Consorci Sanitari Integral

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Organ dysfunction in AHF

PULMONARY EDEMA

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NO CONFLICT OF INTEREST

ACUTE CARDIOVASCULAR CARE 2015

LUNG DYSFUNCTION IN HEART FAILURE

ACUTE

Pulmonary Edema (Hydrostatic)

Starling forces imbalance in pulmonary capillaries

Alveolar fluid reabsorption (NO-dependent)

Alveolar fluid secretion (Cl^- / Na^+ transport-driven)

Pulmonary capillary stress failure

Individual susceptibility and other forms of APE

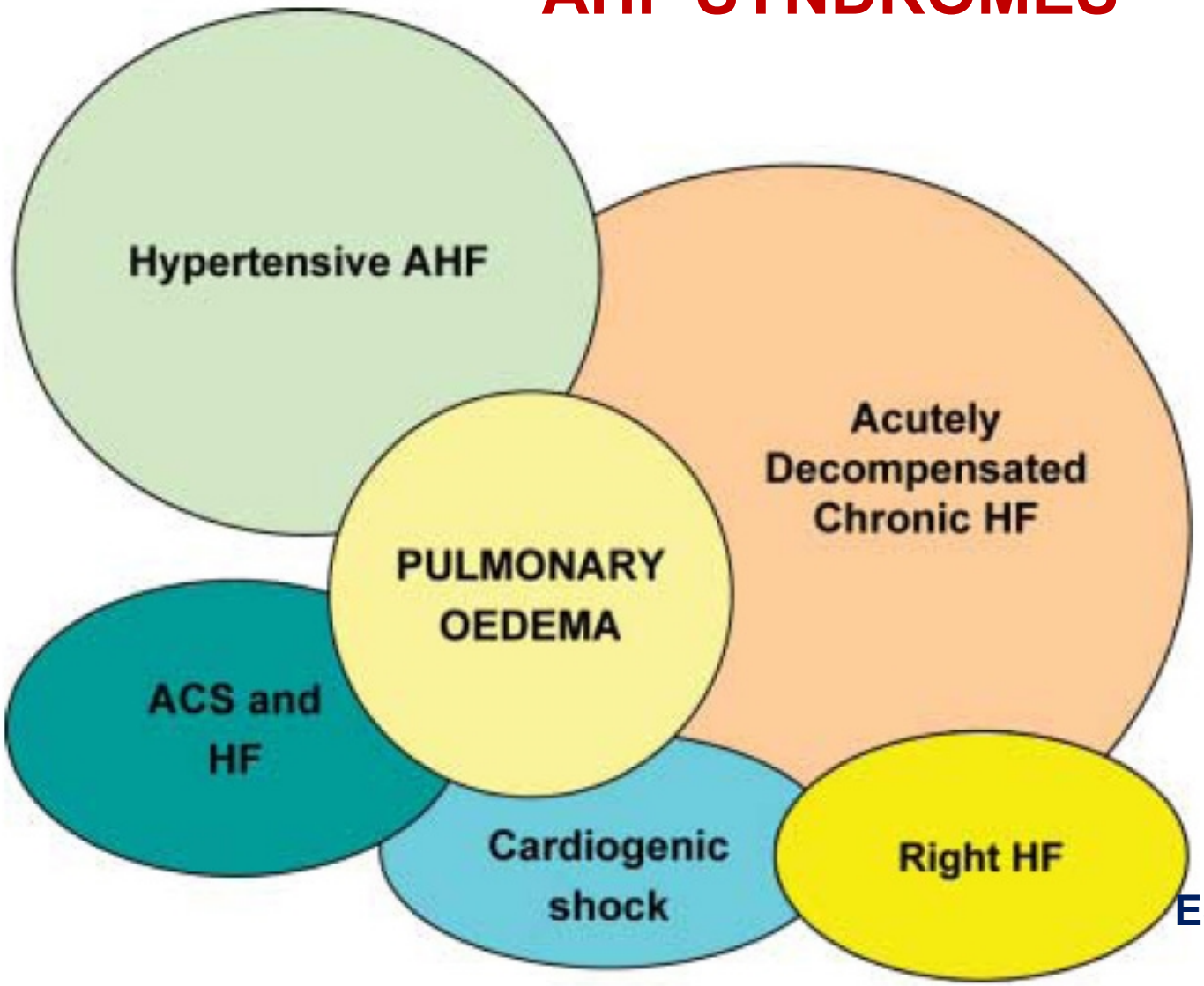
CHRONIC

Restrictive pattern

Cardiac asthma

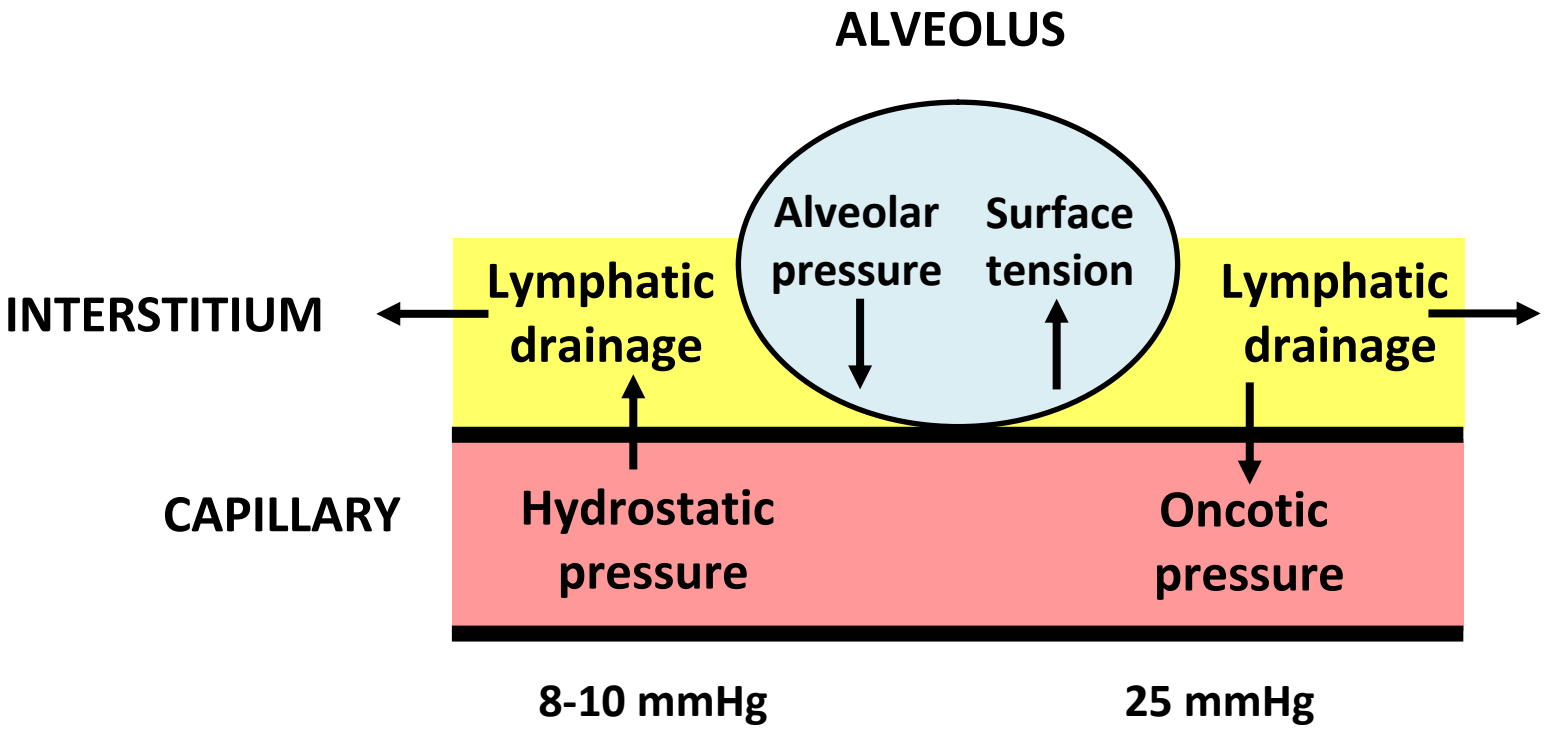
Pulmonary hypertension

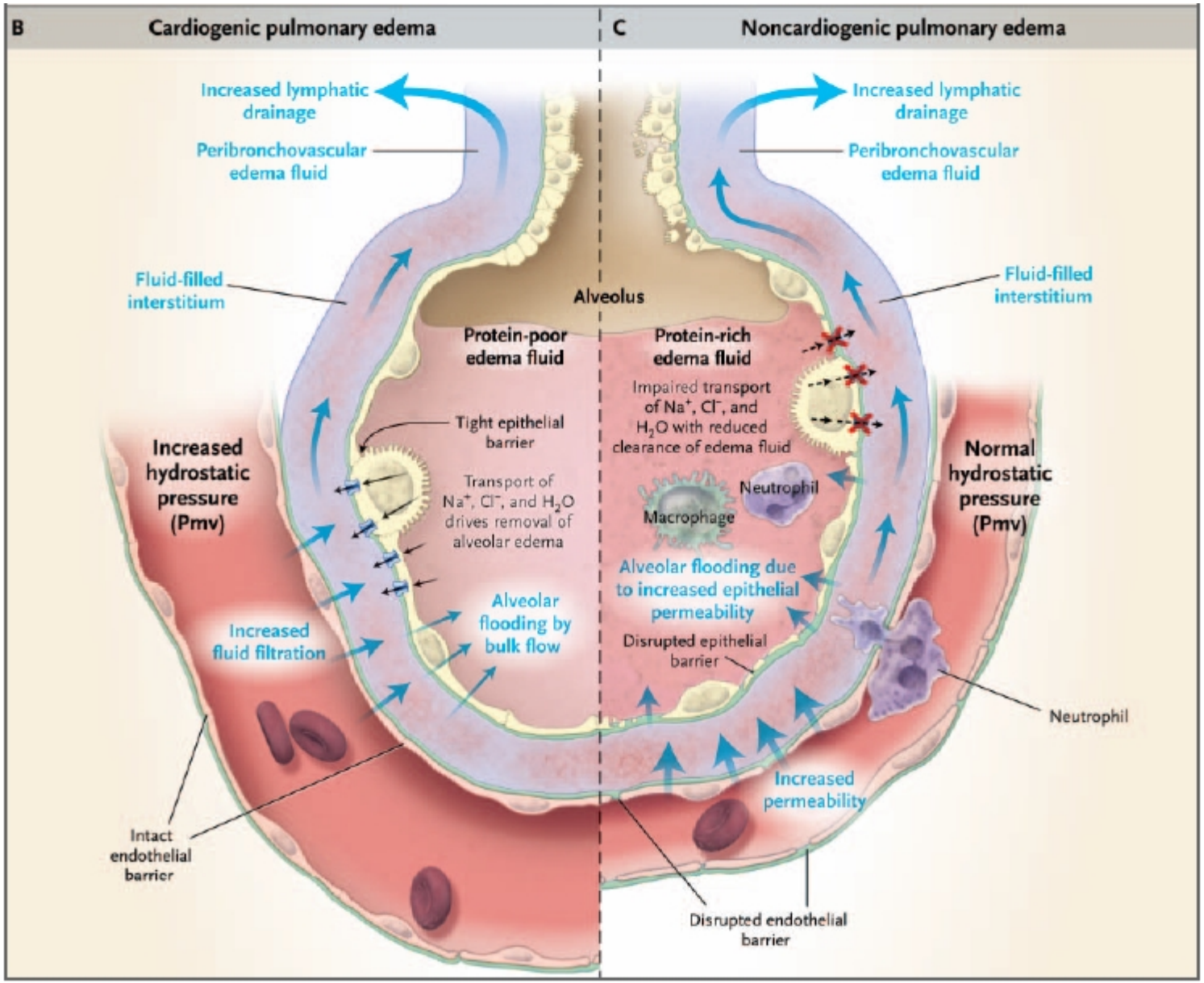
AHF SYNDROMES



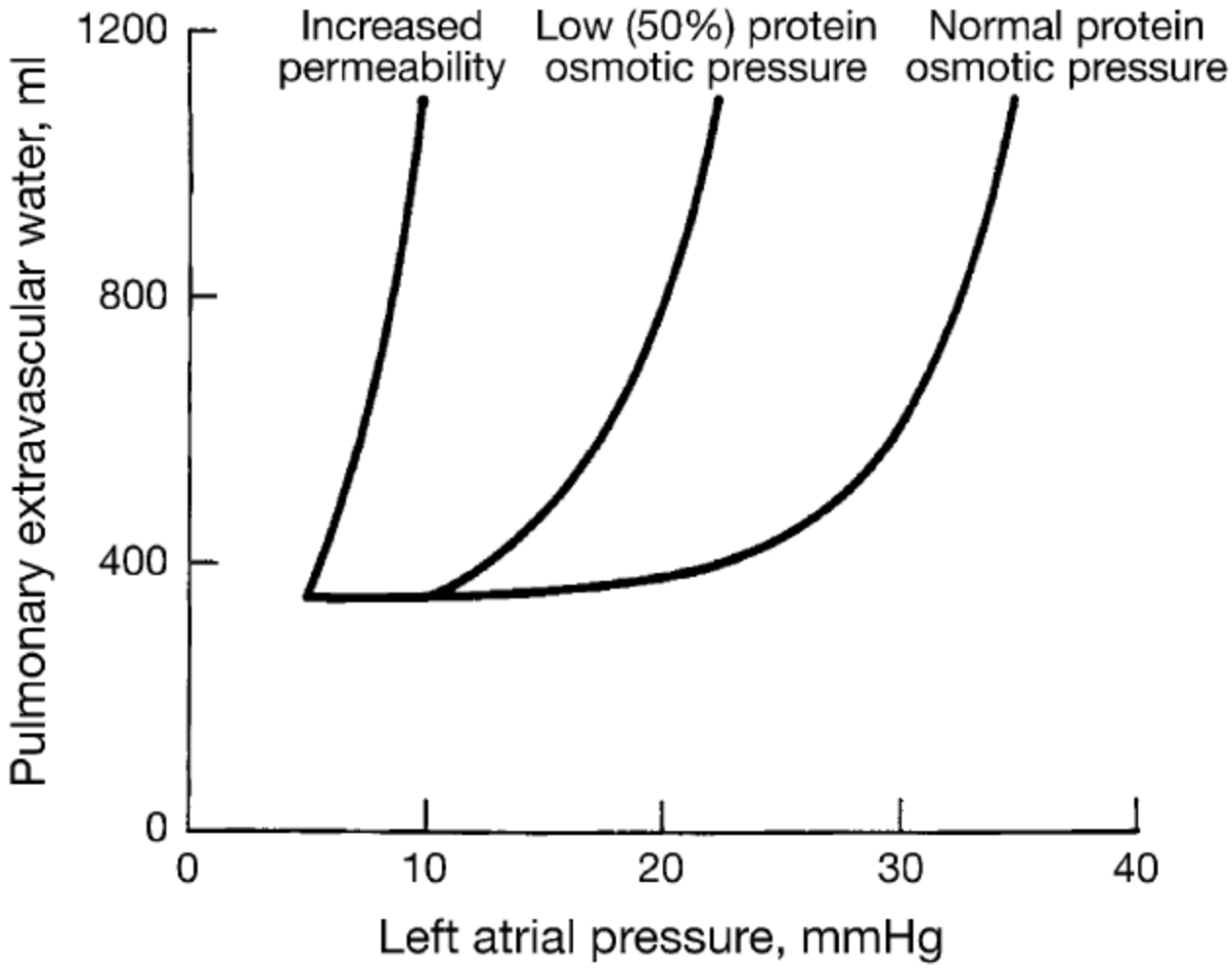
ESC 2008

Starling forces involved in APE



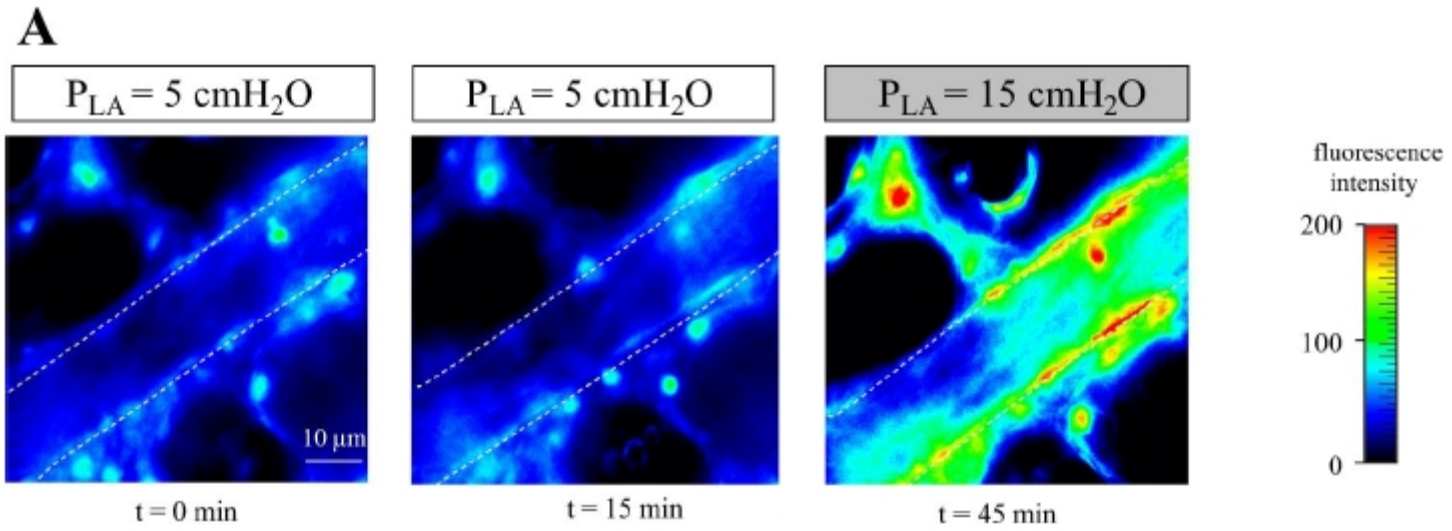


Ware L. N Engl J Med 2005

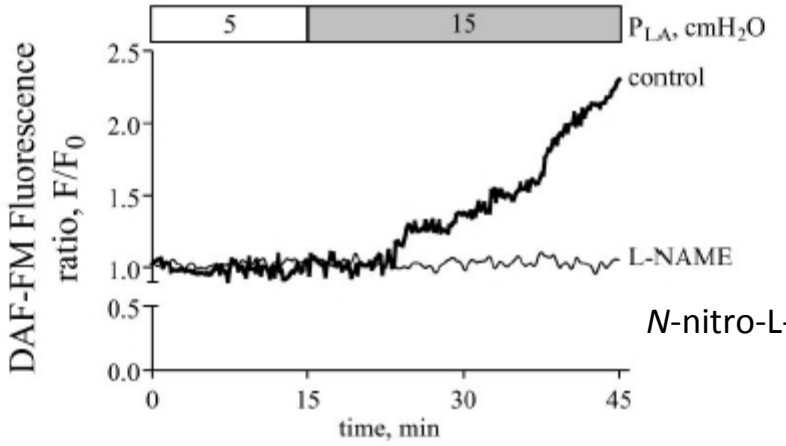


Murral JF- Int J Tuberc Lung Dis 2011

NO dependence of alveolar fluid reabsorption



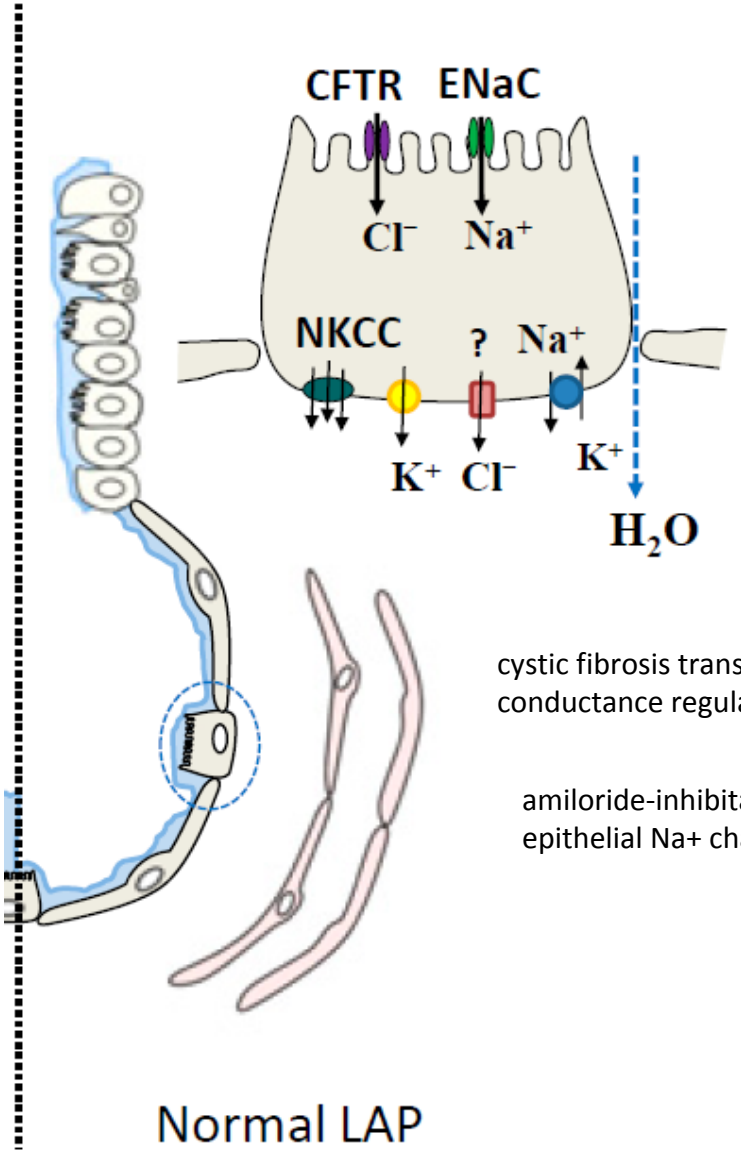
4-amino-5-methylamino-2-7-difluorofluorescein diacetate (DAF-FM DA)



N-nitro-L-arginine methyl ester (L-NAME)

Kaestle SM et al. Am J Physiol Lung Cell Mol Physiol 2007

Transcellular Na+ and Cl− movement across alveolar epithelial cells

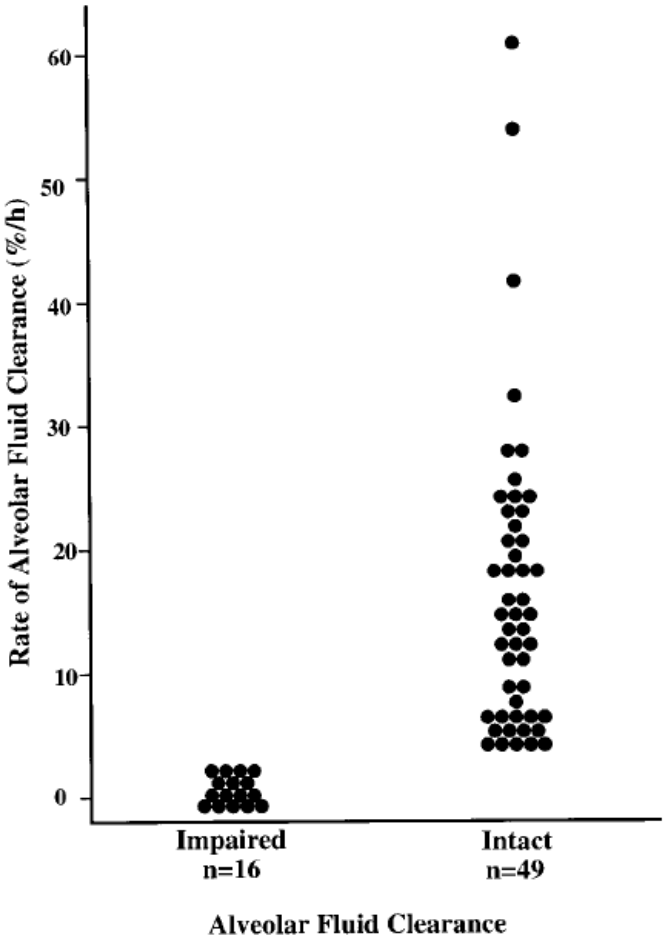


cystic fibrosis transmembrane conductance regulator

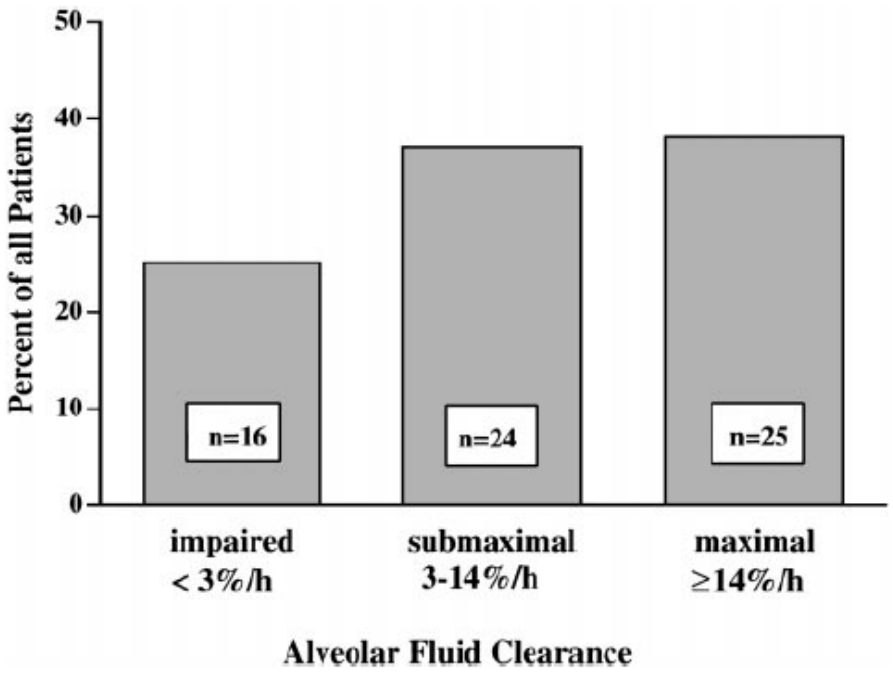
amiloride-inhibitable epithelial Na+ channel

Londino et al. PNAS 2013

ALVEOLAR FLUID CLEARENCE



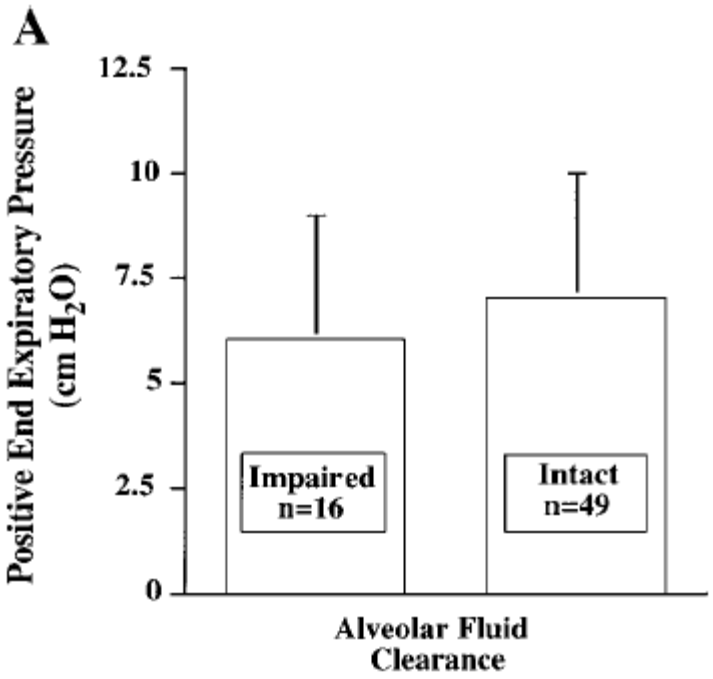
65 mechanically ventilated APE patients



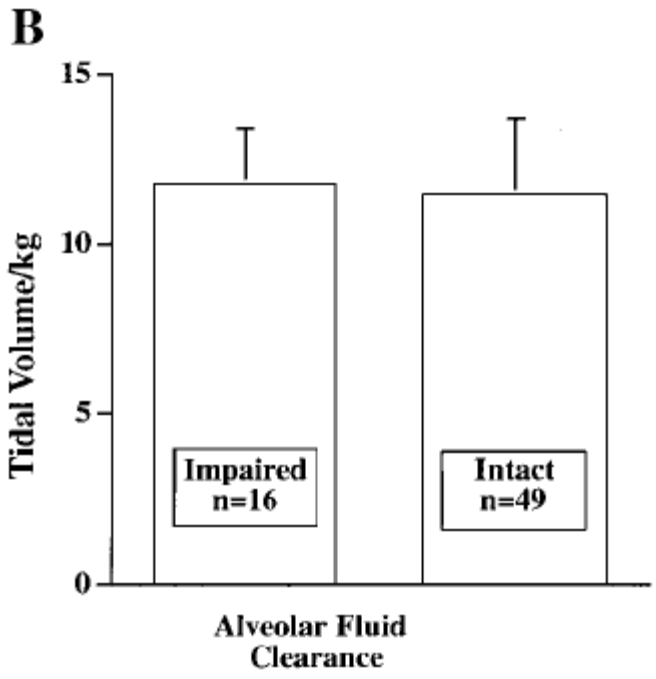
Verghese et al. J Appl Physiol 1999

ALVEOLAR FLUID CLEARENCE

PEEP

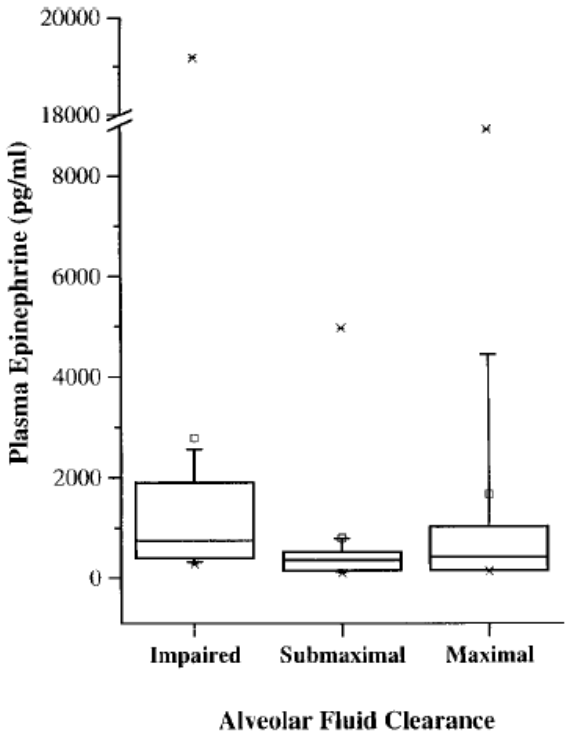


Tidal Volume



Verghese et al. J Appl Physiol 1999

Plasma Epinephrine



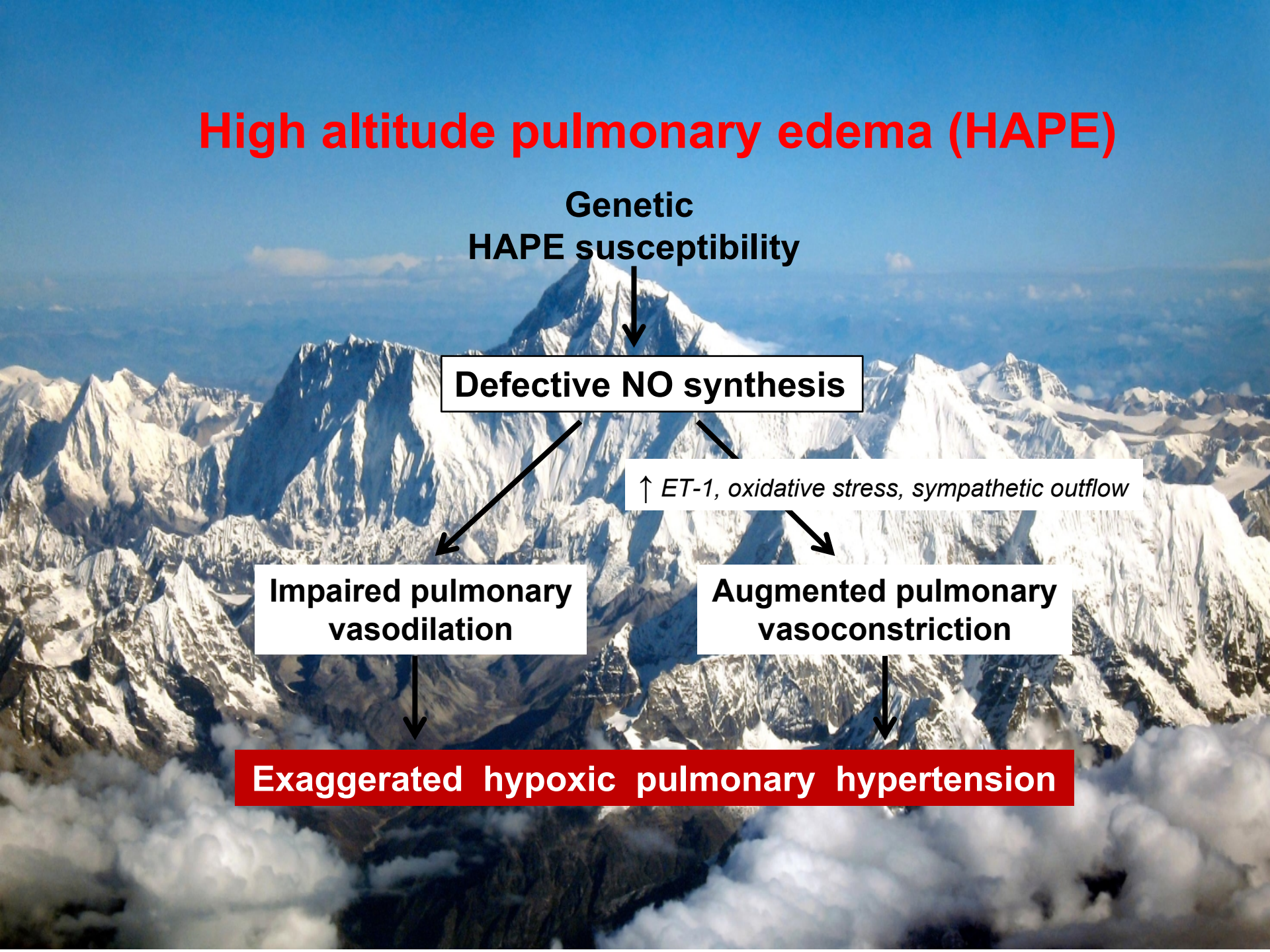
Low reabsorption rate was not related to LVEF or PCWP

Table 6. *Comparison of outcomes in patients with intact vs. impaired alveolar fluid clearance*

Outcome Variable	Alveolar Fluid Clearance: Impaired ($n=16$)	Alveolar Fluid Clearance: Intact ($n=49$)	*P* Value
Change in alveolar-arterial oxygen difference at 4 h	4 ± 100	−40 ± 132	0.19
Change in alveolar-arterial oxygen difference at 24 h	−167 ± 198	−268 ± 172	0.03
Days of unassisted ventilation, median (range)	8 (0–27)	23 (0–27)	0.10
Hospital mortality, %	44%	26%	0.20

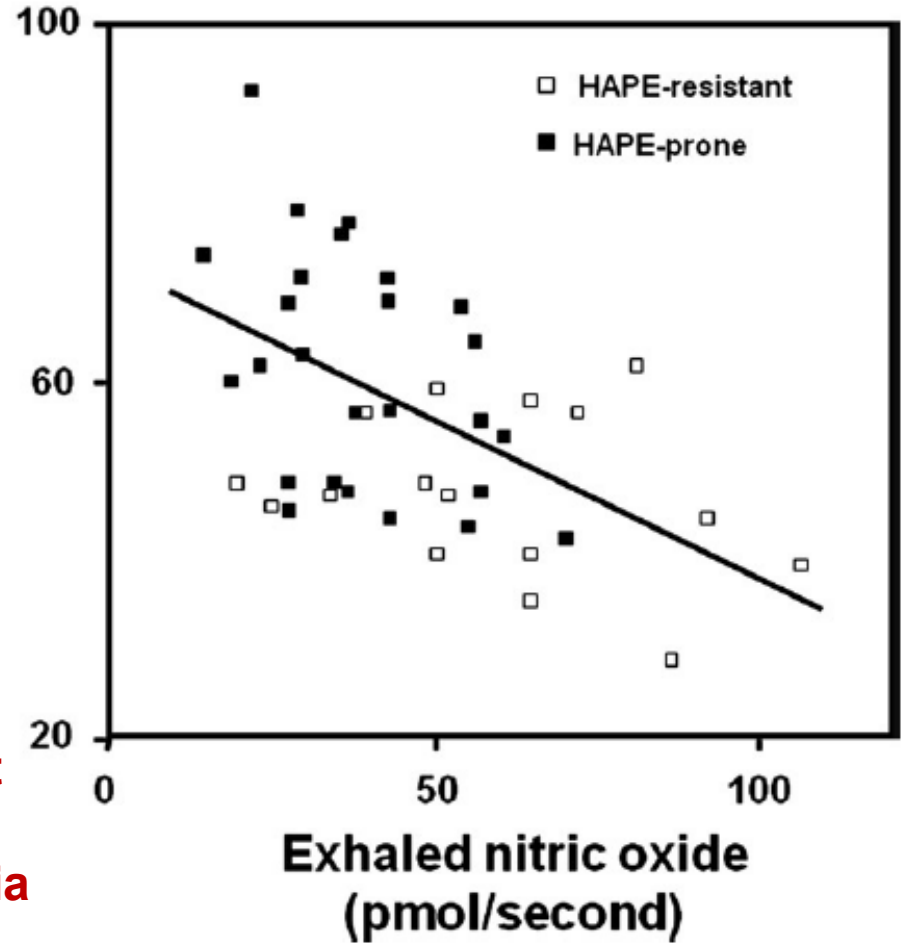
Values of change in alveolar-arterial oxygen difference at 4 and 24 h are means ± SD.

Verghese et al. J Appl Physiol 1999


High altitude pulmonary edema (HAPE)
Genetic
HAPE susceptibility
Defective NO synthesis
↑ ET-1, oxidative stress, sympathetic outflow
Impaired pulmonary vasodilation
Augmented pulmonary vasoconstriction
Exaggerated hypoxic pulmonary hypertension

High altitude pulmonary edema (HAPE)

GREATER HYPOXIC PULMONARY VASOCONSTRICTION



IMPAIRMENT OF ALVEOLAR FLUID CLEARANCE

Altered tansepithelial Na transport

- **Genetic**
- **Induced by hypoxia-hypothermia**

Duplain H, et al. N Engl J Med 2000

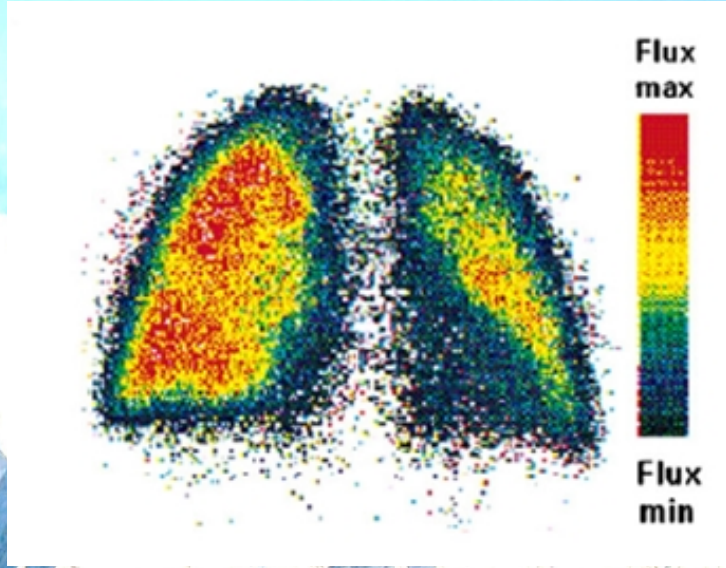
U. Scherrer et al. Prog Cardiovasc Dis 2010

To cause APE, the ↑↑↑ PAP has to be transmitted to the capillaries

Inhomogeneous hypoxic pulmonary vasoconstriction

Some capillaries are not protected
Regional overperfusion with ↑ PCP

Hypoxia→ pulmonary veno-constriction
Increased vascular resistance downstream to the site of fluid filtration
Further increase in PCP



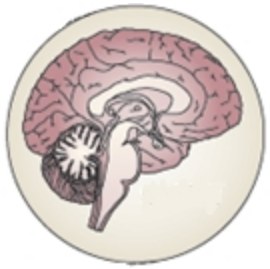
Impairment of alveolar fluid clearence

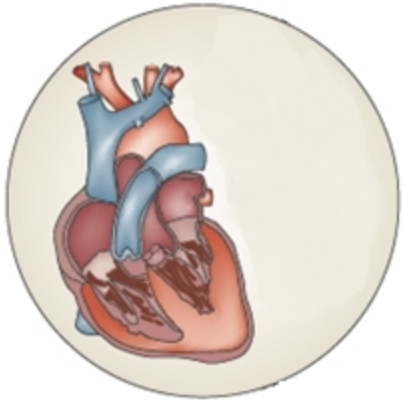
Scherrer U, et al. N Engl J Med 1996

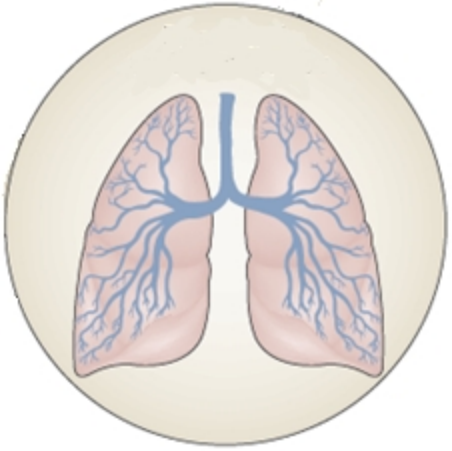
U. Scherrer et al. Prog Cardiovasc Dis 2010

Capilary stress failure
with altered permeability

BAL: erythrocytes and large molecular weight proteins







Neurogenic pulmonary edema

Spinal cord injury, Severe epileptic grand mal seizure,
Primary spinal cord hemorrhage, Intracerebral bleeding,
Brain trauma, Subdural hematoma, Subarachnoid hemorrhage

Elevation of intracranial pressure

Rapid systemic sympathetic discharge

Peripheral vasoconstriction

Increase in systemic blood pressure

Elevated venous return
Reduction LV compliance

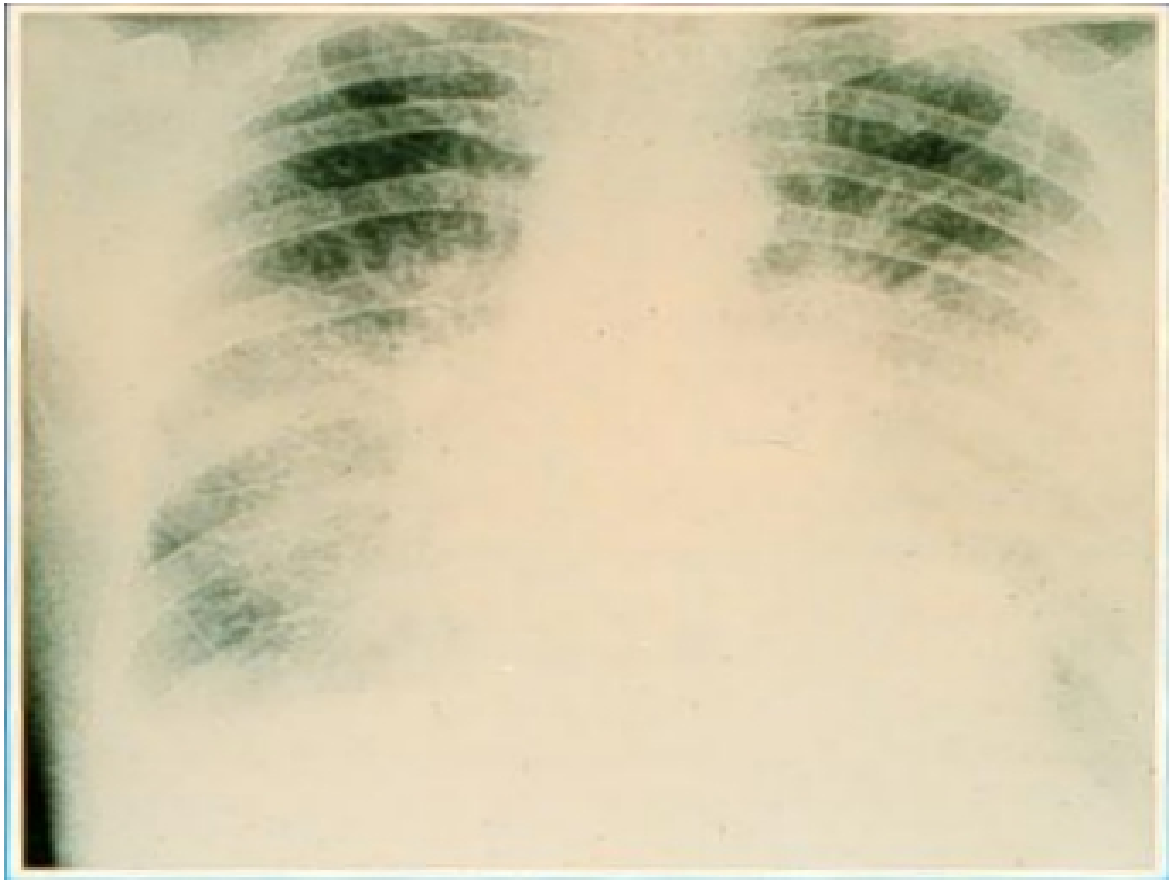
Constriction of the pulmonary veins
Hydrostatic increase in PCP

Damage to the alveolar wall and the leakage of fluid into the interstitium and intraalveolar space, hemorrhage and intra-alveolar accumulation of protein-rich edema fluid

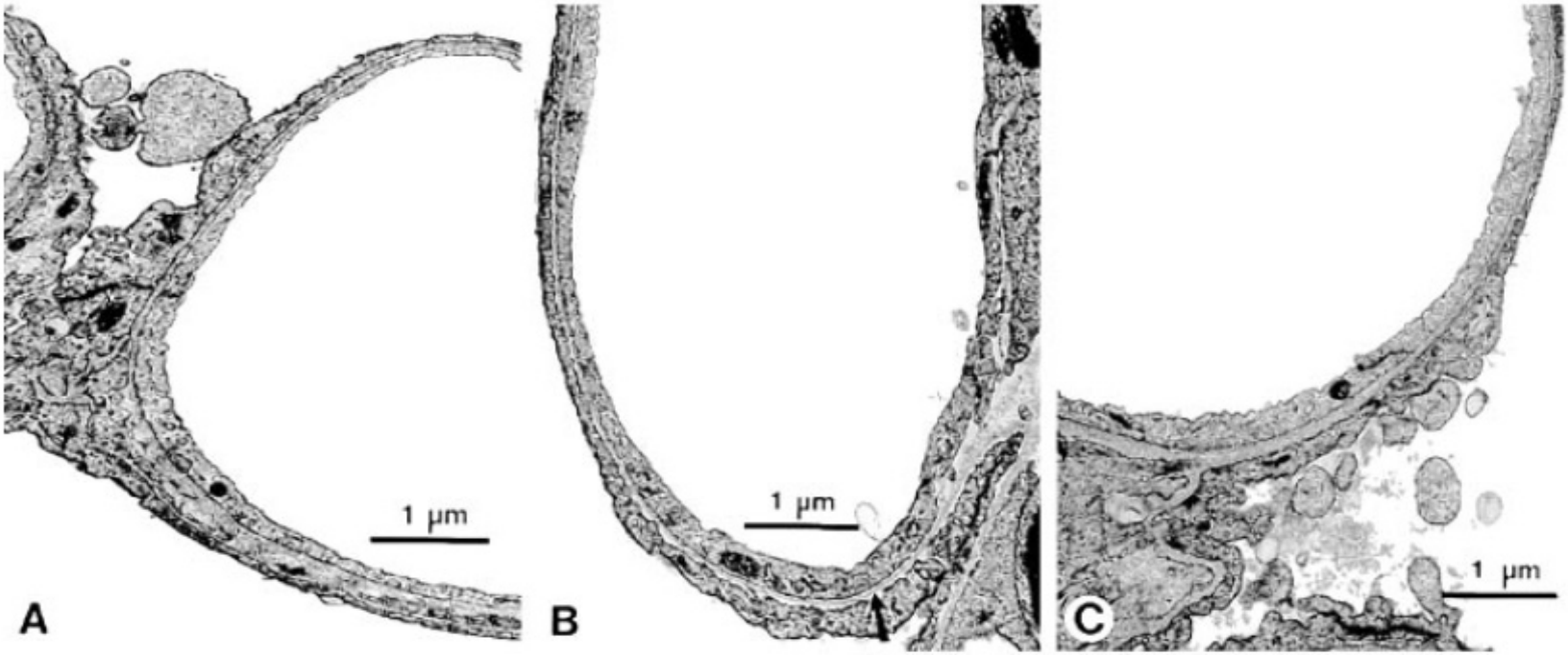
APE in marathon runners

It is likely to occur as a result of overload of the **vascular and lymphatic drainage systems** because of the high cardiopulmonary demands of intense exercise, resulting in APE

SEVERE ACUTE CARDIOGENIC PULMONARY EDEMA

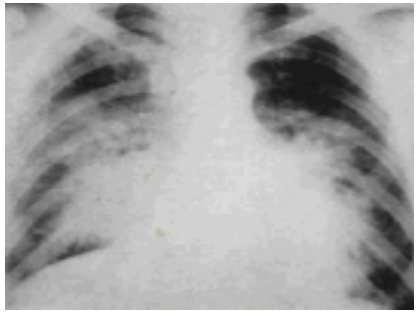


alveolar-capillary stress failure



The increase in capillary pressure or volume disrupts the anatomic configuration of the membrane

M. Guazzi et al. Chest 2003



ACUTE HEART FAILURE

Backward hemodynamic effects
Increasing hydrostatic pressure
Interstitial and Alveolar fluid filtration

Alveolar-capillary stress failure

REVERSIBILITY

CHRONIC

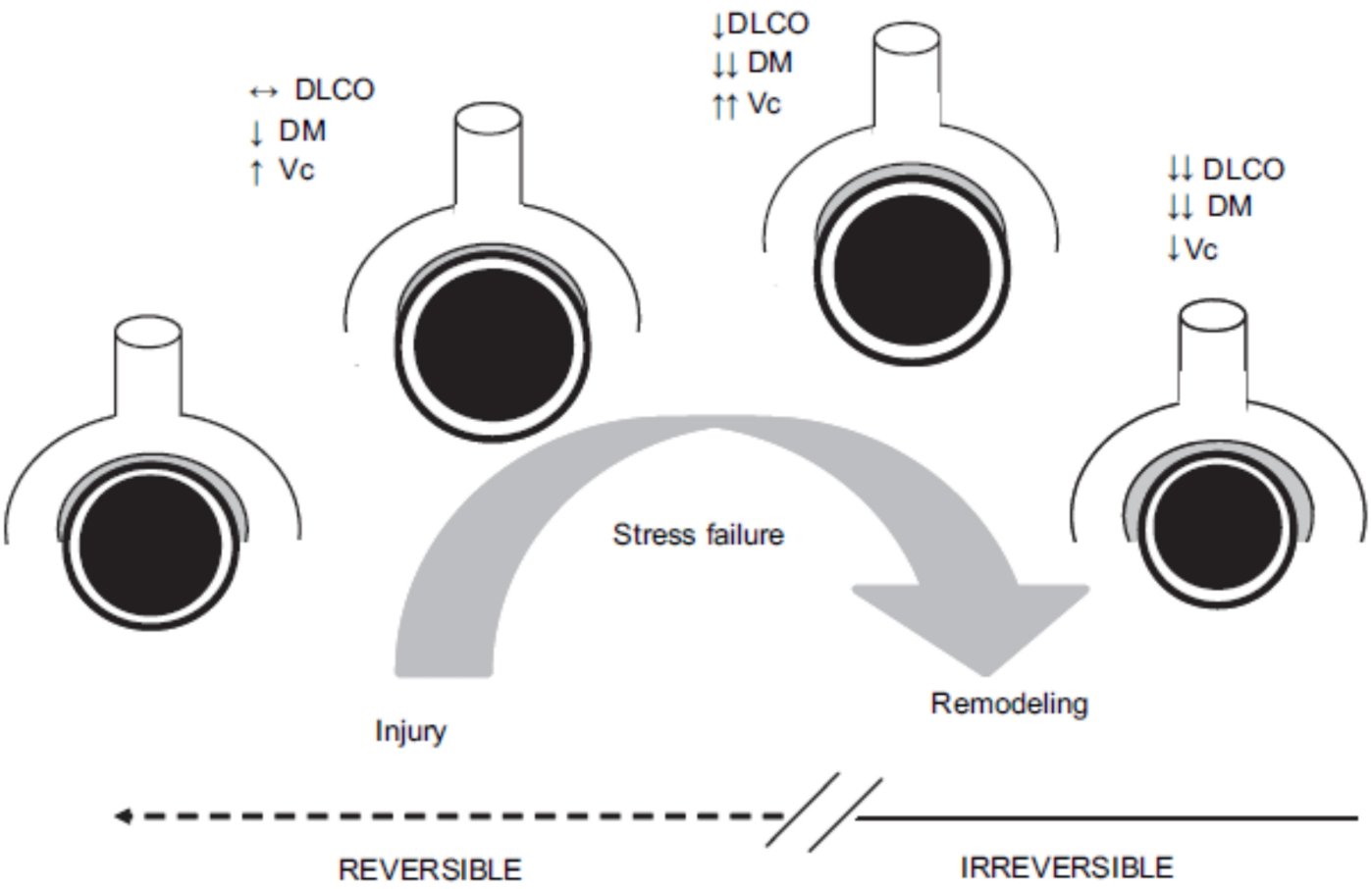
Neurohormonal activation
(Angiotensin II, Norepinephrine)
Inflamatory reaction
(Cytotoxic stimuli: IL,TNFα)
Gene reexpression

Lung capillaries and Tissue membrane
REMODELING

Impaired endothelial permeability
Loss of active alveolar clearence capacity
Extracellular matrix thickening

Permanent lung dysfunction

Modified from M. Guazzi et al. Chest 2003



DM: Alveolar-capillary membrane gas conductance
DLCO: Diffusion capacity
Vc: Capillary Volume

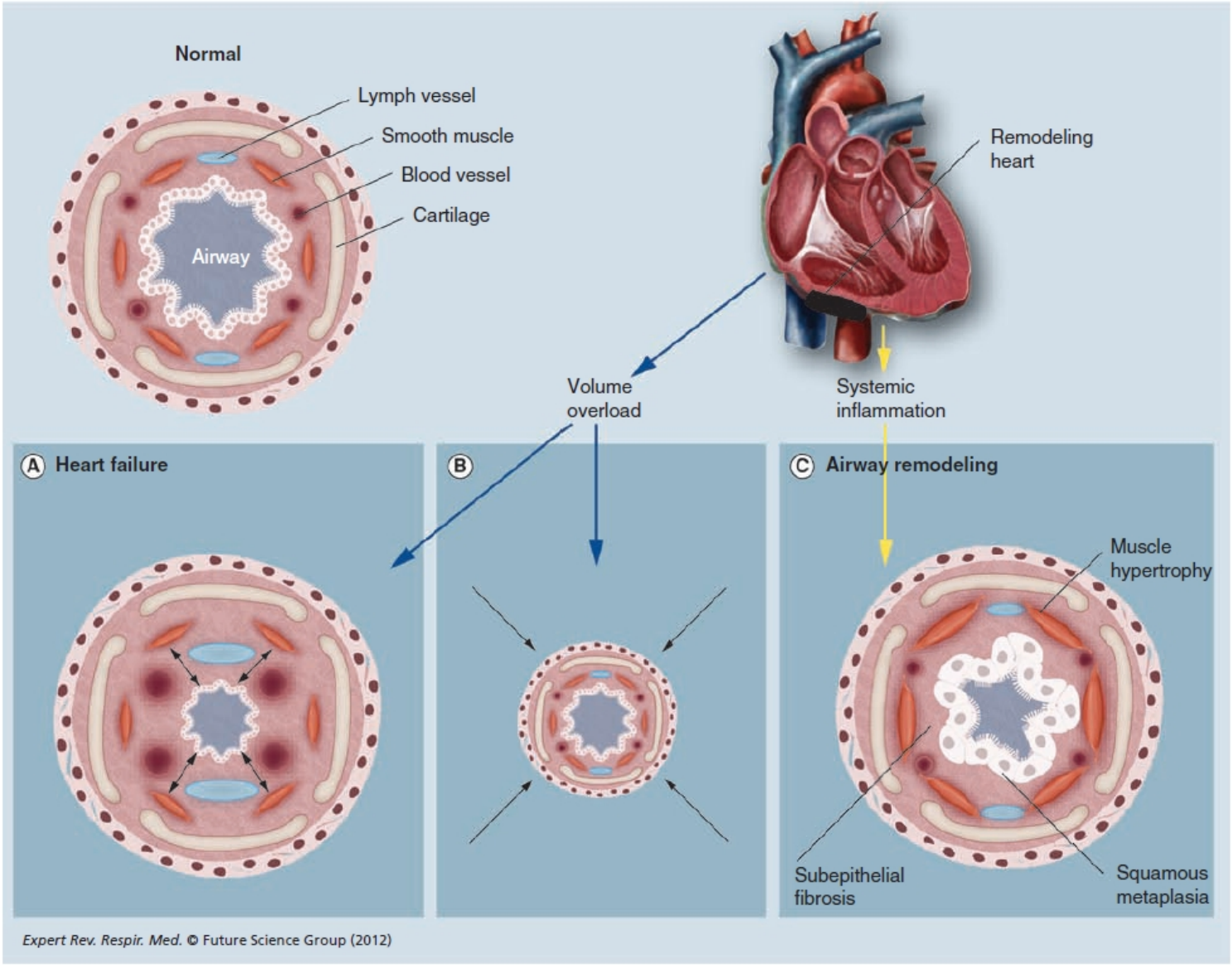
M. Guazzi. J Cardiac Failure 2008

Pulmonary function in CHRONIC HF patients according to Peak-VO2

$_{Peak}VO_2$	n	FVC	FEV-1	DLCO	DM	VC
<12	25	67%	76%	65	27.7	83
12-16	75	80%*	85%*	80*	30.3	104
16-20	64	85%*	90%*	80*	31.1	103*
>20	26	87%*	98%*	90*	42.3*	111*

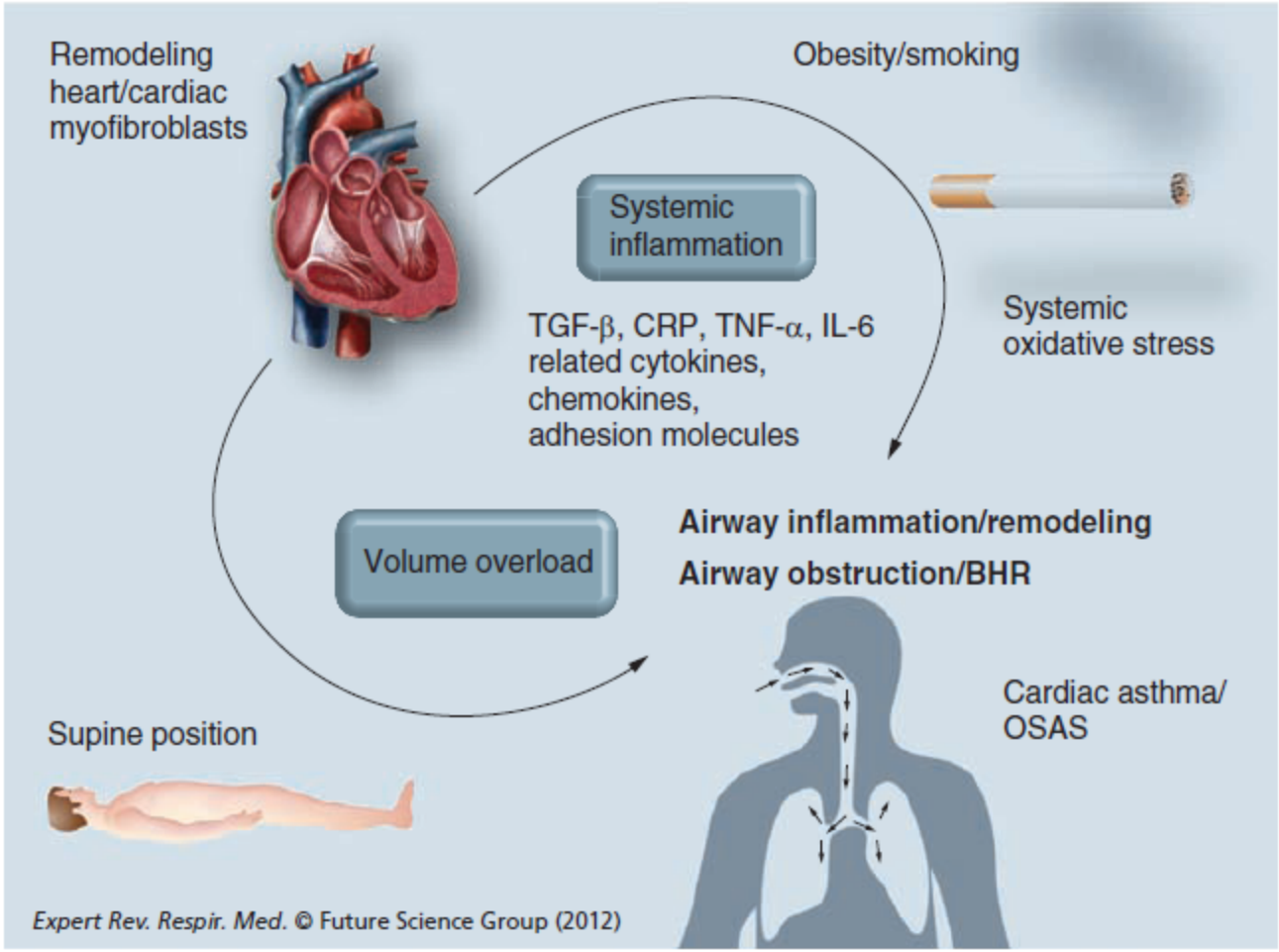
* p> 0.05 or 0.01

P. Agostoni. Pulmonary Pharmacology & Therapeutics 2007

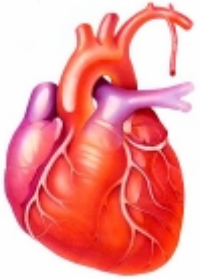


Tanabe T Expert Rev Resp Med 2012

Prevalence asthma syndromes in > 65 years is 6-10%
Elderly with CHF have 35% cardiac asthma (3.5 times greater)

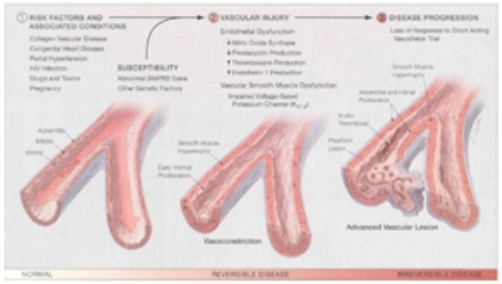


Tanabe T Expert Rev Resp Med 2012

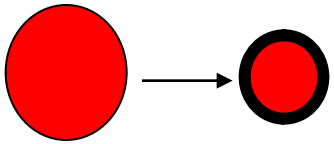


LV Dysfunction

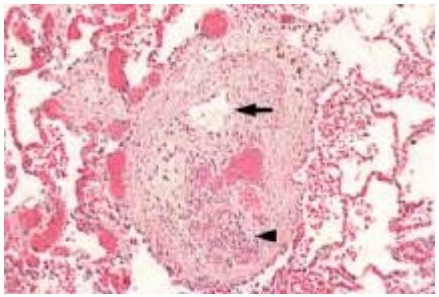
↑ EDP | ↑ Neurohormones (local/systemic) | ↑ Cytokines (local)



Pulmonary EC Dysfunction (↑ ET/↓ NO)



Pulmonary Vasoconstriction | Pulmonary Vascular Remodeling



Secondary Pulmonary Hypertension

RV Dysfunction
↑ Morbidity/Mortality

Denzil L. Moraes. Circulation. 2000

Conclusions

- Hydrostatic pulmonary edema is the common clinical presentation of LV-AHF. An imbalance in the starling forces in the capillaries is the main pathophysiological mechanism, but NO-dependent alveolar fluid reabsorption, Cl^- and Na^+ transport alveolar fluid secretion and alveolar-capillary stress failure with inflammatory activation are other important contributing factors
- Individual susceptibility may explain why in different scenarios some patients tend to present severe APE
- Chronic and severe decompensations may lead to persisting alterations in the lung parenchyma and bronchi with a restrictive pattern, cardiac asthma and finally, pulmonary hypertension