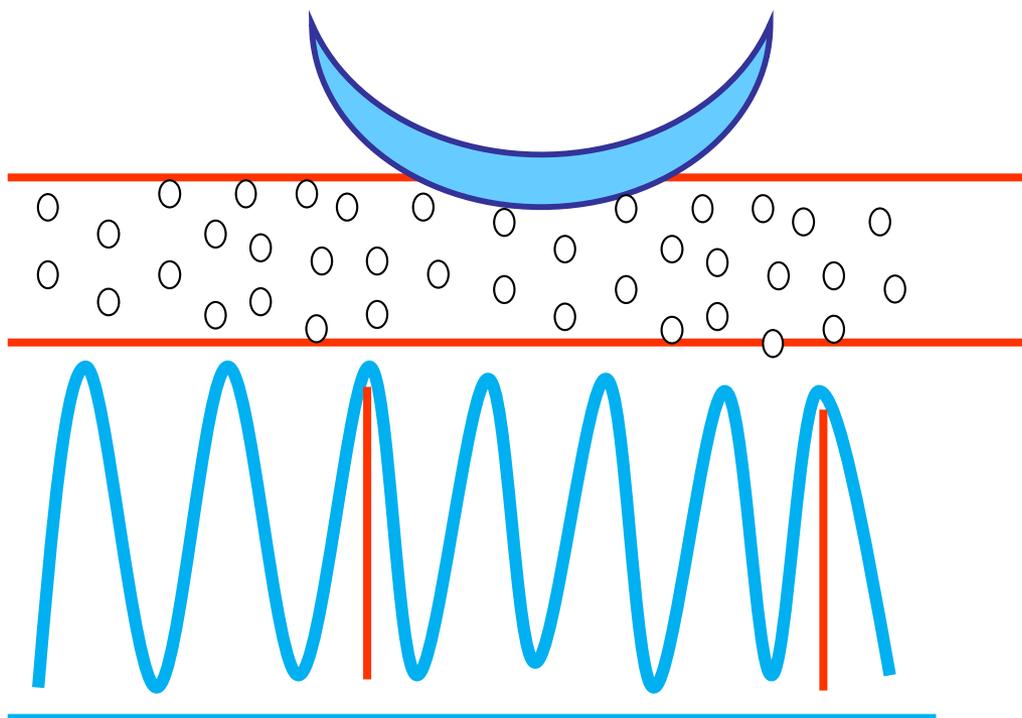


$$\Delta PP(\%) = \frac{(PP_{\max} - PP_{\min}) \times 2}{(PP_{\max} + PP_{\min})} \times 100$$

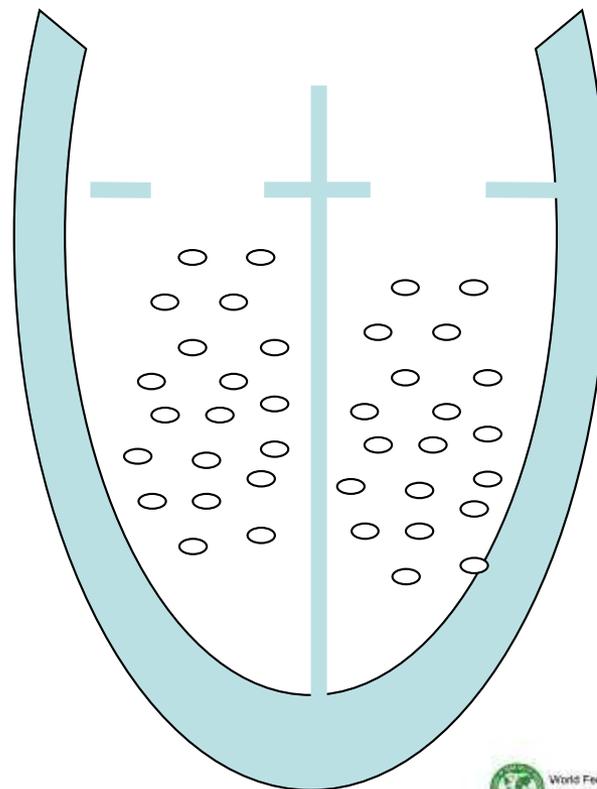
$$PP_{\min} = PAS_{\min} - PAD_{\min}$$

$$PP_{\max} = PAS_{\max} - PAD_{\max}$$

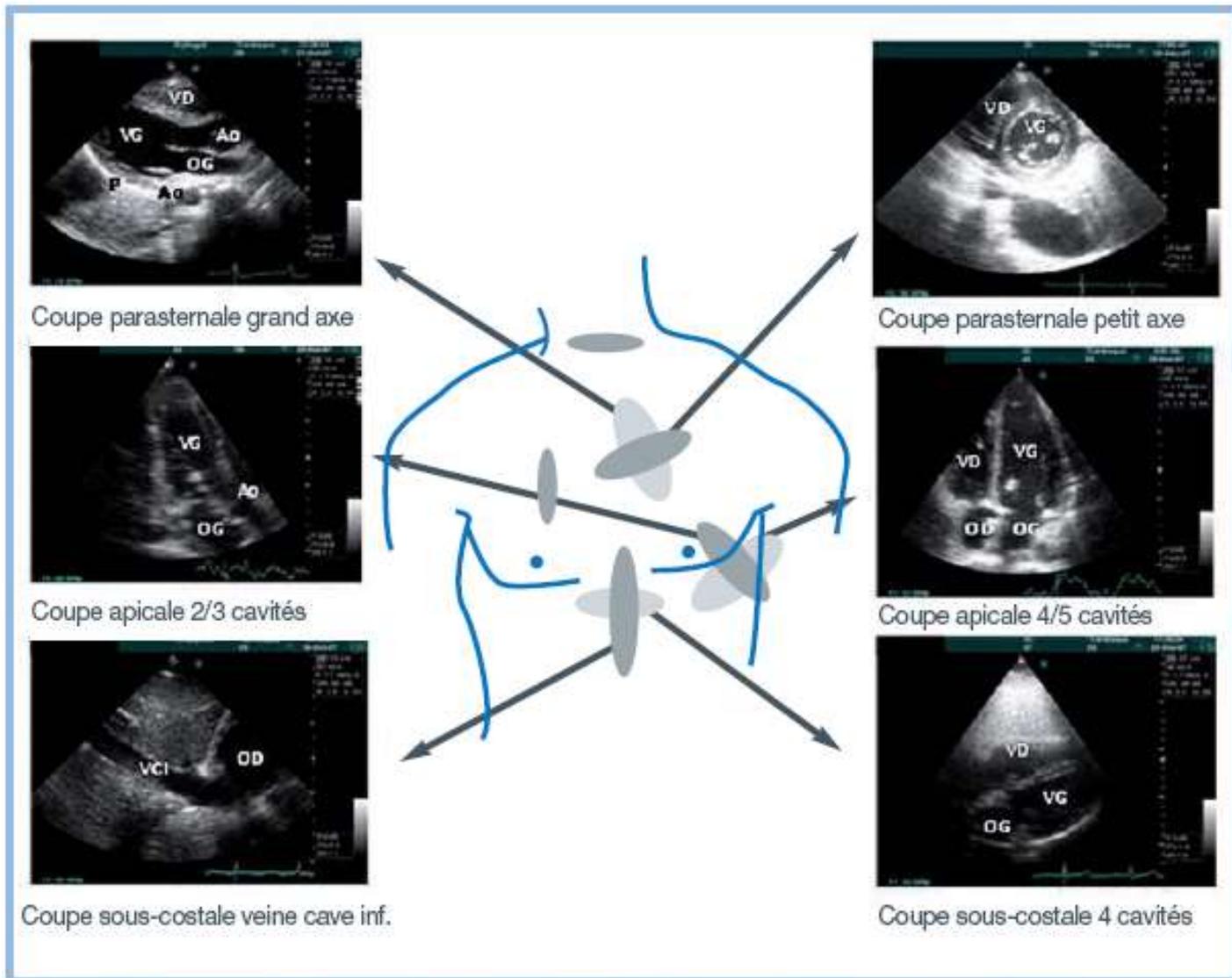
$\Delta PP < 13\%$

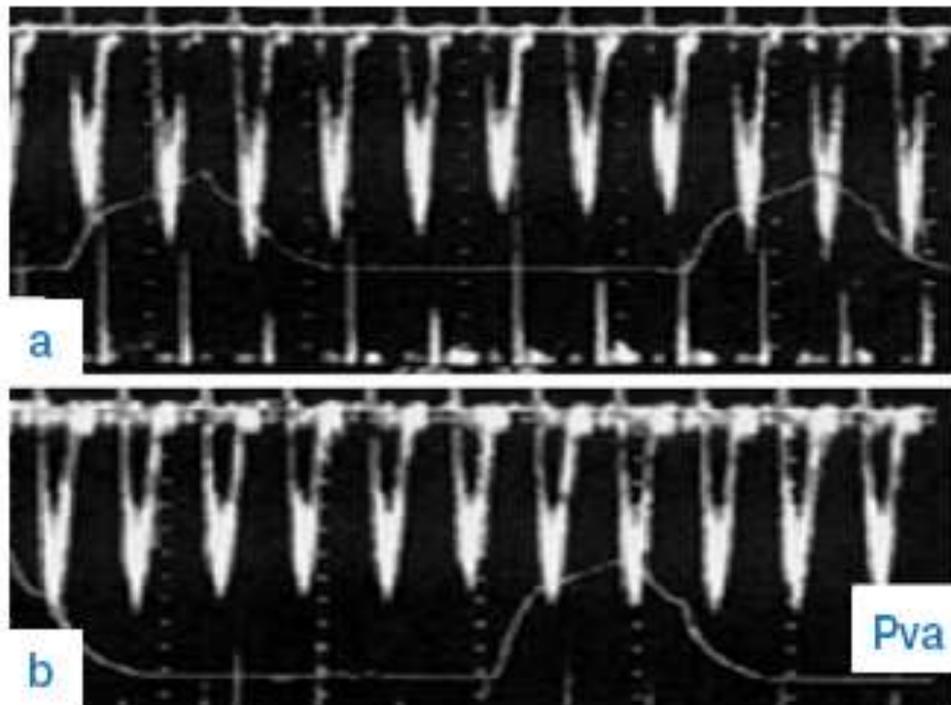


1 ciclu respirator



# Ecocardiografia – un instrument util pentru testarea responsivitatii DC la umplerea vasculara



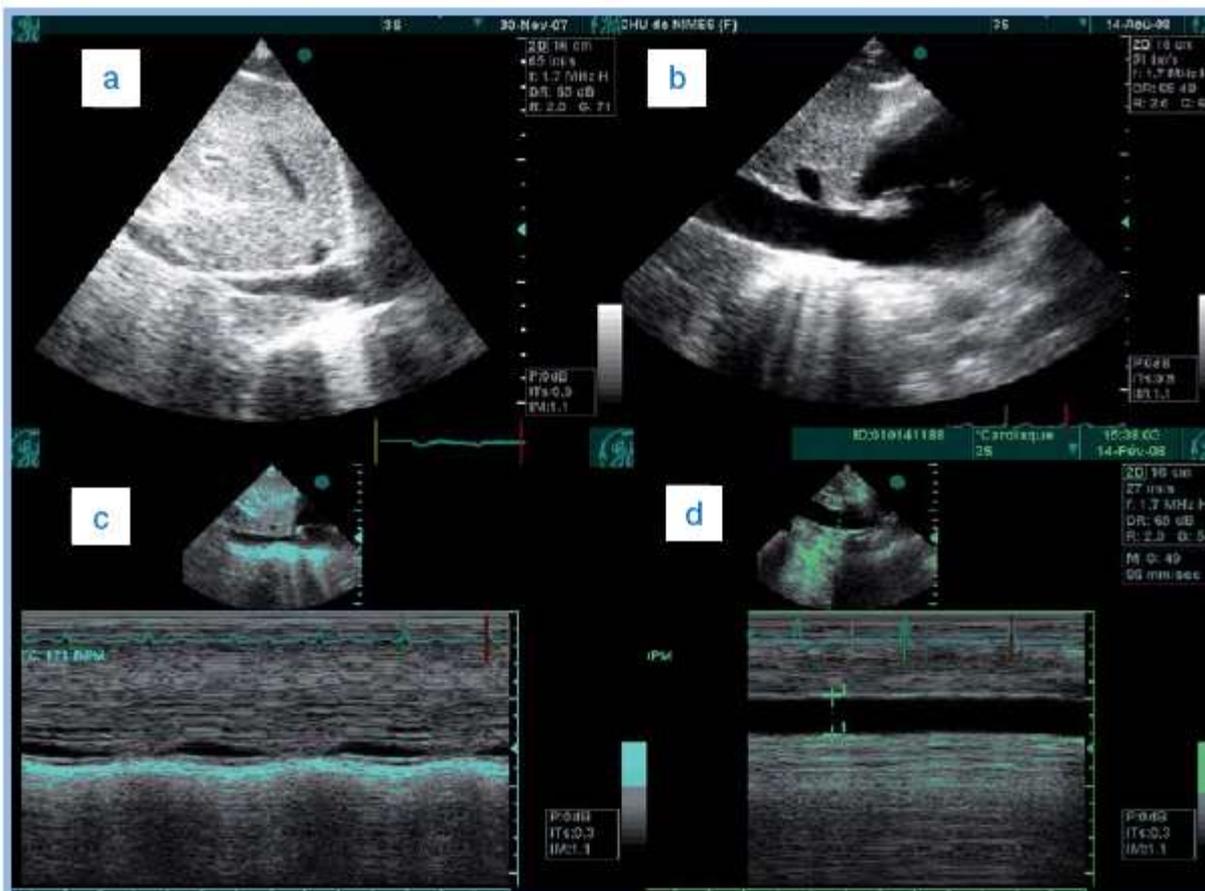


**Variatiile respiratorii a velocitatii fluxului subaortic ( $\Delta V_{peak}$ ):**

- a. ( $\Delta V_{peak}$ ) >12% - dependenta de presarcina → **umplere vasc. necesara**
- b. ( $\Delta V_{peak}$ ) <12% - independenta de presarcina (**x**)

# Ecocardiografia – un instrument util pentru testarea responsivitatii DC la umplerea vasculara

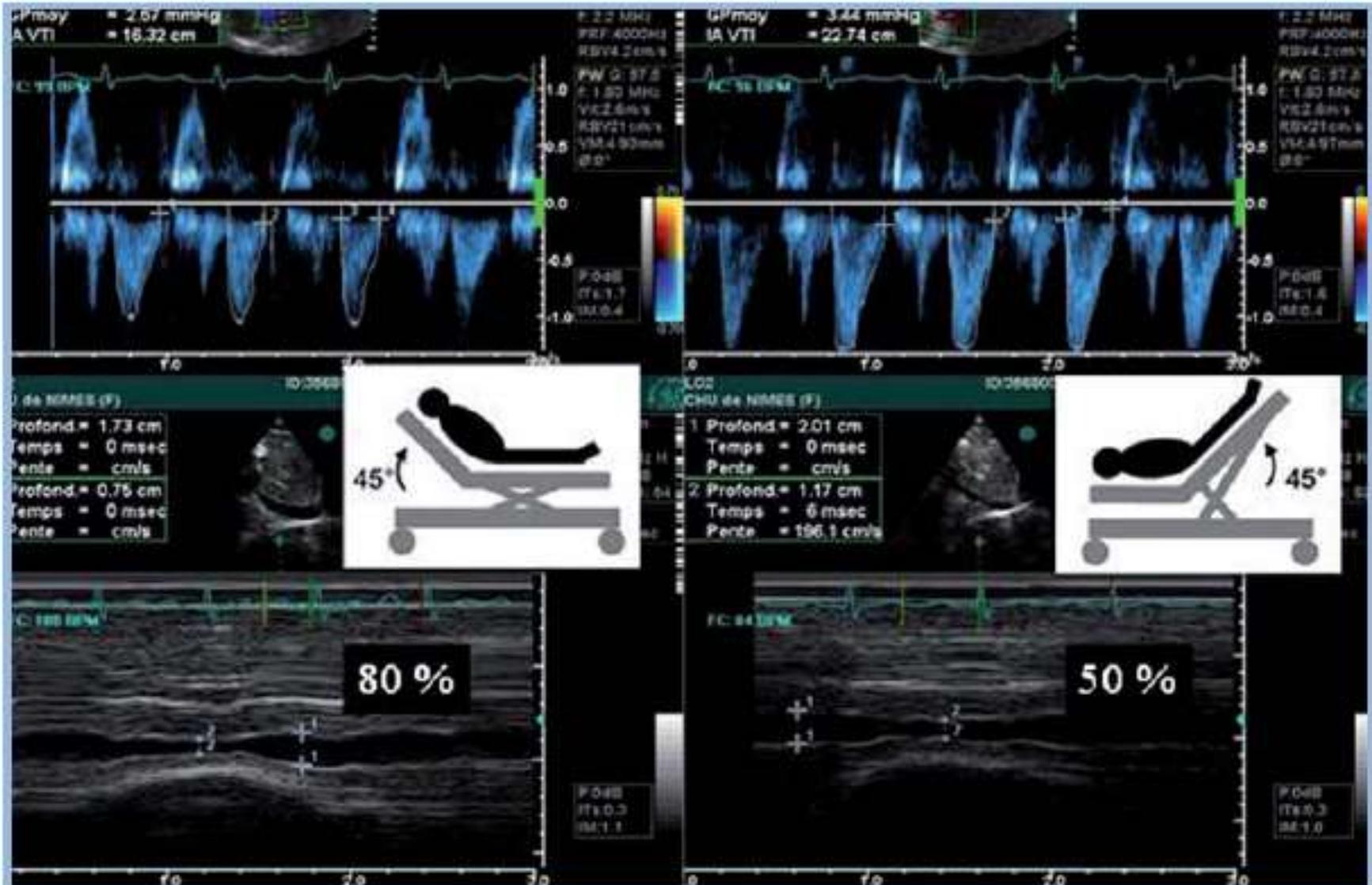
**i.v. → OK**



**i.v. → STOP**

**i.v. → OK**

**i.v. → STOP**



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*Clinical Study*

# **Extravascular Lung Water Does Not Increase in Hypovolemic Patients after a Fluid-Loading Protocol Guided by the Stroke Volume Variation**

**Carlos Ferrando,<sup>1</sup> Gerardo Aguilar,<sup>1</sup> and F. Javier Belda<sup>1,2</sup>**

<sup>1</sup> *Department of Anesthesiology and Critical Care, Hospital Clínico Universitario de Valencia, 46010 Valencia, Spain*

<sup>2</sup> *Department of Surgery, School of Medicine, University of Valencia, 46010 Valencia, Spain*

Correspondence should be addressed to Gerardo Aguilar, [gerardo.aguilar@uv.es](mailto:gerardo.aguilar@uv.es)

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PMCID: PMC3357553

## Why Do We have to Move Fluid to be Able to Breathe?

[Martin Fronius](#)<sup>1,\*</sup>, [Wolfgang G. Clauss](#)<sup>1</sup> and [Mike Althaus](#)<sup>1</sup>

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### Abstract

Go to:

The ability to breathe air represents a fundamental step in vertebrate evolution that was accompanied by several anatomical and physiological adaptations. The morphology of the air-blood barrier is highly conserved within air-breathing vertebrates. It is formed by three different plies, which are represented by the alveolar epithelium, the basal lamina, and the endothelial layer. Besides these conserved

### Related citations in PubMed

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Ion transport by pulmonary epithelia.

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[Am J Physiol Lung Cell Mol Phy...]

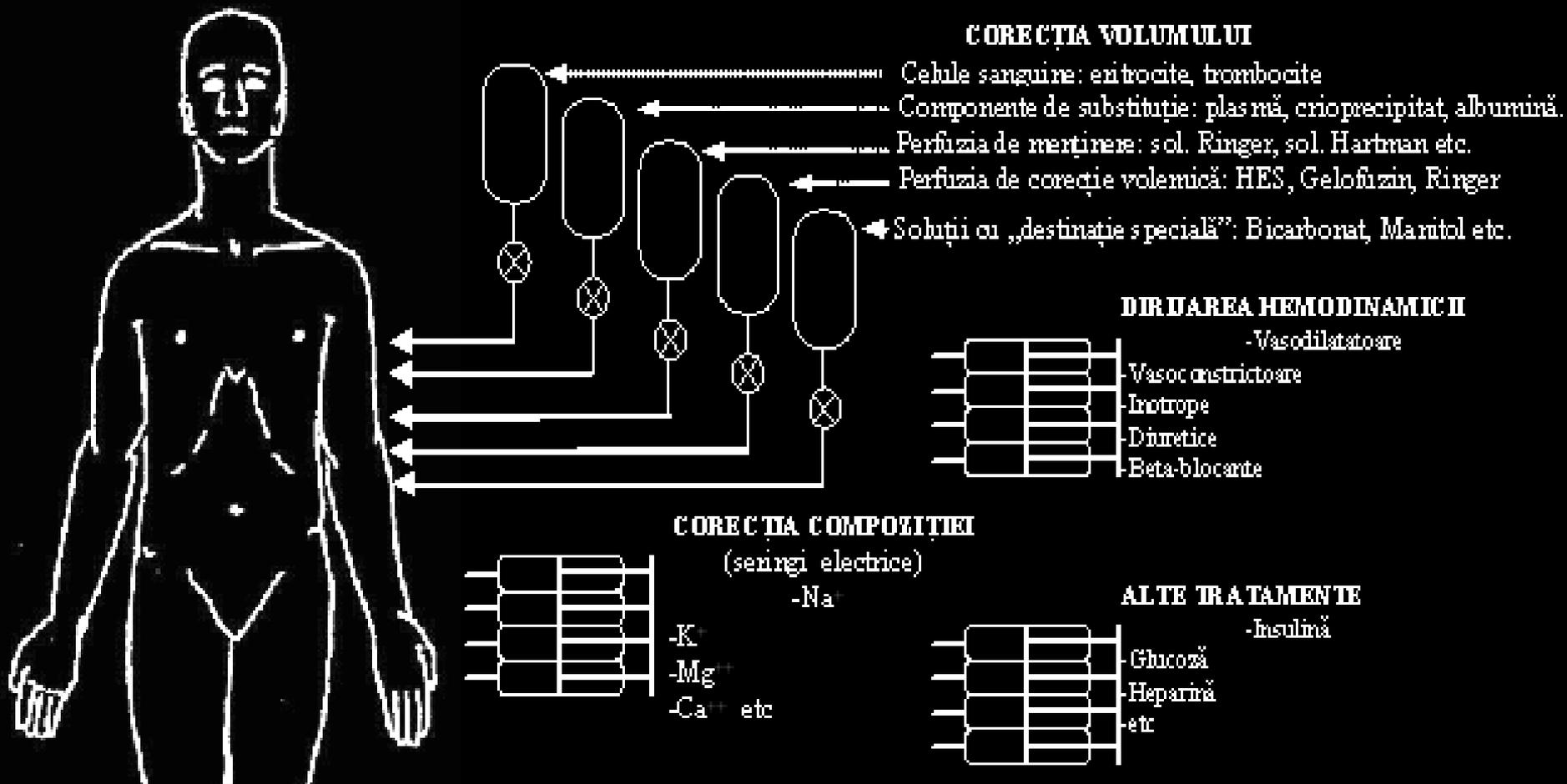
Electrolyte and fluid transport across the mature alveolar epithelium.

[J Appl Physiol. 1993]

Salt and water transport across the alveolar epithelium in the developing lung: correlations between functic [Int J Mol Med. 1998]

See reviews...

# Schema de principiu pentru realizarea unui program de perfuzie



1. Pacientul cu EPA deseori este hipovolemic;
2. Edemele si hipervolemia venoasa pot coexista cu hipovolemia arteriala;
3. Reechilibrarea relatiei Starling-Pappenheimer-Staverman nu intotdeauna va conduce la rezolvarea EPA;
4. Hipervolemia venoasa (= «rezerva interna») poate fi sursa compensarii lente a hipovolemiei arteriale in EPA si IC.
5. Perfuzarea intravenoasa de lichide in EPA se face doar in cazul unui test (+) de responsivitate la umplere ( $\Delta PP$ , SVV...)
6. Ce solutii perfuzabile? – Asteptam decizia FDA...

