Fluid and electrolyte balance in the surgical patient

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WATER

- involved in every level of body function
  creates environment for life

global hemodynamics
microcirculatory hemodynamics
cells
mitochondria
biochemical pathways

plays crucial role in the treatment

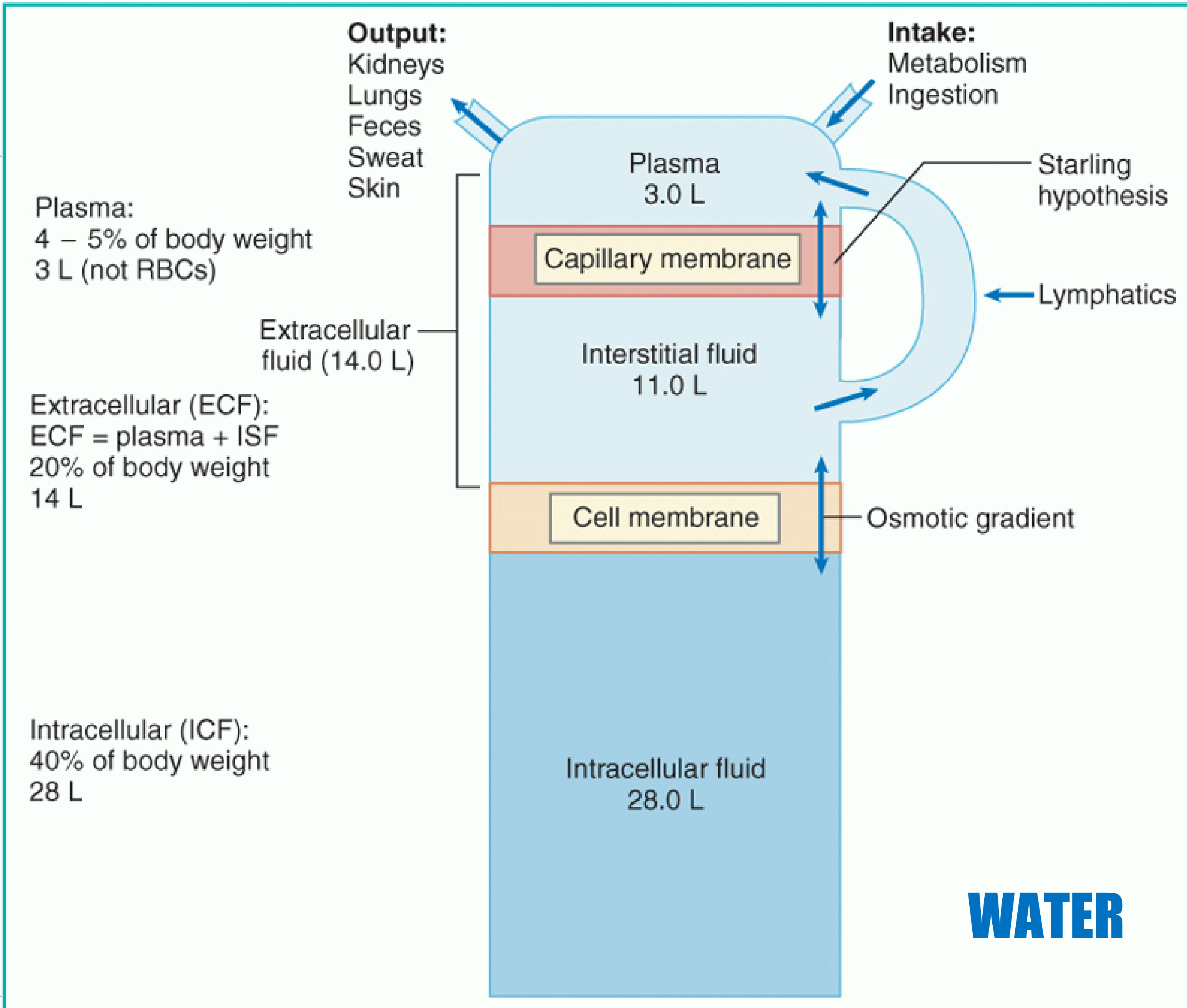
TBW (Total Body Water)

- Total volume of water within the body
- Decreases with: increasing body fat; increasing age
- General rule: TBW - **60 % body weight in men**
  - 50 % body weight in women

TBW

- ICF (Intracellular fluid) = 2/3 TBW

- ECF (Extracellular fluid) = 1/3 TBW
  - Intravascular space (25 % ECF, 8 % TBW) - plasma
  - Interstitial space (75 % ECF, 25 % TBW)
    - free phase of fully exchangeable water
    - bound phase of minimally exchangeable water
    - transcellular compartment (cerebrospinal fluid, water in the cartilages, eye fluid, lubricants of serous membranes)



Output:
Kidneys
Lungs
Feces
Sweat
Skin
Intake:
Metabolism
Ingestion
Plasma:
4 – 5% of body weight
3 L (not RBCs)
Plasma
3.0 L
Starling hypothesis
Capillary membrane
Lymphatics
Extracellular fluid (14.0 L)
Interstitial fluid
11.0 L
Extracellular (ECF):
ECF = plasma + ISF
20% of body weight
14 L
Cell membrane
Osmotic gradient
Intracellular (ICF):
40% of body weight
28 L
Intracellular fluid
28.0 L
WATER

Effective circulating volume

- Portion of the ECF that perfuses the organs
- Normally = intravascular volume
- Under pathological contitions

i.e. bowel obstruction, pancrteatitis, sepsis

↓

”third space loss”

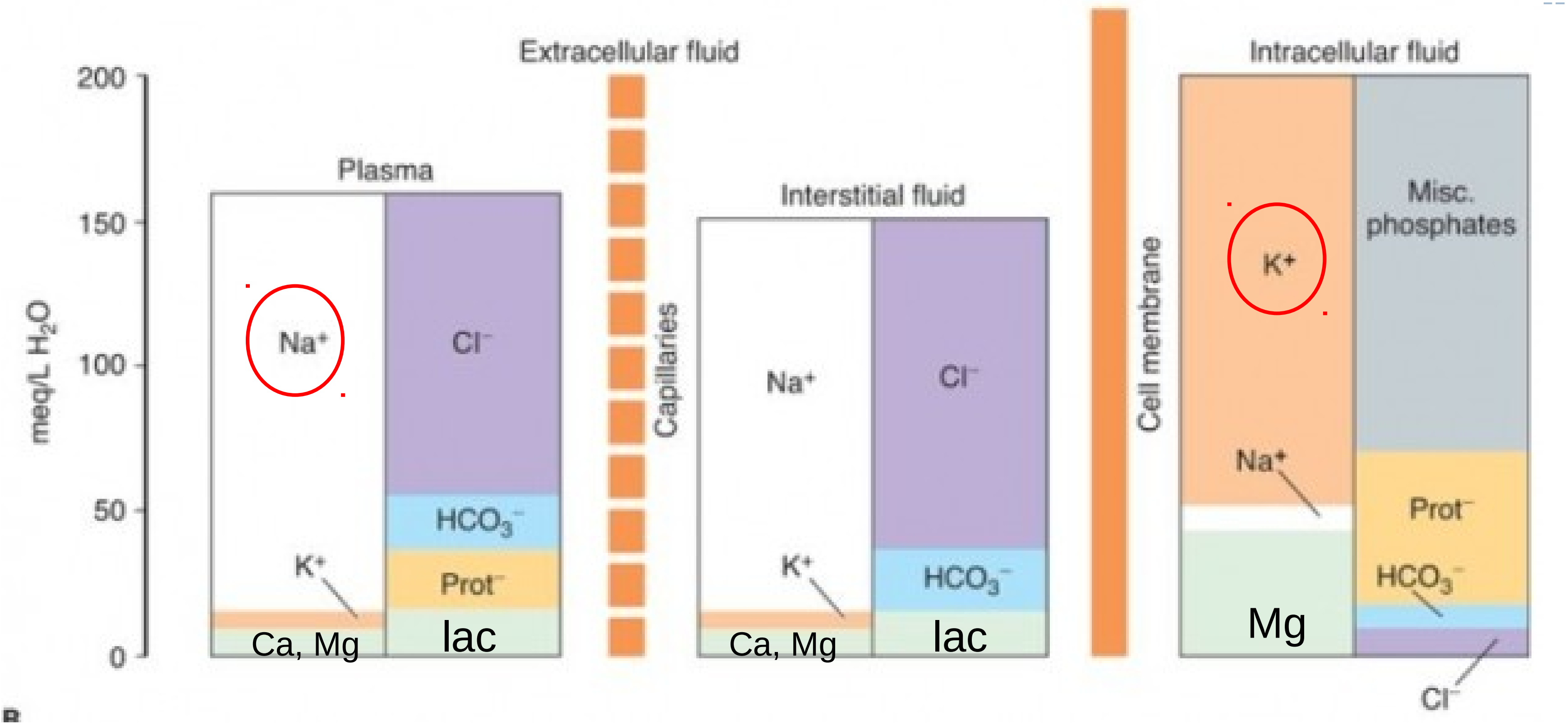
↓

intravascular volume – diminished

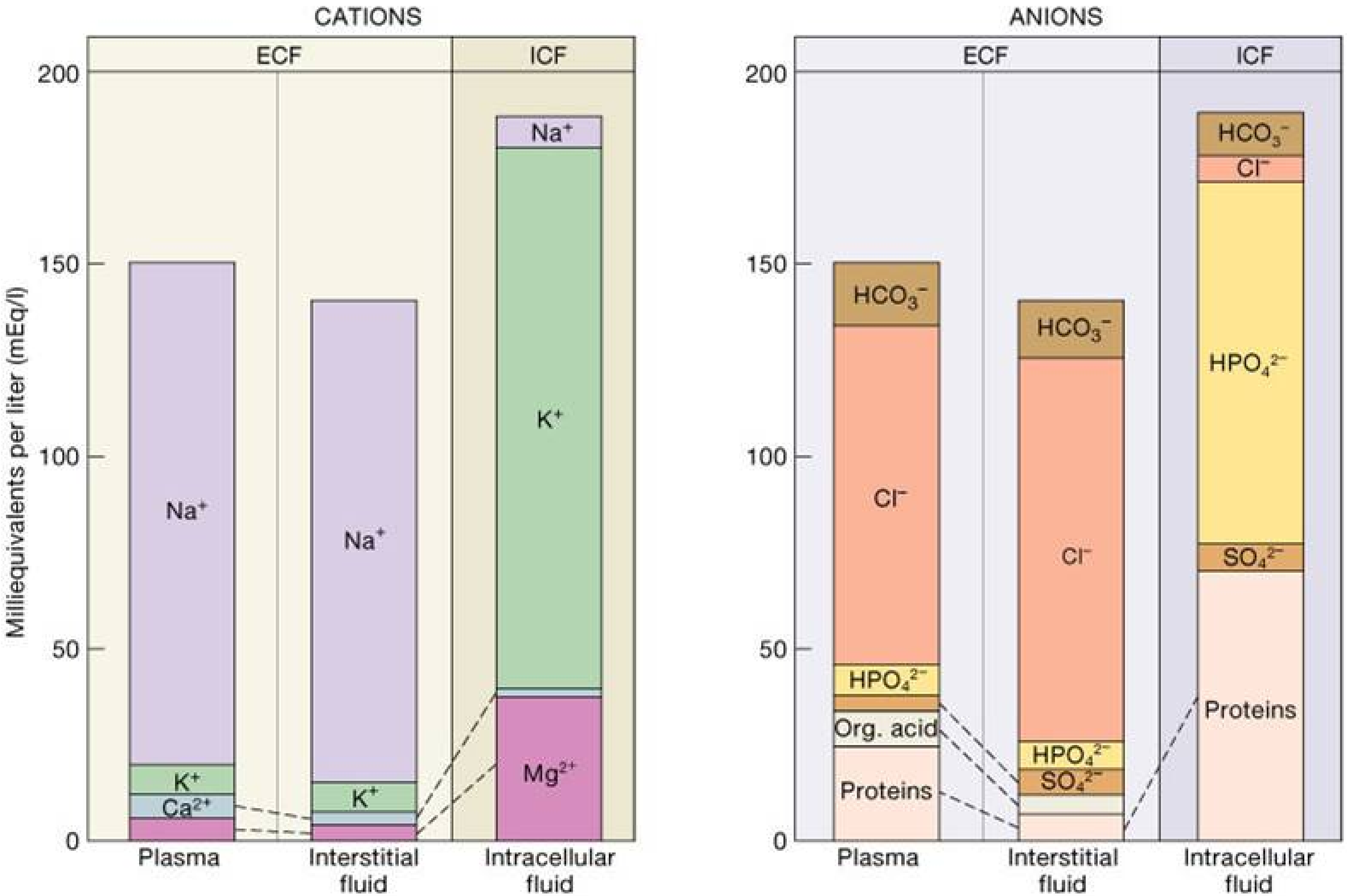
hypoperfusion

Needs: restoration of circulating volume and treatment of vasodysregulation

ECF ICF



Electrochemical equilibrium



Electrochemical equilibrium

Volume Control Mechanisms

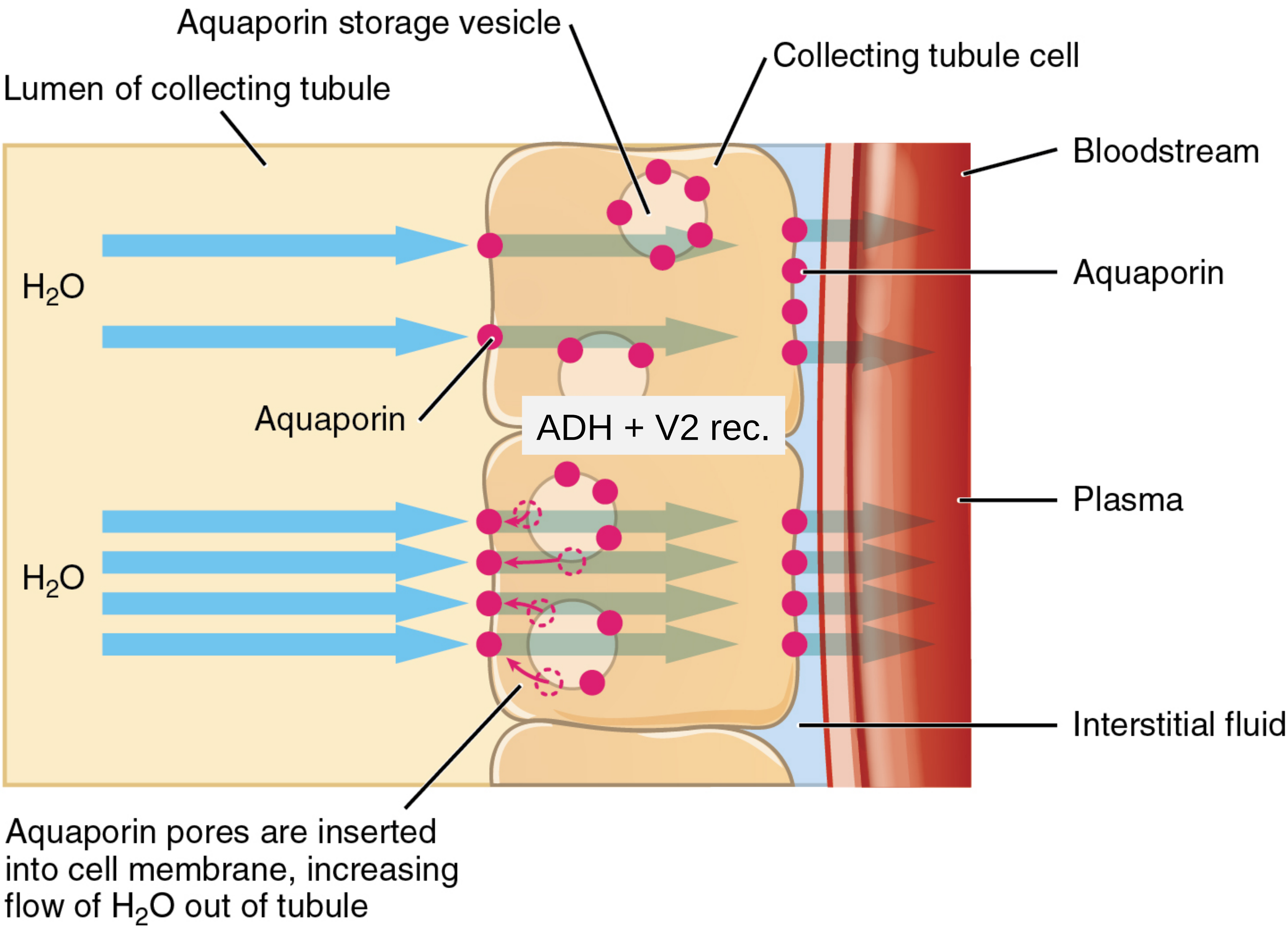
- Plasma osmolality – controlled **289 mOsm/kg H_2O**
- Regulators:

THIRST

ADH (Antidiuretic Hormone)

Osmoreceptor cells in the paraventricular and supraoptic nuclei of the hypothalamus

ADH + nicotine, ether, morphine, barbiturates, tissue injury
ADH - ethanol



Renal collecting ducts

- Drugs ! V2 antagonists (vaptans)

Volume Control Mechanisms

- Baroreceptors: sympathetic and parasympathetic connections but less precise than osmoreceptors

  - vena cava
  - atria
  - aortic arch (extreme changes)
  - carotid arteries (extreme changes)
  - intra-renal at the afferent arteriole (renin)

Volume Control Mechanisms

- Endocrine and hormonal factors:

  renin – angiotensin – aldosterone (RAA) system

  natriuretic peptide system

  (ANP – atrial; BNP – brain; CNP)

  renal prostaglandins (PGE2, PGI2)

  endothelins

  NO

Water losses

- SENSIBLE

  urine (800-1500 ml/24h)

  stool (0-250 ml/24h)

  sweat (minimal unless hot climate)

- INSENSIBLE

  skin

  lungs 600-900 ml/24h

  fever + 10% for each degree > 37.2

Maintenance Fluid Therapy

- Replaces fluids normally lost during the course of a day

Weight - based formulas to calculate requirements

„4-2-1 rule”

first 10 kg BW:	4 ml/kg/h
second 10 kg BW:	2 ml/kg/h
each additional 10 kg BW:	1 ml/kg/h

In severe obesity – ABW (Adjusted Body Weight)

ABW = IBW + 1/3 (Actual BW – IBW)

Maintenance Fluid Therapy

- Daily about 25-30 ml/kg BW

- Maintenance fluid – hypotonic

5 % dextrose (glucose)/1 + 2/ 0,9% NaCl + 20 mEq KCl

- provides appropriate quantity of Na, K

Resuscitative Fluid Therapy

- Replaces preexisting deficits or additional ongoing losses
- Crystalloid – the most common category of fluids used
- Isotonic (or nearly isotonic) salt solution without dextrose

Lactated Ringer’s solution

or new salt solutions

Fluid escape

- Capillary endothelium is permeable

  - crystalloid distributes between

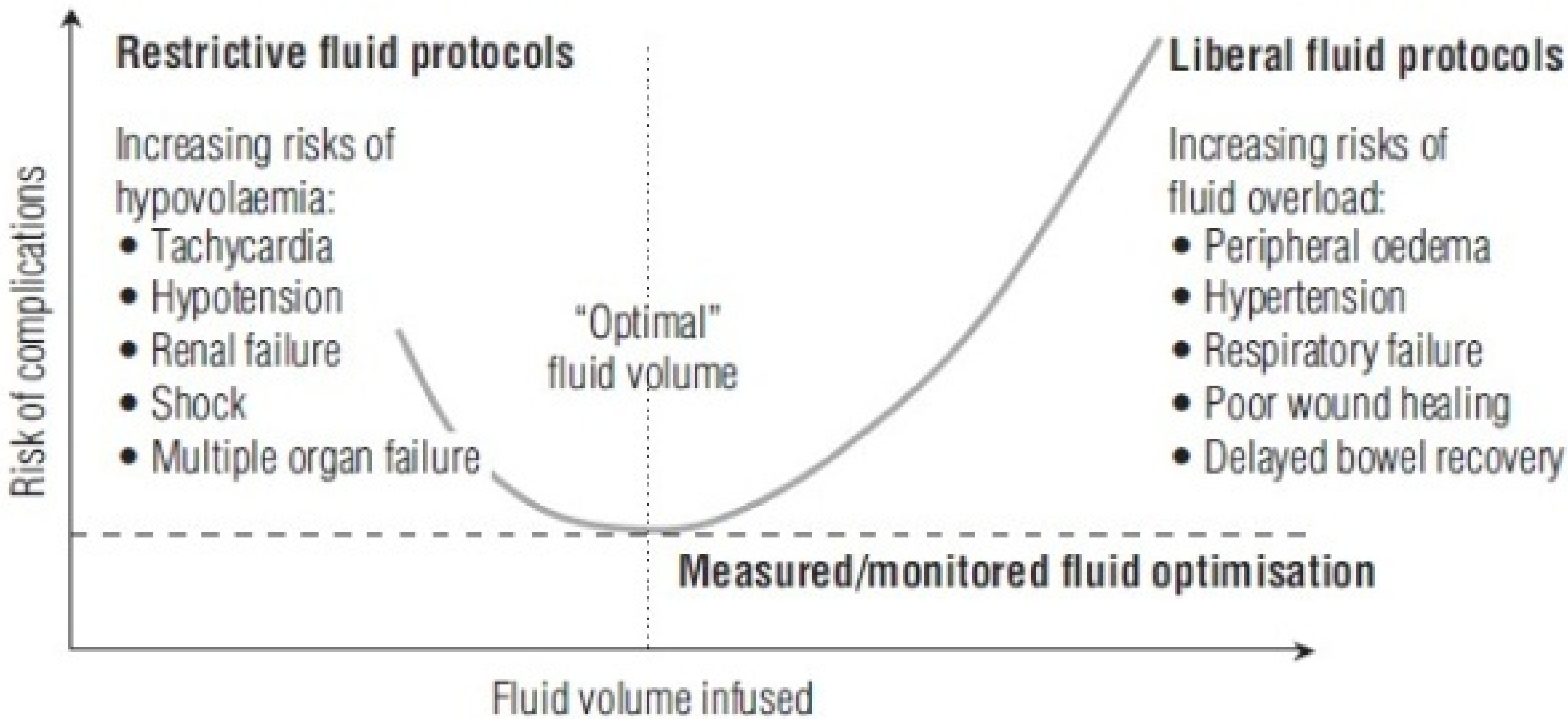
  the intravascular space (25% ECF) and

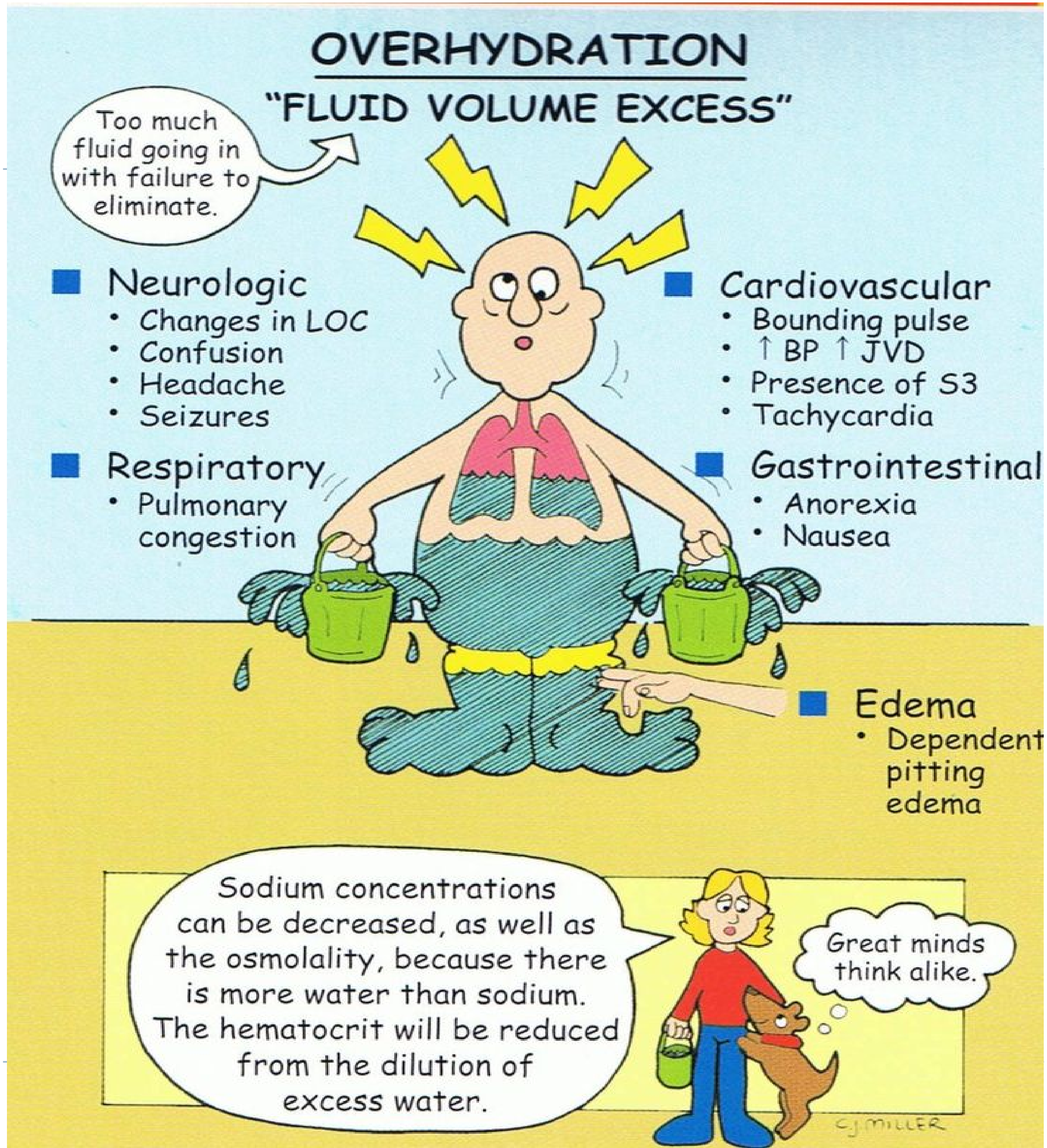
  the interstitial space (75% ECF)   1: 3

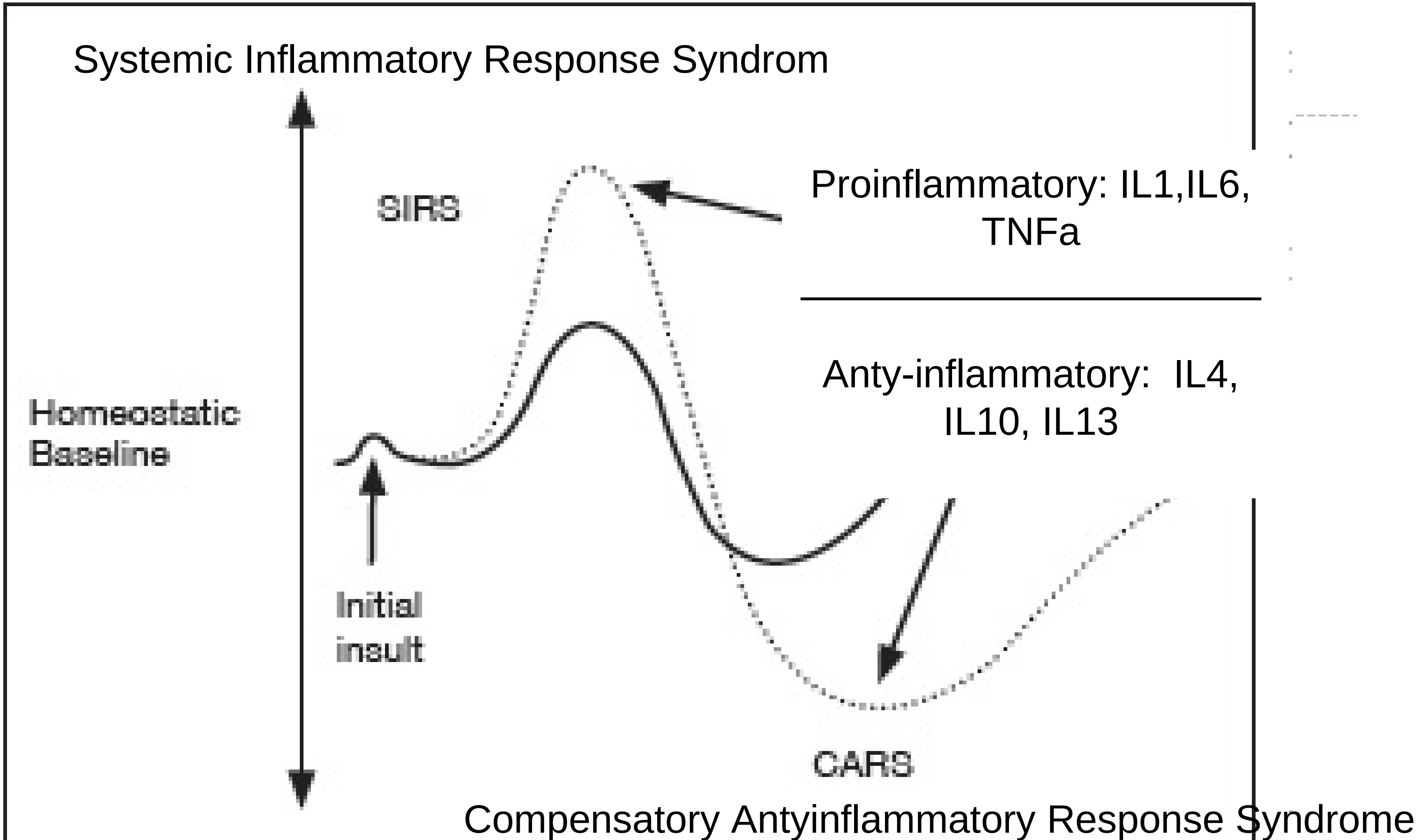
  so FOR EACH LITER OF CRYSTALLOID INFUSED IV 250 ml remains IV and 750 ml diffuses into interstitial space

Crystalloids have their own pro-inflammatory effect !

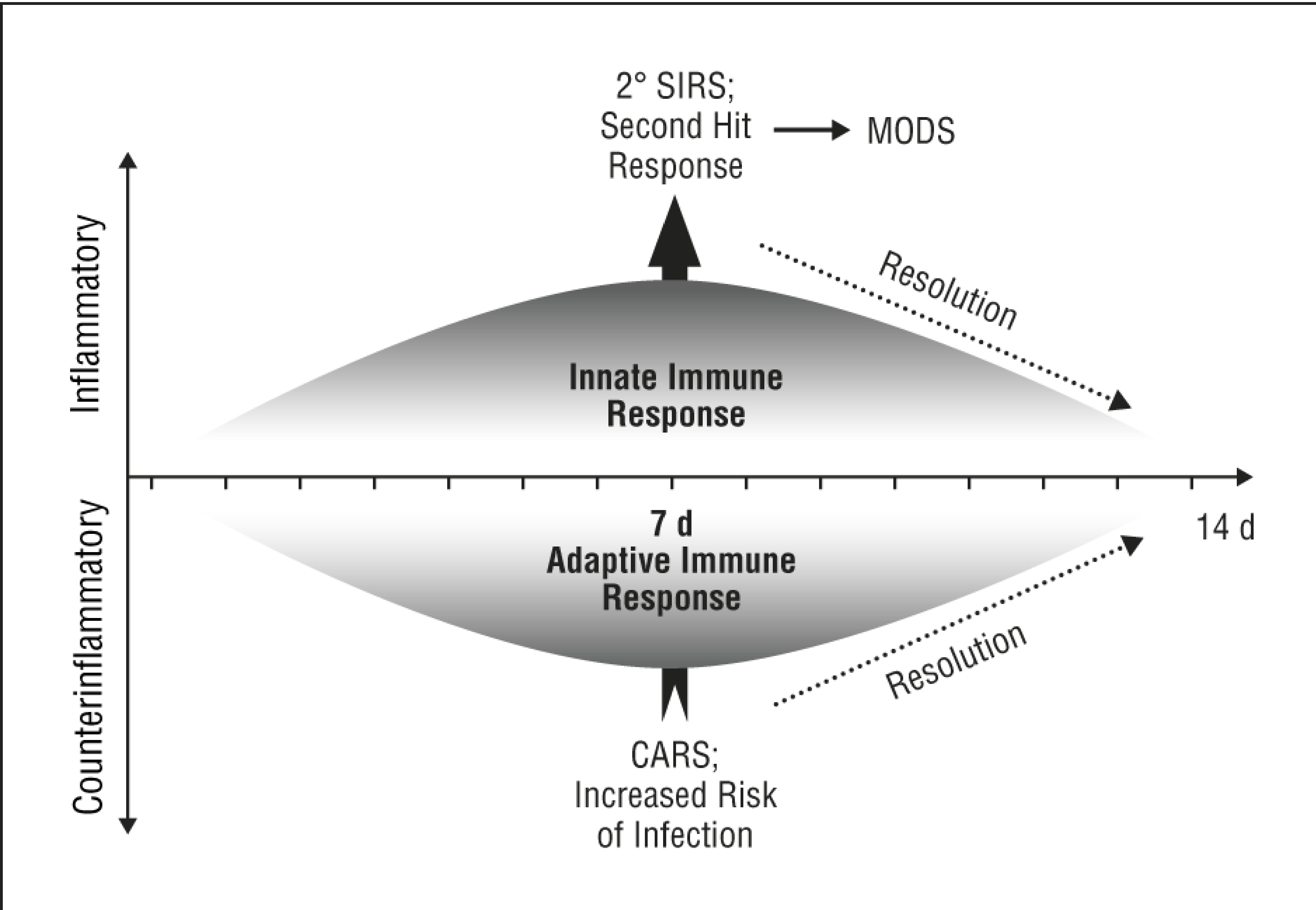
2 Hypothetical curve of the risk of fluid therapy-related complications versus volume of fluid infused




OVERHYDRATION
"FLUID VOLUME EXCESS"
Too much fluid going in with failure to eliminate.
Neurologic
• Changes in LOC
• Confusion
• Headache
• Seizures
Respiratory
• Pulmonary congestion
Cardiovascular
• Bounding pulse
• ↑ BP ↑ JVD
• Presence of S3
• Tachycardia
Gastrointestinal
• Anorexia
• Nausea
Edema
• Dependent pitting edema
Sodium concentrations can be decreased, as well as the osmolality, because there is more water than sodium. The hematocrit will be reduced from the dilution of excess water.
Great minds think alike.
C.J. MILLER



Hypothetical biphasic metabolic/inflamatory response to trauma



2° SIRS;
Second Hit
Response
MODS
Resolution
Inflammatory
Innate Immune
Response
Counterinflammatory
7 d
14 d
Adaptive Immune
Response
Resolution
CARS;
Increased Risk
of Infection


NaCl 0,9 %

STEROFUNDIN ISO

	Osocze	Sterofundin® ISO	NaCl 0.9%
Na^+ (mmol/l)	142	145	154
K^+ (mmol/l)	4	4	-
Ca^{2+} (mmol/l)	2.5	2.5	-
Mg^{2+} (mmol/l)	1.25	1	-
Cl^- (mmol/l)	103	127	154
HCO_3 (mmol/l)	24	-	-
acetate	-	24	-
malate	-	5	-
osmolarity (mOsmol/kg H_2O)	290	290	286

Volta C.A., Alvisi V., Campi M., et al.: Influence of different strategies of volume replacement on the activity of matrix metallopreoteinases. Anesthesiology 2007;106:85-91

Volta et al.: Effects of two different strategies of fluid administration on inflammatory mediators, plasma electrolytes and acid/base disorders in patients undergoing major abdominal surgery: a randomized double blind study. Journal of Inflammation 2013 10:29.

Colloids

- Stay longer in the circulation then crystalloids
- Albumins (effective but expensive, often lost to the interstitial space)
- HES (hydroxy ethyl starch) 3%, 6%, 10%
- Gelatins

- effective but rather for resuscitative therapy

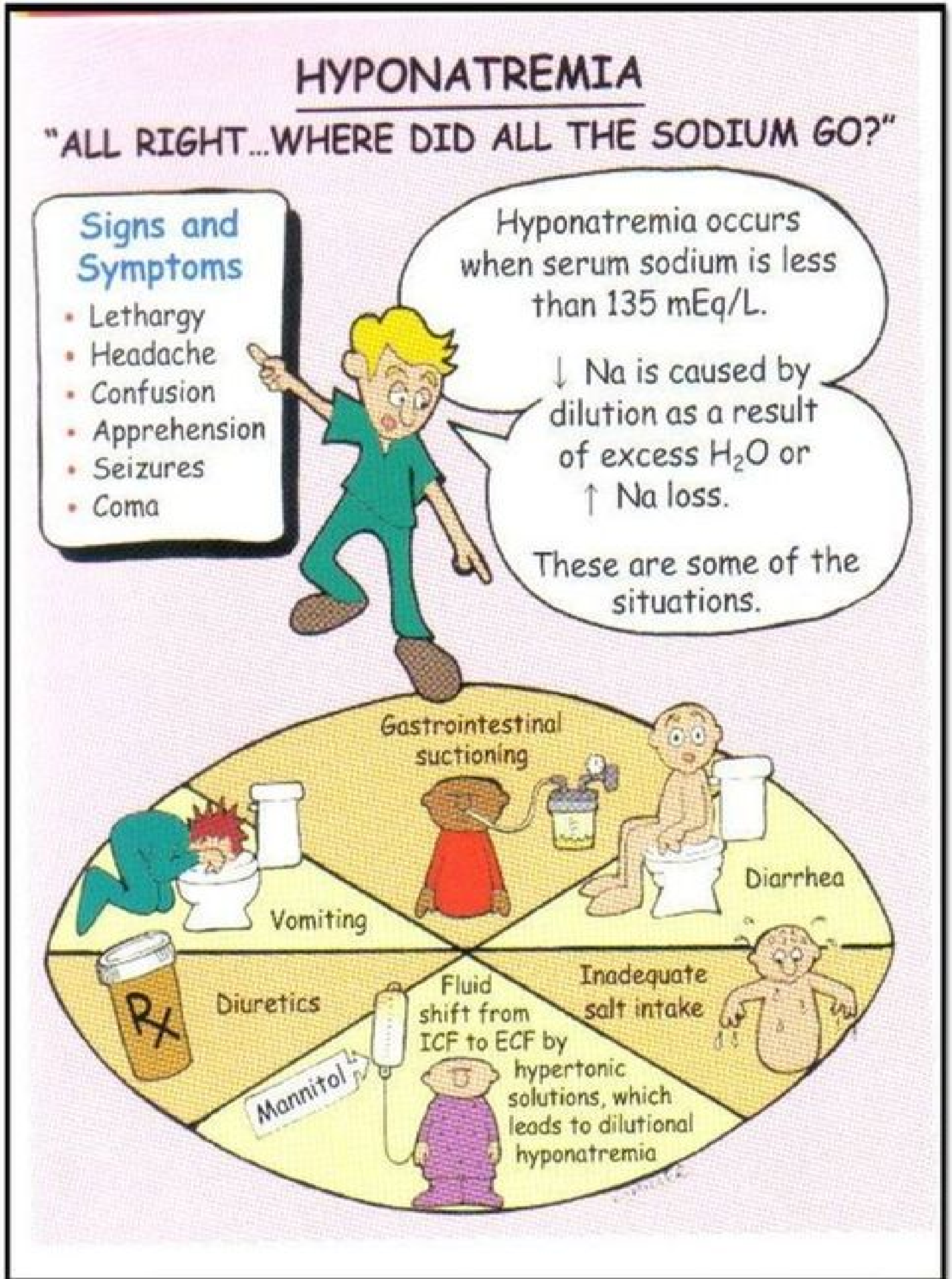
higher incidence of acute renal insufficiency

Sodium

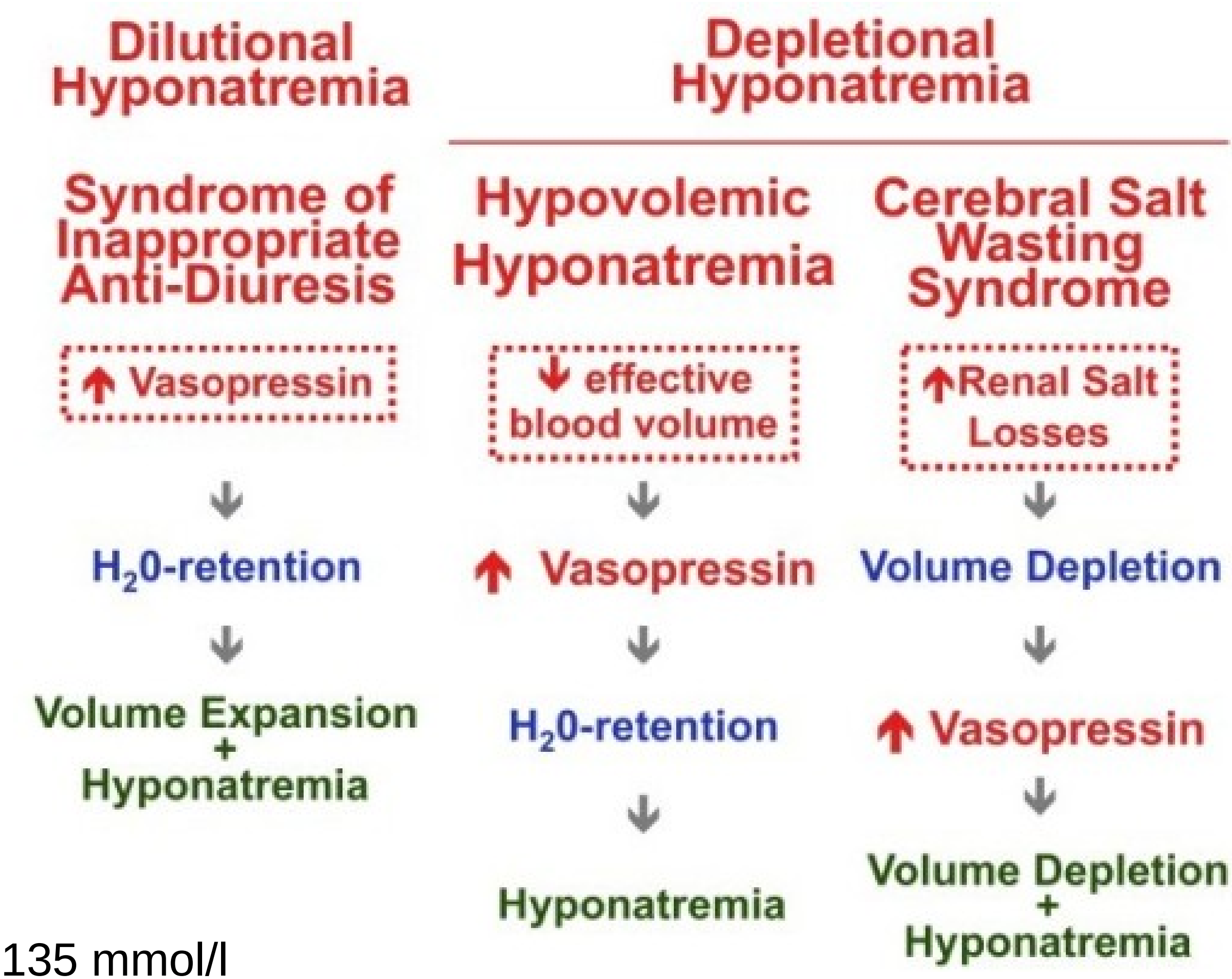
- Normal daily Na requirement 1-2 mEq/kg/24 h
- Primary extracellular cation
- Inverese relationship between Na and TBW \
  (when TBW increases, the Na level decreases)

→ **the Na level is a marker of TBW**

Sodium disorders are often in clinical practice usually secondary to changes in water balance NOT sodium levels !!!


HYPONATREMIA
"ALL RIGHT...WHERE DID ALL THE SODIUM GO?"
Signs and Symptoms
• Lethargy
• Headache
• Confusion
• Apprehension
• Seizures
• Coma
Hyponatremia occurs when serum sodium is less than 135 mEq/L.
↓ Na is caused by dilution as a result of excess H_2O or ↑ Na loss.
These are some of the situations.
Gastrointestinal suctioning
Diarrhea
Vomiting
Diuretics
Rx
Inadequate salt intake
Fluid shift from ICF to ECF by hypertonic solutions, which leads to dilutional hyponatremia
Mannitol

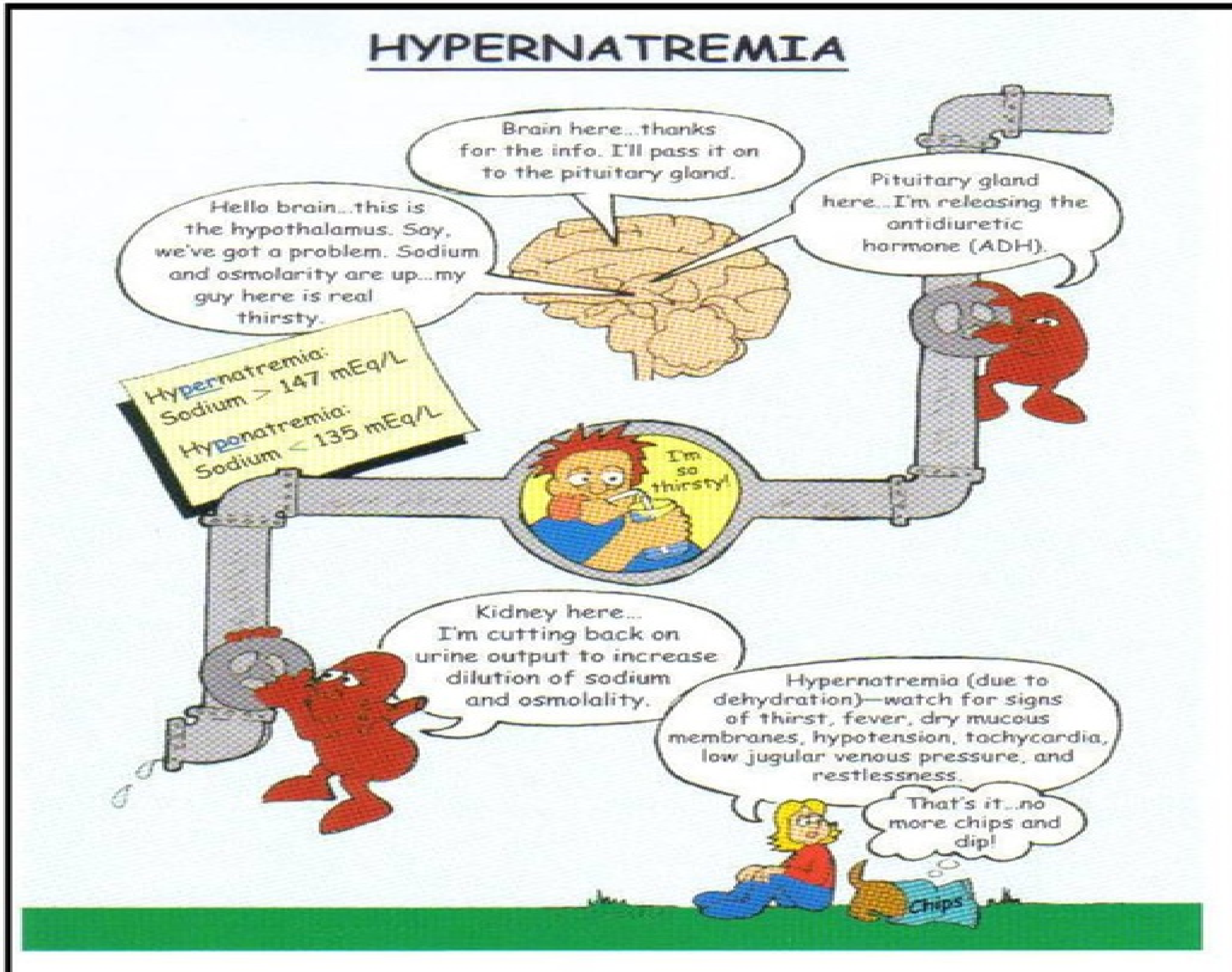
Hyponatremia (common, 20-25% pts.)



Na < 135 mmol/l

Hyponatremia

- Must be corrected slowly !
- Too rapid – osmotic pontine demyelination (central pontine demyelination)
- Symptoms:generalised encephalopathy, behavioral changes, cranial nerve palsies, quadriplegia
- Patients: alkoholics, malnourished, geriatric, thermal injury
- 3% NaCl used, slow infusion + diuretics


HYPERNATREMIA
Hello brain...this is the hypothalamus. Say, we've got a problem. Sodium and osmolarity are up...my guy here is real thirsty.
Brain here...thanks for the info. I'll pass it on to the pituitary gland.
Pituitary gland here...I'm releasing the antidiuretic hormone (ADH).
Hypernatremia: Sodium > 147 mEq/L
Hyponatremia: Sodium < 135 mEq/L
I'm so thirsty!
Kidney here... I'm cutting back on urine output to increase dilution of sodium and osmolality.
Hypernatremia (due to dehydration)—watch for signs of thirst, fever, dry mucous membranes, hypotension, tachycardia, low jugular venous pressure, and restlessness.
That's it...no more chips and dip!
Chips

Hypernatremia

- Na level > 145 mmol/l; 2% of pts.. 15% ICU pts.
- Mortality rate 70 %
- Causes: Water deficit or excess total body Na
- Symptoms: CNS – confusion, weakness, lethargy, coma, death
- Slow infusion of water (avoid cerebral oedema)

- 0,9% NaCl infusions – most common reason of hypernatremia (hypernatremia with hiperchloremic metabolic acidosis)154 mmol Na + 154 mmol Cl

- Potassium
- Calcium
- Magnesium
- Phosphorous

Shock

- Intravascular volume (ab. 5 l)

  - significant decreases of mean arterial pressure are poorly tolerated and lead to hypovolemic shock

  MAP = DP + 1/3 [SP- DP] 75-100 mmHg

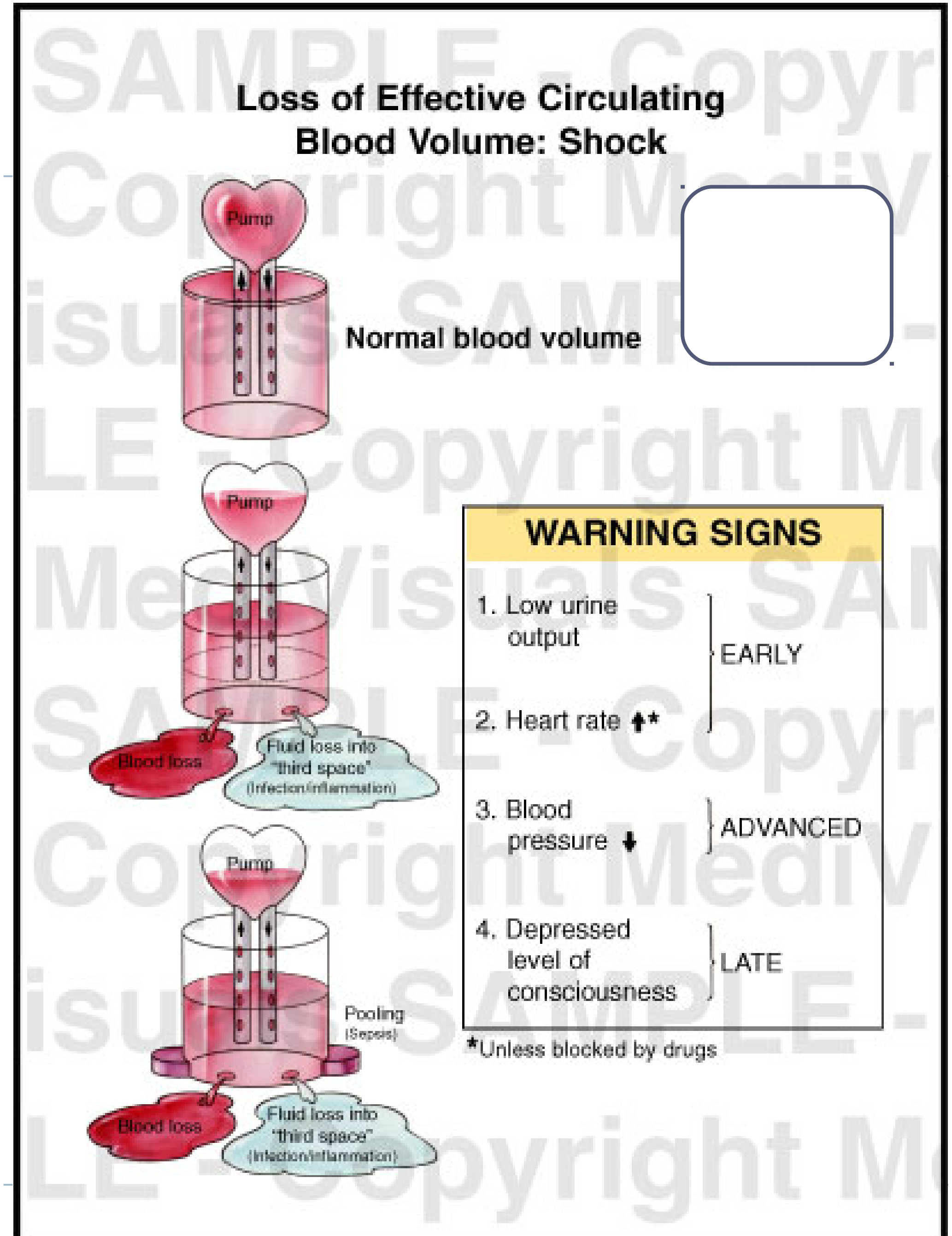
blood loss = hemorrhagic shock

class I < 15 % blood volume

class II 15-30 % blood volume

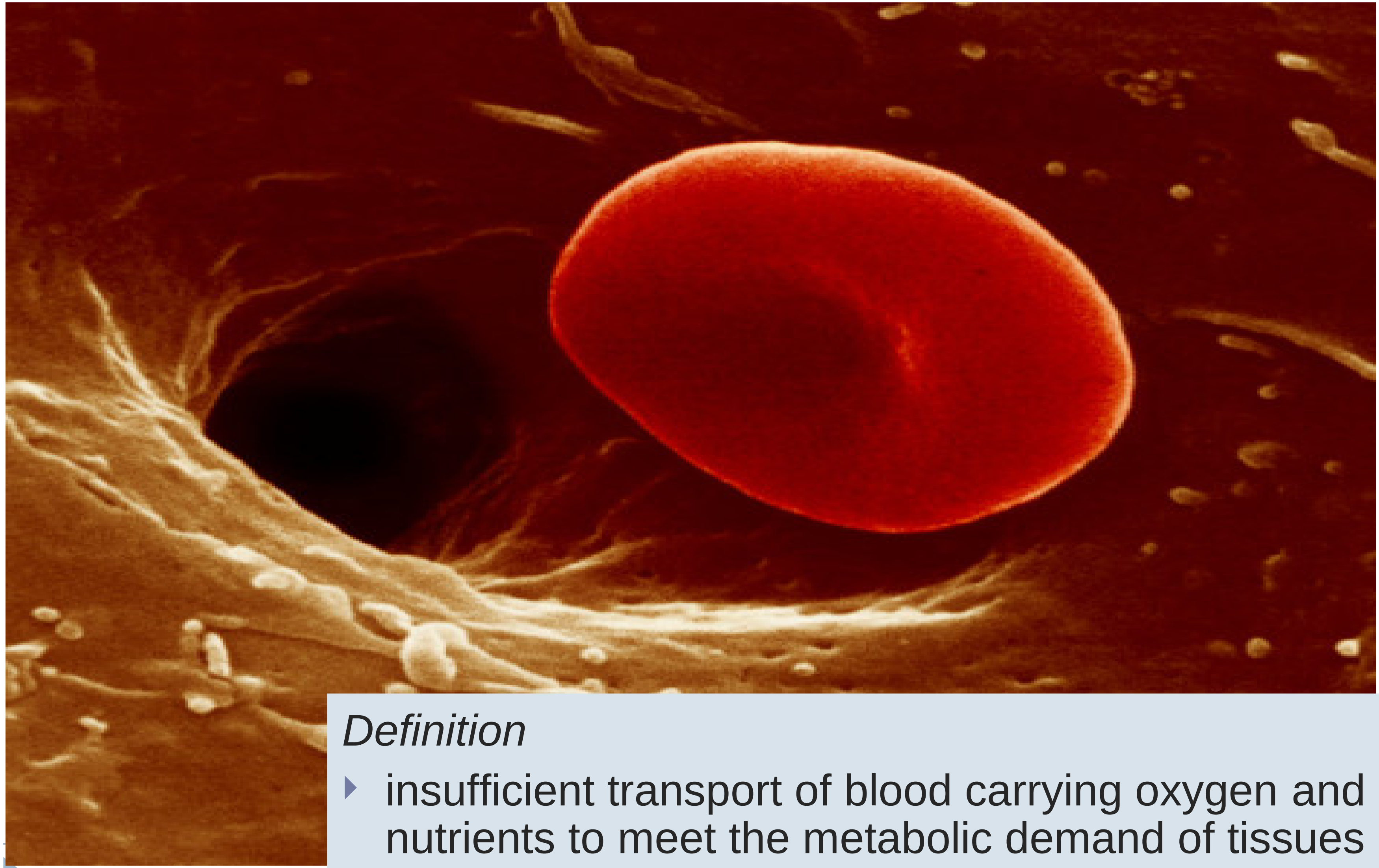
class III 30-40 % blood volume (hypotension)

class IV > 40 % blood volume (> 50 % cardiac arrest)



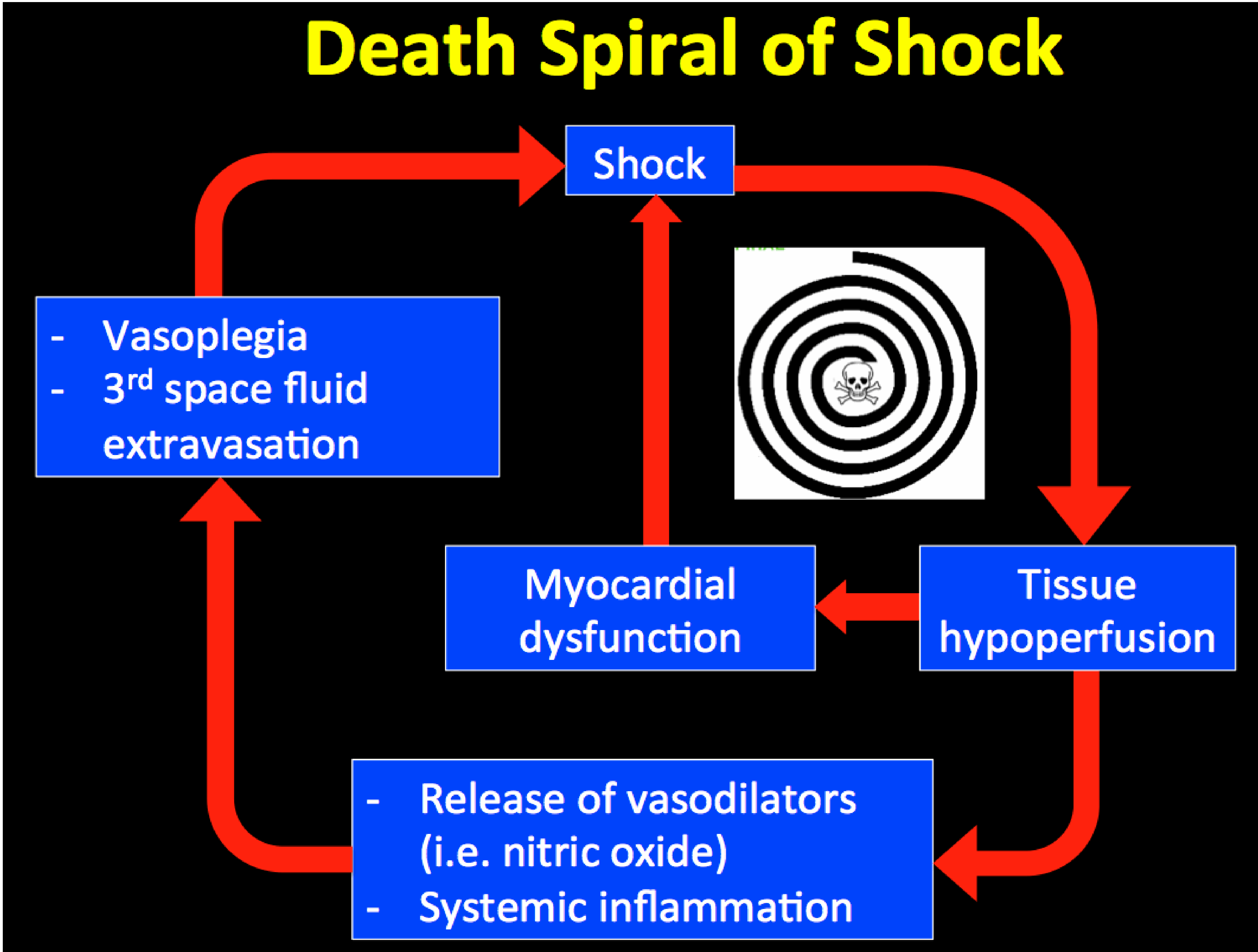
Exhibit# 390006-03X

Shock



Definition

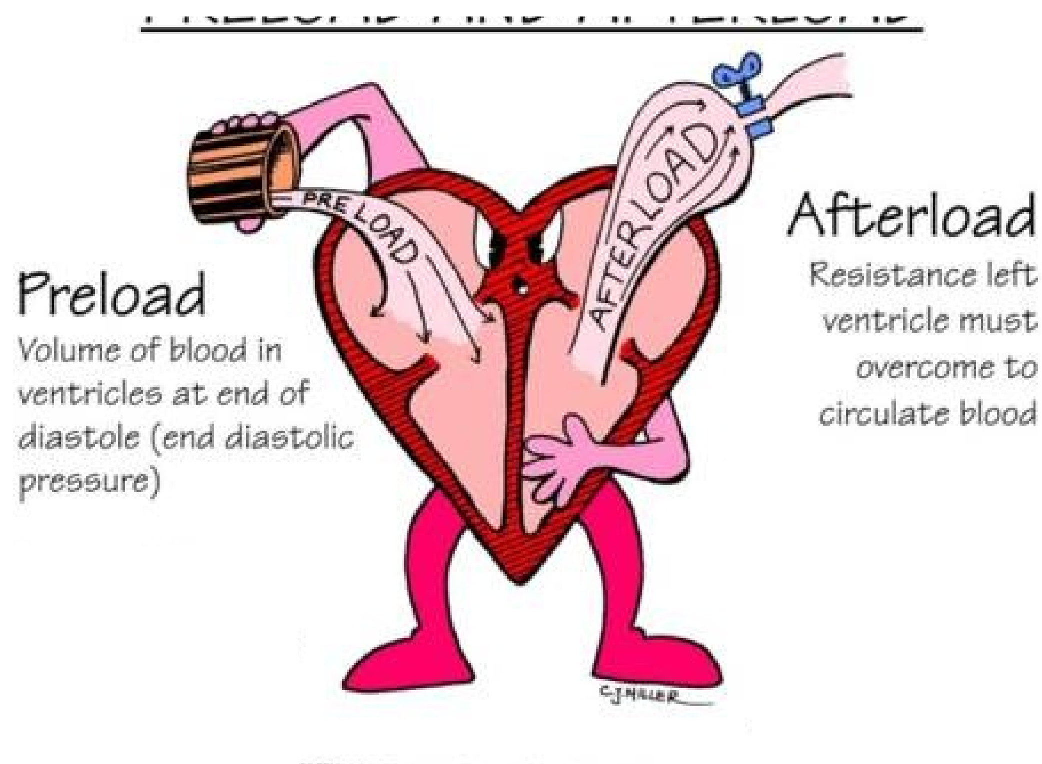
- insufficient transport of blood carrying oxygen and nutrients to meet the metabolic demand of tissues


Death Spiral of Shock
Shock
- Vasoplegia
- 3rd space fluid extravasation
Myocardial dysfunction
Tissue hypoperfusion
- Release of vasodilators (i.e. nitric oxide)
- Systemic inflammation

Hypovolemic shock

PRELOAD

Decreased



1. Hemorrhage
2. Fluid loss

Circulating blood volume

- Neonates 85-90 ml/kg
- Infants 75-80 ml/kg
- Children 70-75 ml/kg
- Adults 65-70 ml/kg

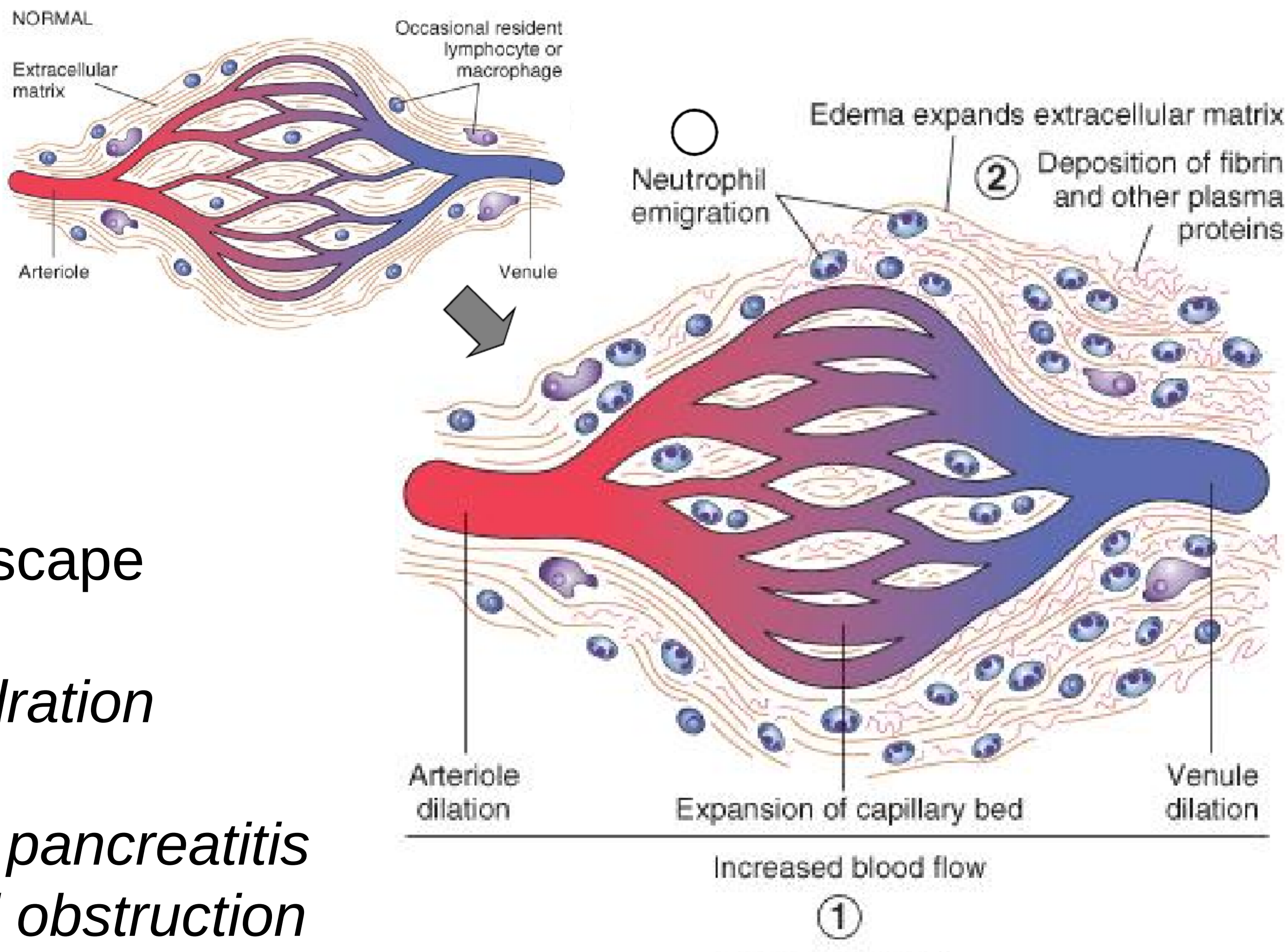
M > W

7 % of IBW (adults)
8-9 % of IBW (children)

70 kg man ≈ 5 liters

Hemorrhage
- *trauma*
- *pathological bleeding (GI hemorrhage)*
- *surgery (unexpected injury of large vessles)*

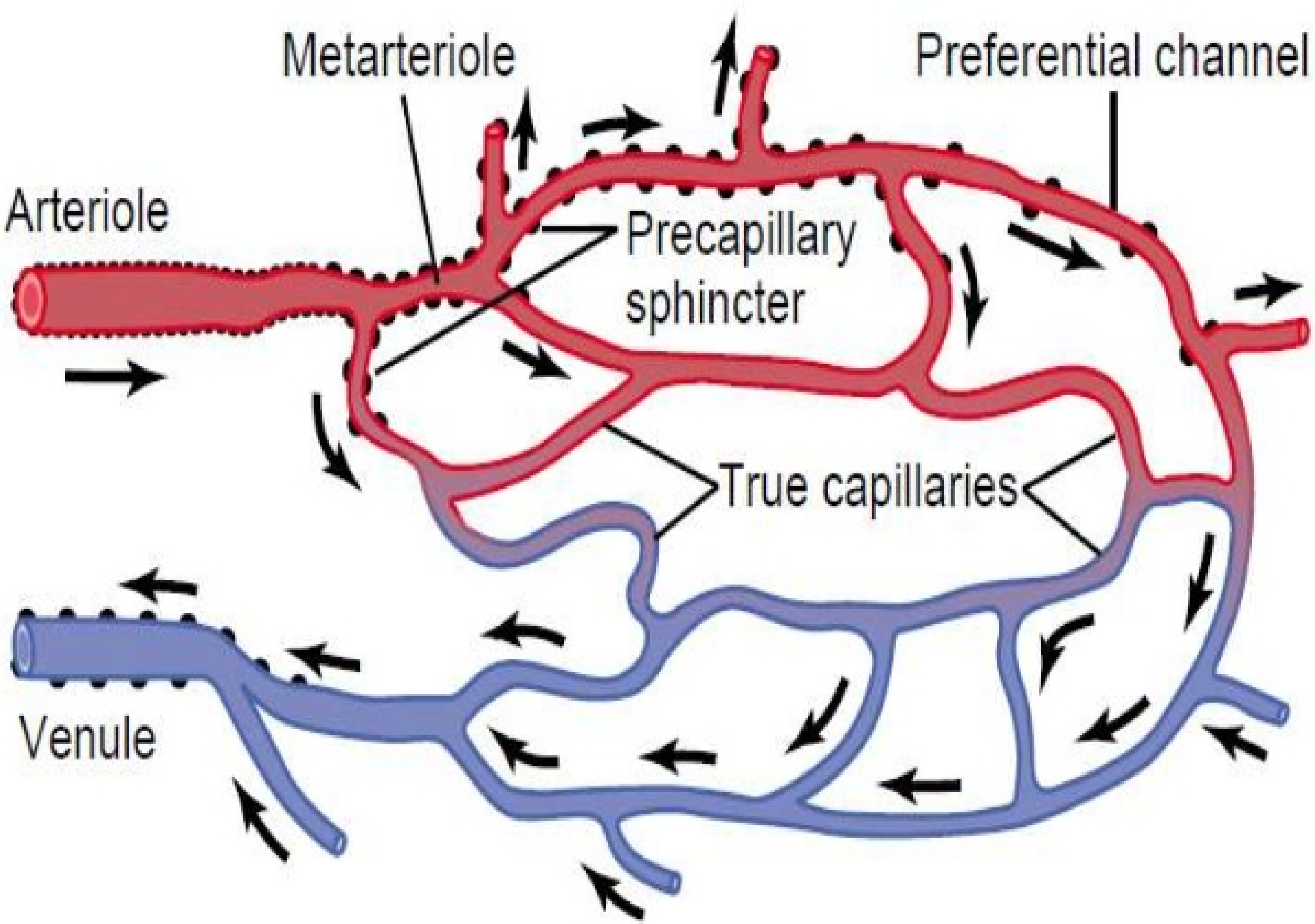
Fluid shift



Fluid escape

- *dehydration*
- *burns*
- *acute pancreatitis*
- *bowel obstruction*

Microcirculation network *"DRAMA SCENE"*

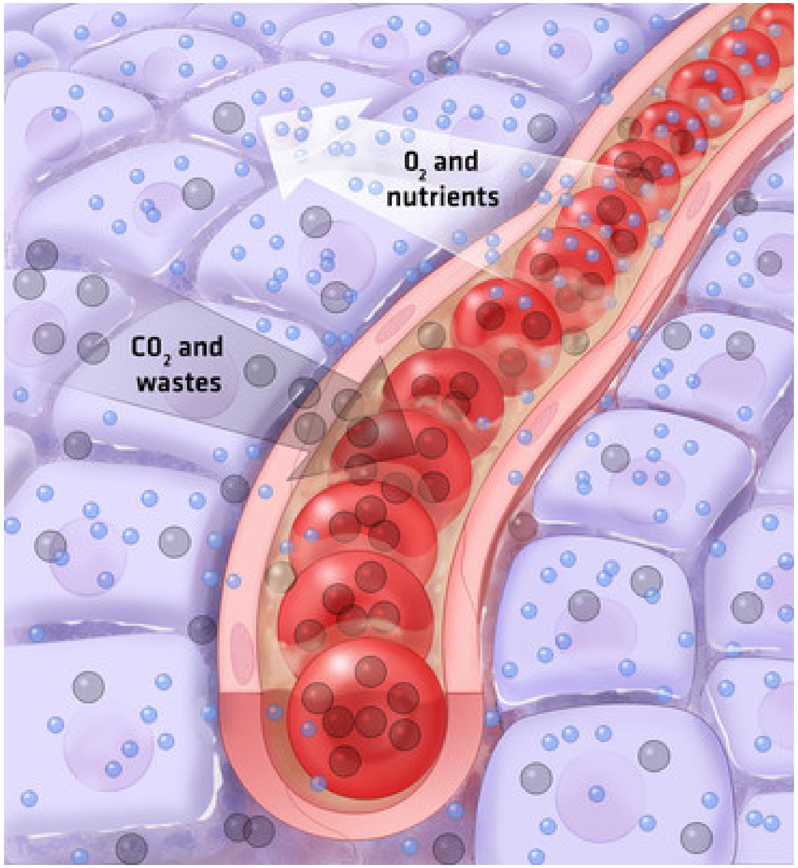


Microcirculation

- the principal function –
  to permit the transfer of substances between the tissues and the circulation

- transfer occurs predominantly across the walls of the capillaries + some exchange occurs in the small venules also

- substances involved include water, electrolytes, gases (O2, CO2), nitrogenous wastes, glucose, lipids and drugs + heat



Microcirculation

Electrolytes and other small molecules cross the membrane through pores.
Lipid soluble substances (including oxygen and carbon dioxide) can easily across the thin capillary walls.
Proteins are large and do not cross easily via pores but some transfer does occur via pinocytosis (endocytosis/exocytosis).

Water molecules are smaller than the size of the pores in the capillary and can cross the capillary wall very easily.

The capillary endothelial cells in some tissues (eg glomerulus, intestinal mucosa) have gaps (fenestrations) in their cytoplasm which are quite large - the water conductivity across these capillaries is much higher then in non-fenestrated capillaries in other tissues of the body.

The transfer of water across the capillary membrane occurs by two processes: **diffusion and filtration**

Microcirculation

Diffusion

The total daily diffusional turnover of water across all the capillaries in the body is huge (eg **80,000 liters per day**) and is much larger than the total capillary blood flow (cardiac output) of about 8,000 liters per day.

Diffusion occurs in both directions and does not result in net water movement across the capillary wall => net diffusion is dependent on the presence of a concentration gradient for the substance (Fick's Law of Diffusion) and there is ordinarily no water concentration difference across the capillary membrane.

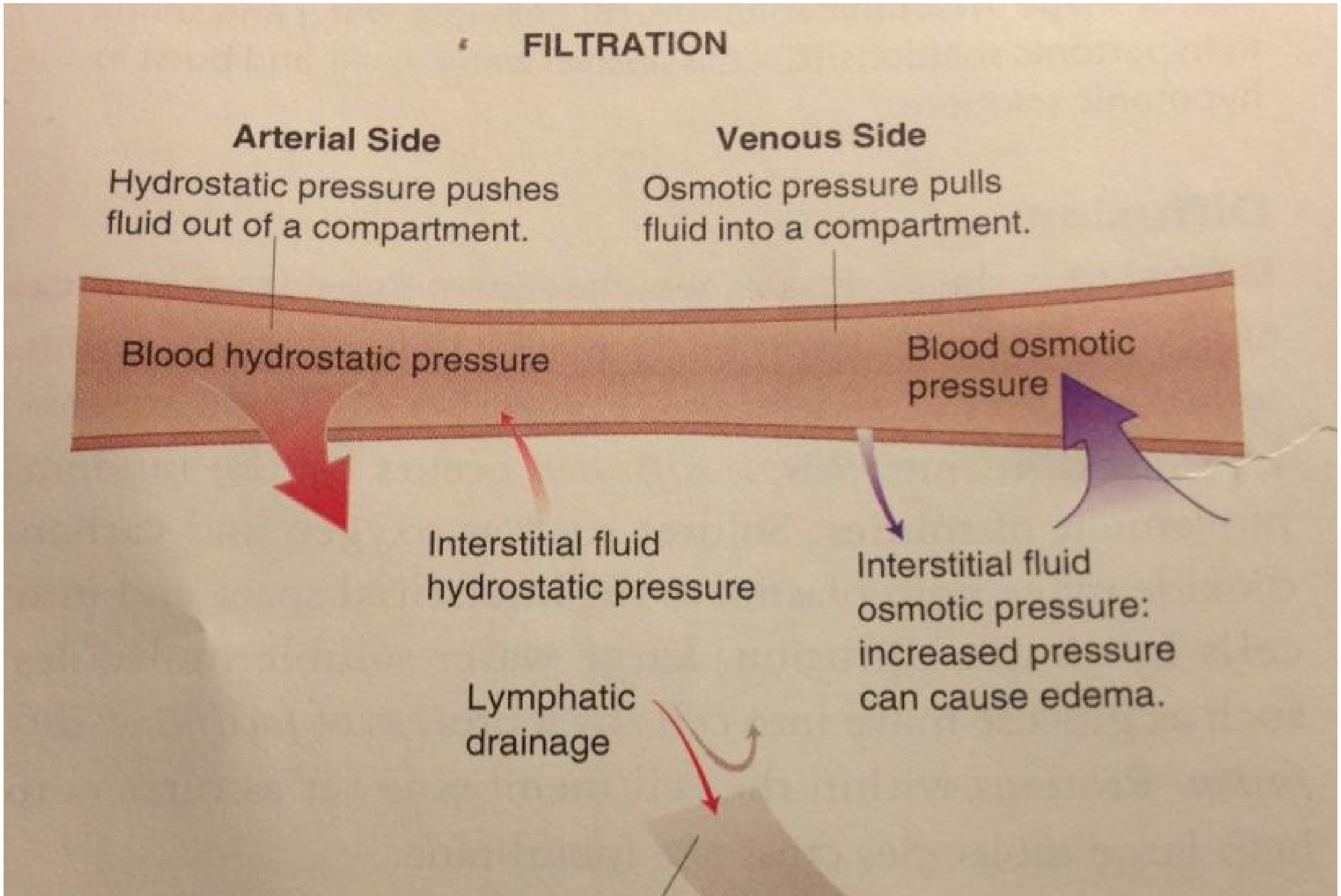
Net diffusional flux is zero.

Microcirculation

Filtration

- actually ultrafiltration as the plasma proteins do not cross the capillary membrane in most tissues
- considered to occur because of the imbalance of hydrostatic pressures and oncotic pressures across & along the capillary membrane (Starling's hypothesis)
- for the whole body, there is an ultrafiltration **outward of 20 liters per day** and **inwards of 18 liters per day**. The difference (about 2 liters/day) is returned to the circulation as lymph.
- filtration <u>results in net movement of water because</u> there is an imbalance between the forces promoting outward flow and the forces promoting inward flow. These forces are variable so net movement could be inwards or outwards in a particular tissue at a certain time.
- the forces also change in value along the length of the capillary and the typical situation is to have net movement outward at the arterial end and to have net movement inward at the venous end of the capillary.

Microcirculation



SHOCK - Compensatory mechanisms

- Heart rate increases
- Sympathetic stimulation
- Stress hormones (NA, A)
- RAA
- Wazopresin
- Water shift from extravascular space to vessels

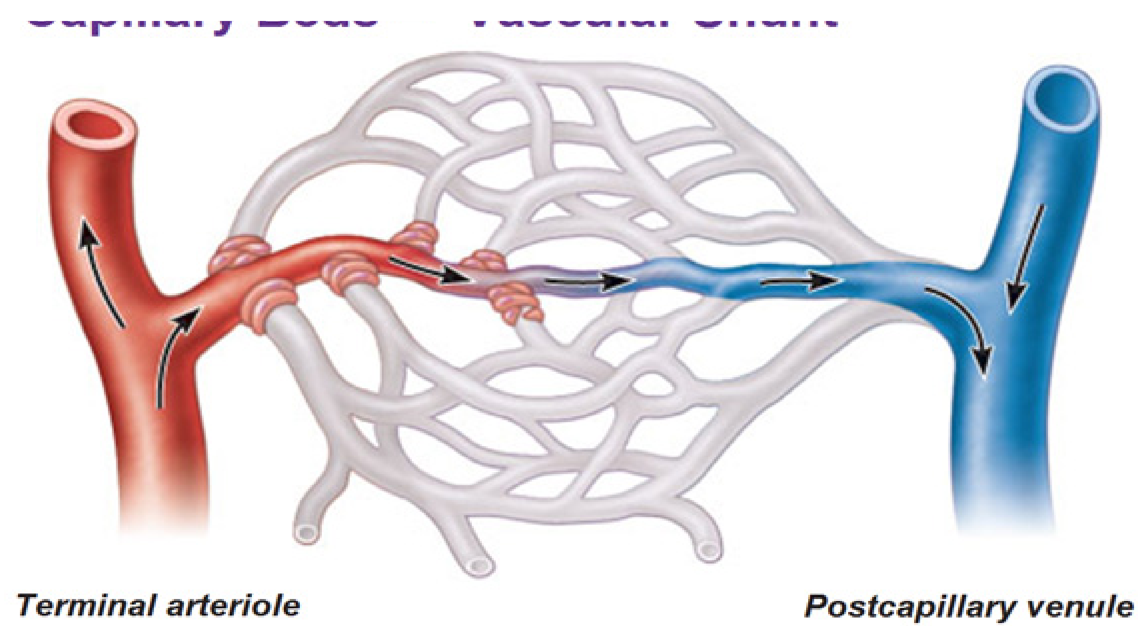
….

Compensatory mechanisms

- Sphincters closed due to sympathetic stimulation

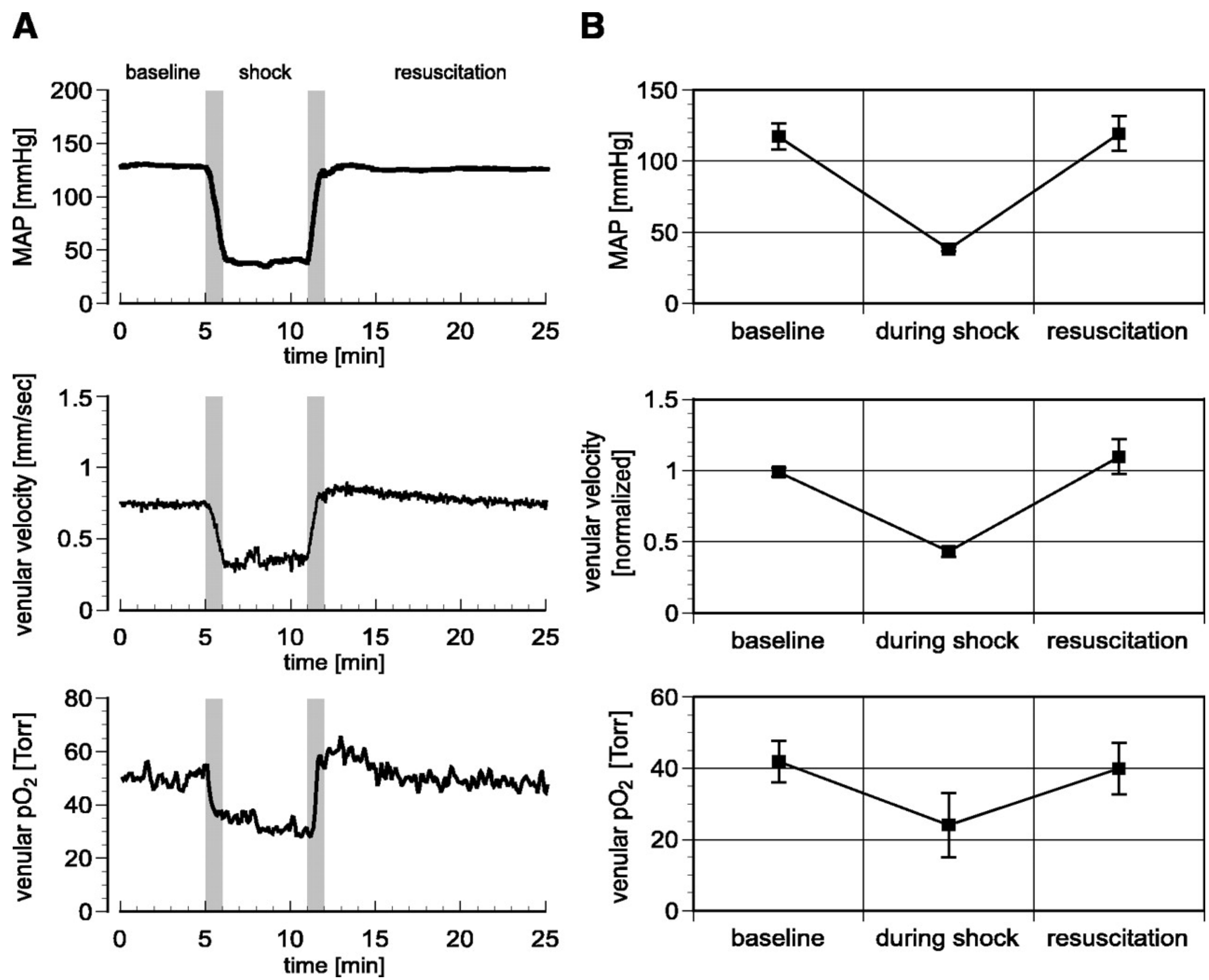
  - blood flows straight through metarteriole and bypasses the capillaries

  „shunting strategy”

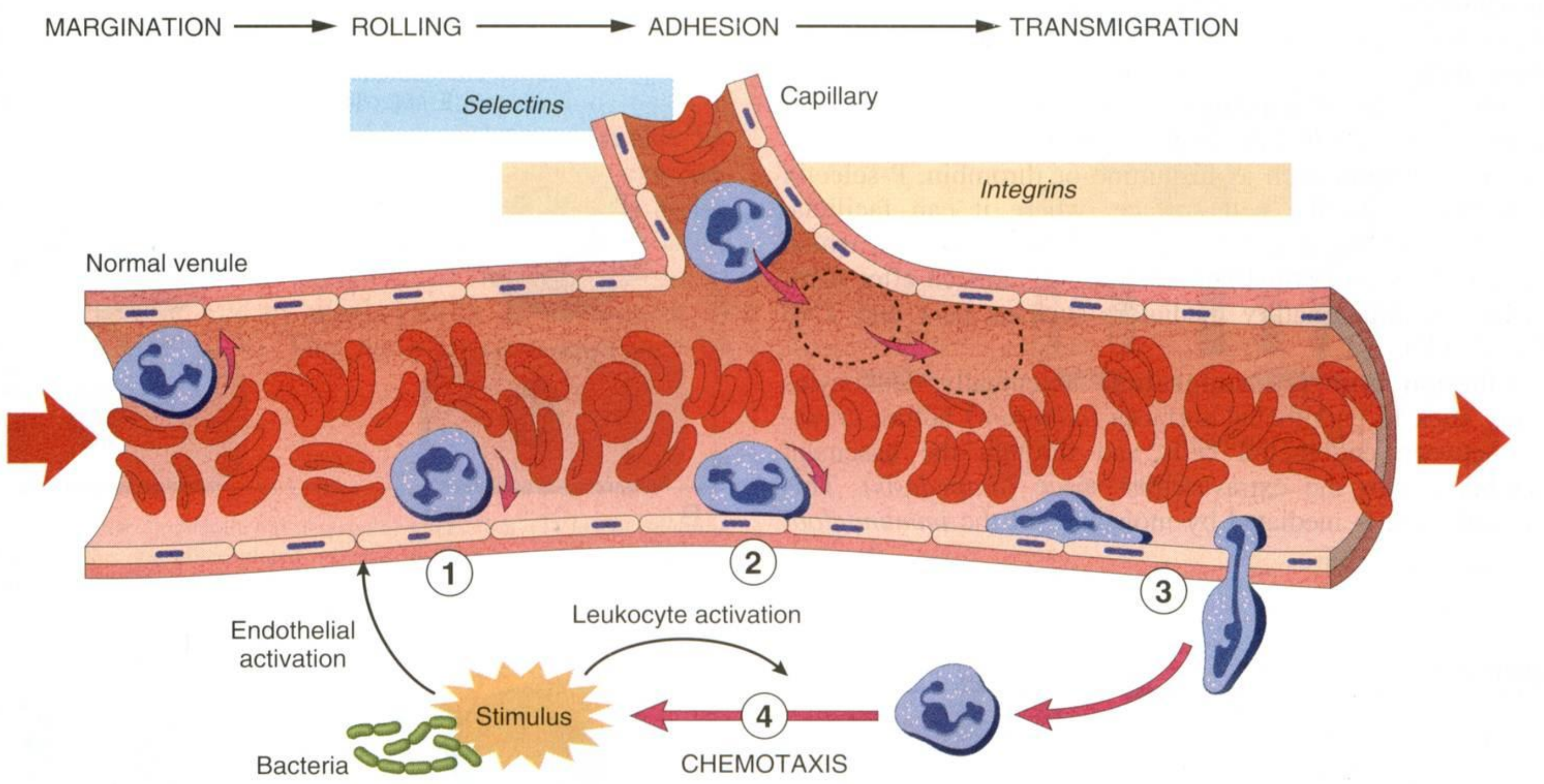


(b) Sphincters closed (sympathetic stimulation)—blood flows

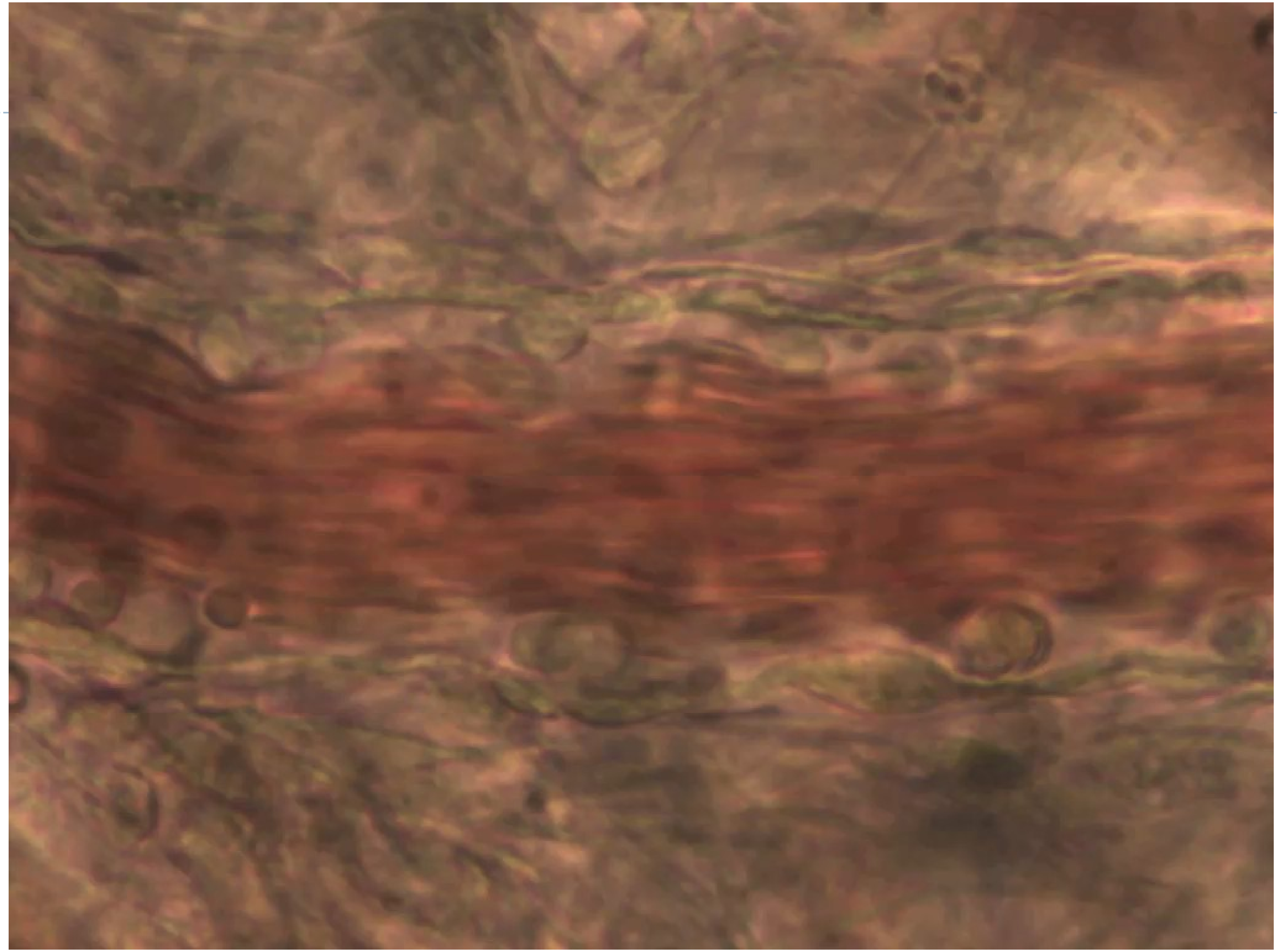
Microcirculatory hemodynamics

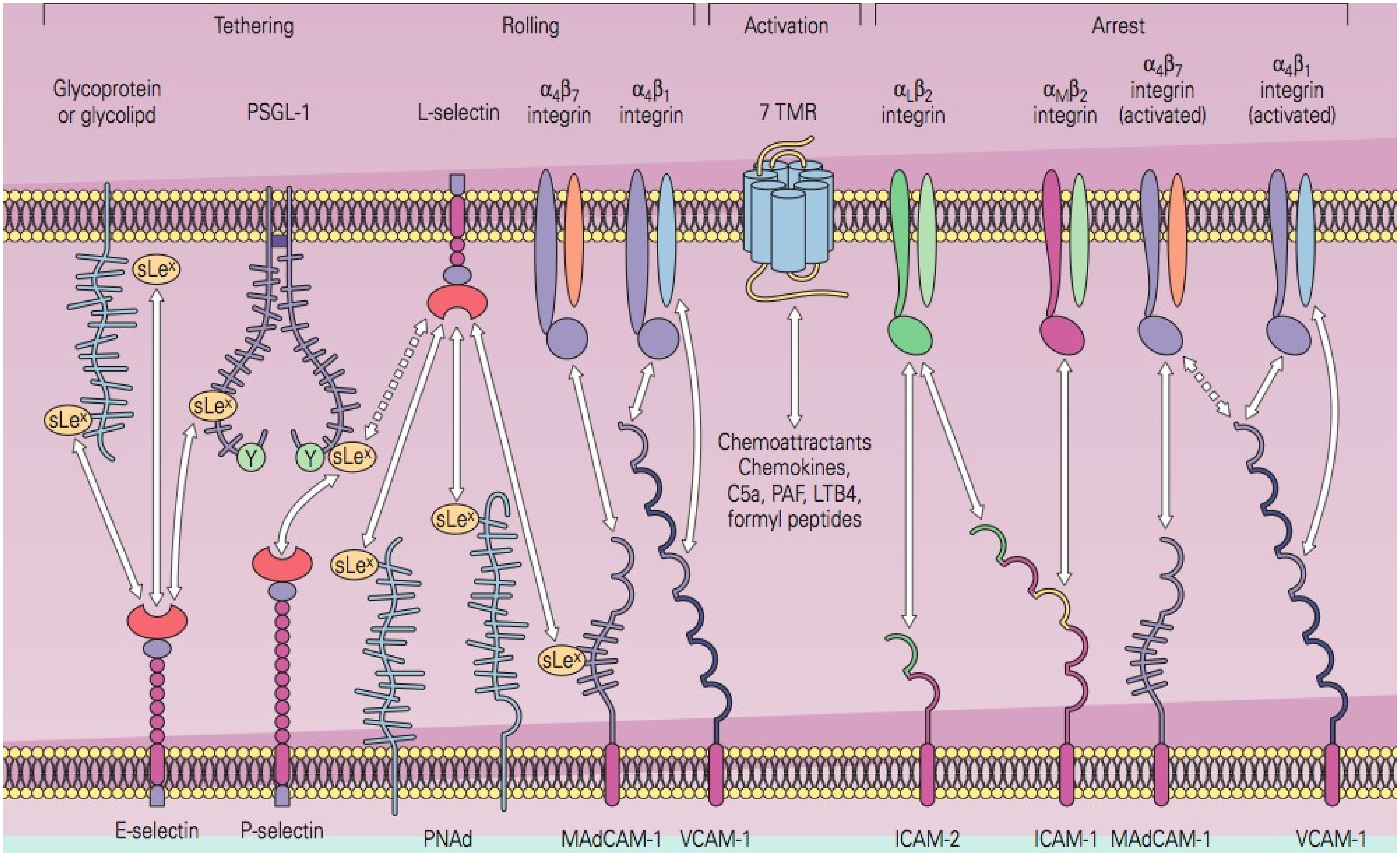


Endothelium – leukocyte interactions



SHOCK

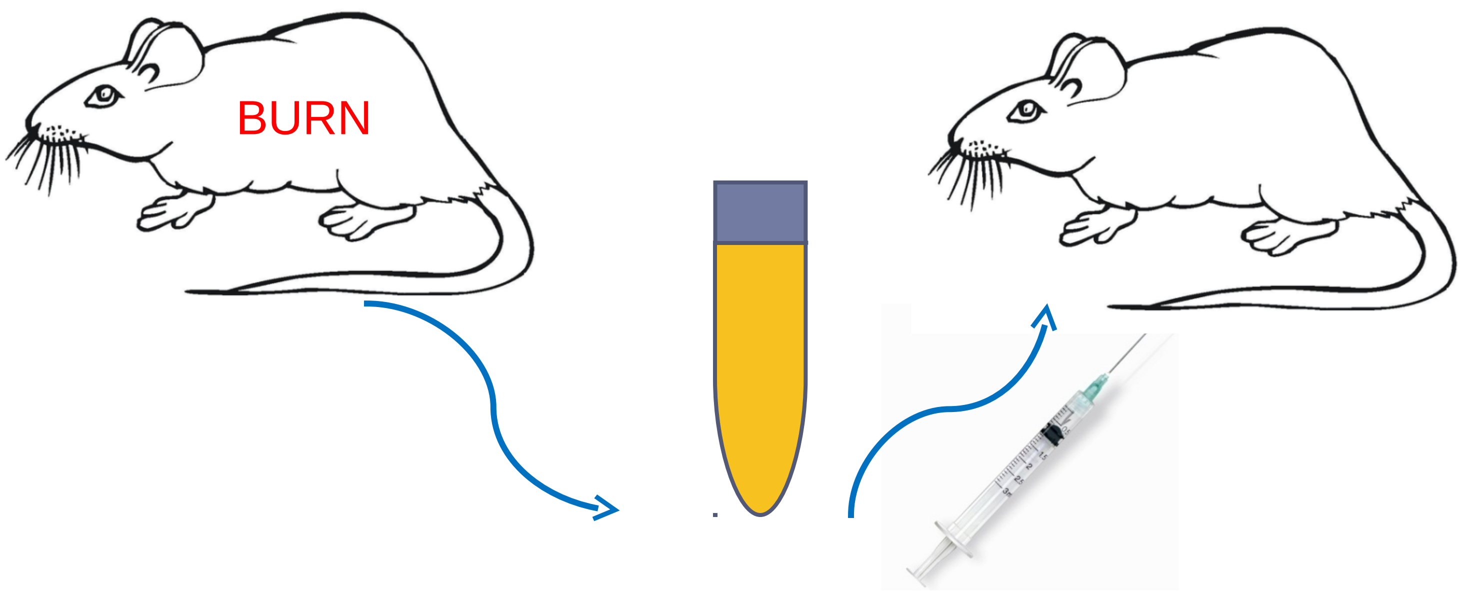




Tethering
Rolling
Activation
Arrest
Glycoprotein or glycolipd
PSGL-1
L-selectin
$\alpha_4\beta_7$ integrin
$\alpha_4\beta_1$ integrin
7 TMR
$\alpha_L\beta_2$ integrin
$\alpha_M\beta_2$ integrin
$\alpha_4\beta_7$ integrin (activated)
$\alpha_4\beta_1$ integrin (activated)
sLe^x
Y
Chemoattractants
Chemokines,
C5a, PAF, LTB4,
formyl peptides
E-selectin
P-selectin
PNAd
MAdCAM-1
VCAM-1
ICAM-2
ICAM-1
MAdCAM-1
VCAM-1

Cytokines are co-responsible for microcirculatory insufficiency & fluid shift

- Burn plasma transfer induces systemic burn edema in healthy individuals, which is identical to burn edema after direct thermal injury in this rat model.



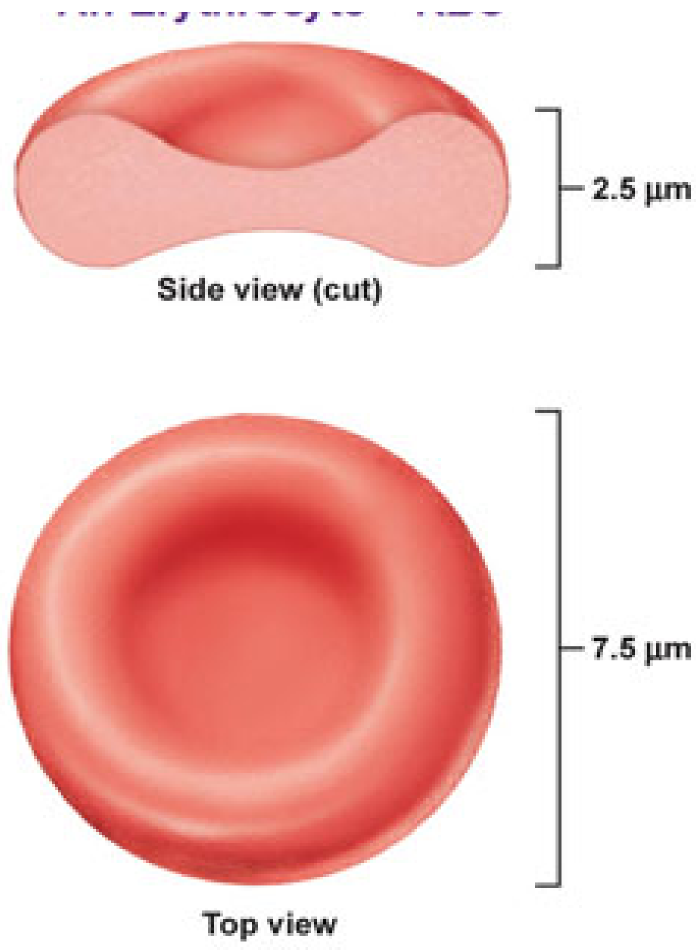
Burn plasma transfer induces burn edema in healthy rats.
Kremer T[1], Abé D, Weihrauch M, Peters C, Gebhardt MM, Germann G, Heitmann C, Walther A. Shock, 2008 Oct;30(4):394-400.

Erythrocytes (RBCs)

- Biconcave disc shape (less volume for a given surface area – decrease bending energy with the membrane)
- no nucleus
- cell volume: 90 fl
- surface: 136 μm^2
- Hb solution + cytoplasm
- lifetime: 100-120 days
- deformability !

  lost with age => rupture in spleen

WATER

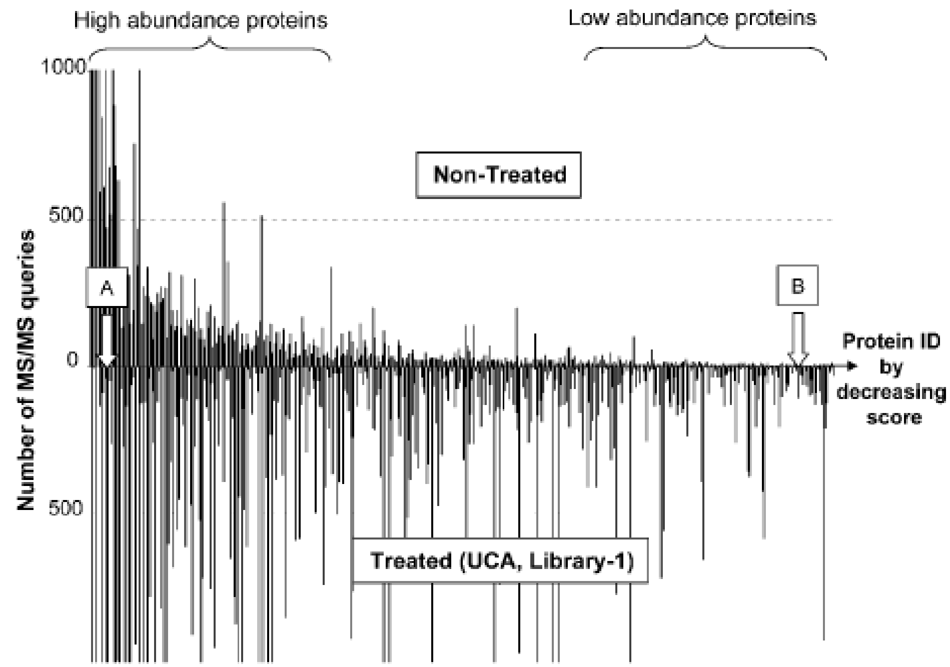


K. Kenneth, 2010 Williams hematology McGraw-Hill New York

Cytoplasm of the erythrocyte

- 98 % Hb
- 2 % mostly unknown

1578 proteins



WATER

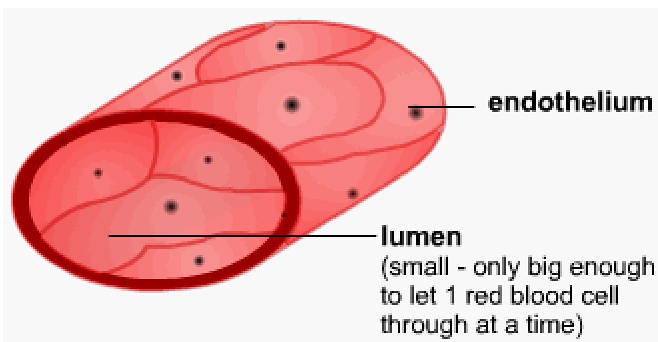
Extensive Analysis of the Cytoplasmic Proteome of Human Erythrocytes Using the Peptide Ligand Library Technology and Advanced Mass Spectrometry*

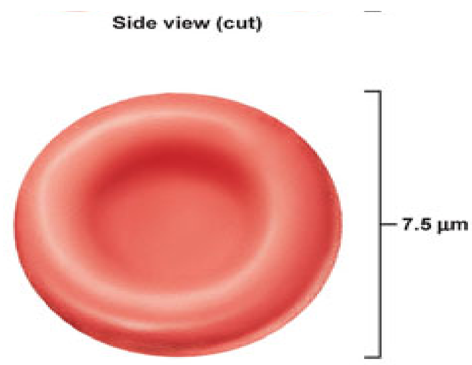
Florence Roux-Dalvai‡§, Anne Gonzalez de Peredo‡§, Carolina Simó¶, Luc Guerrier‖, David Bouyssié‡, Alberto Zanella**, Attilio Citterio¶, Odile Burlet-Schiltz‡, Egisto Boschetti‖, Pier Giorgio Righetti¶‡‡, and Bernard Monsarrat‡§§

Erythrocyte deformability

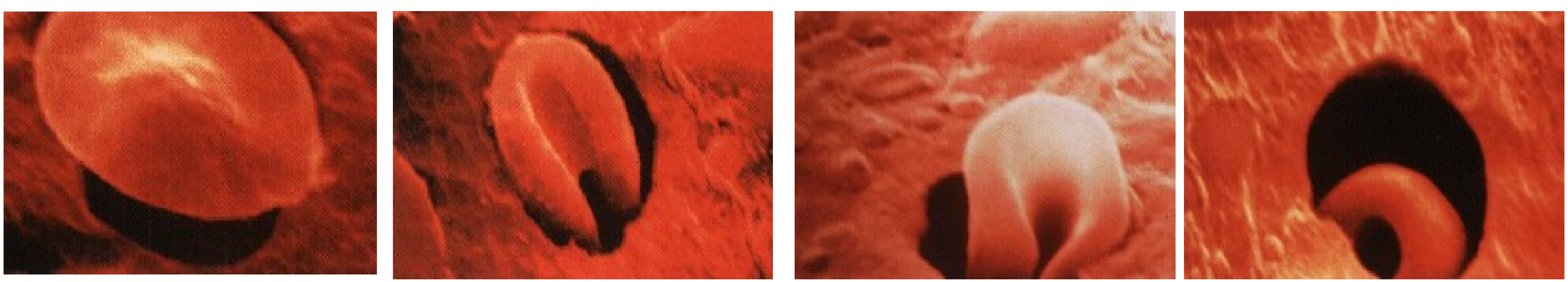
The arterial side of vessels in the microcirculation, surrounded by smooth muscle cells, has the inner diameter of ~ **10 – 100 µm**.

Capillaries have only one RBC thick ~ **5 – 10 µm.**

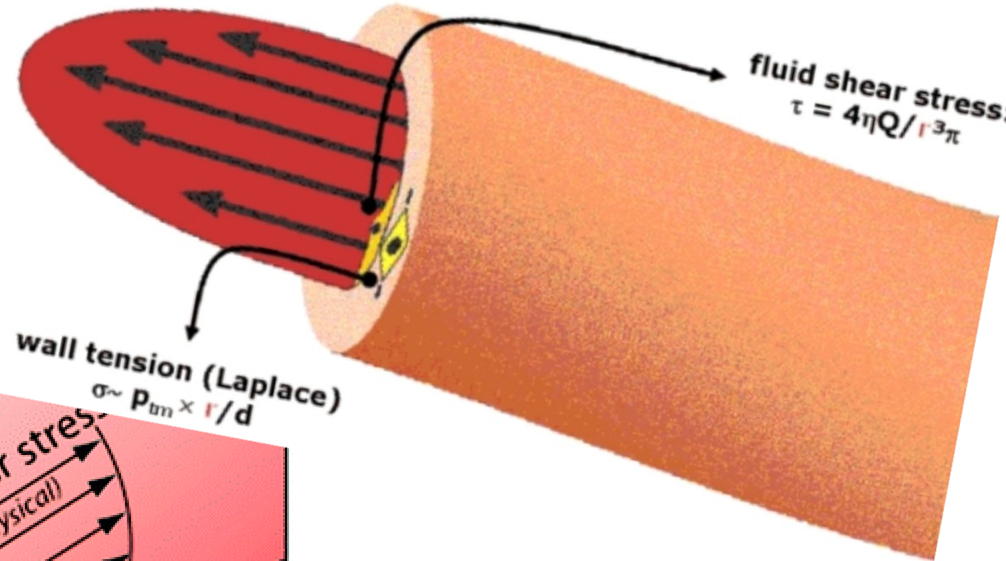


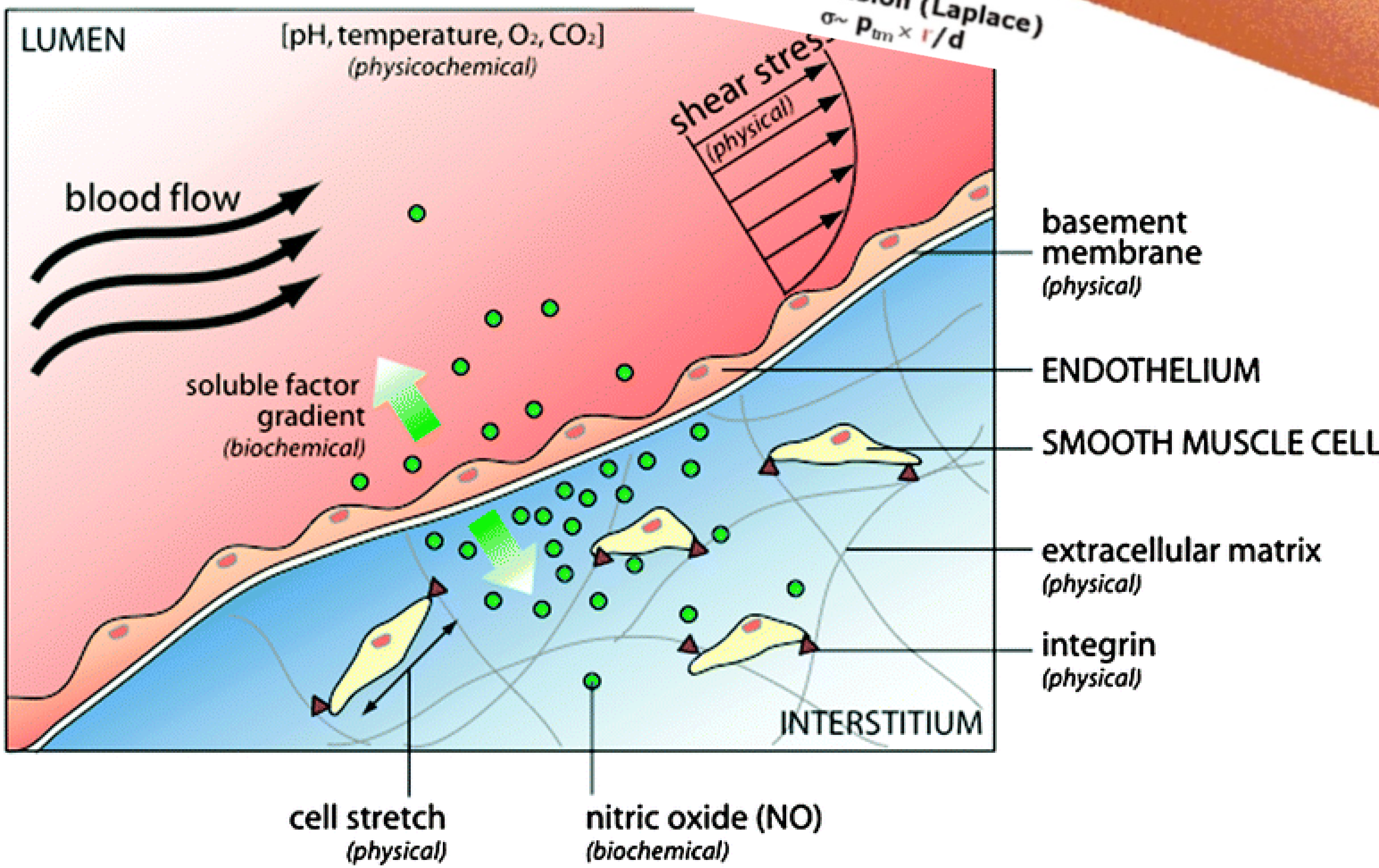


WATER



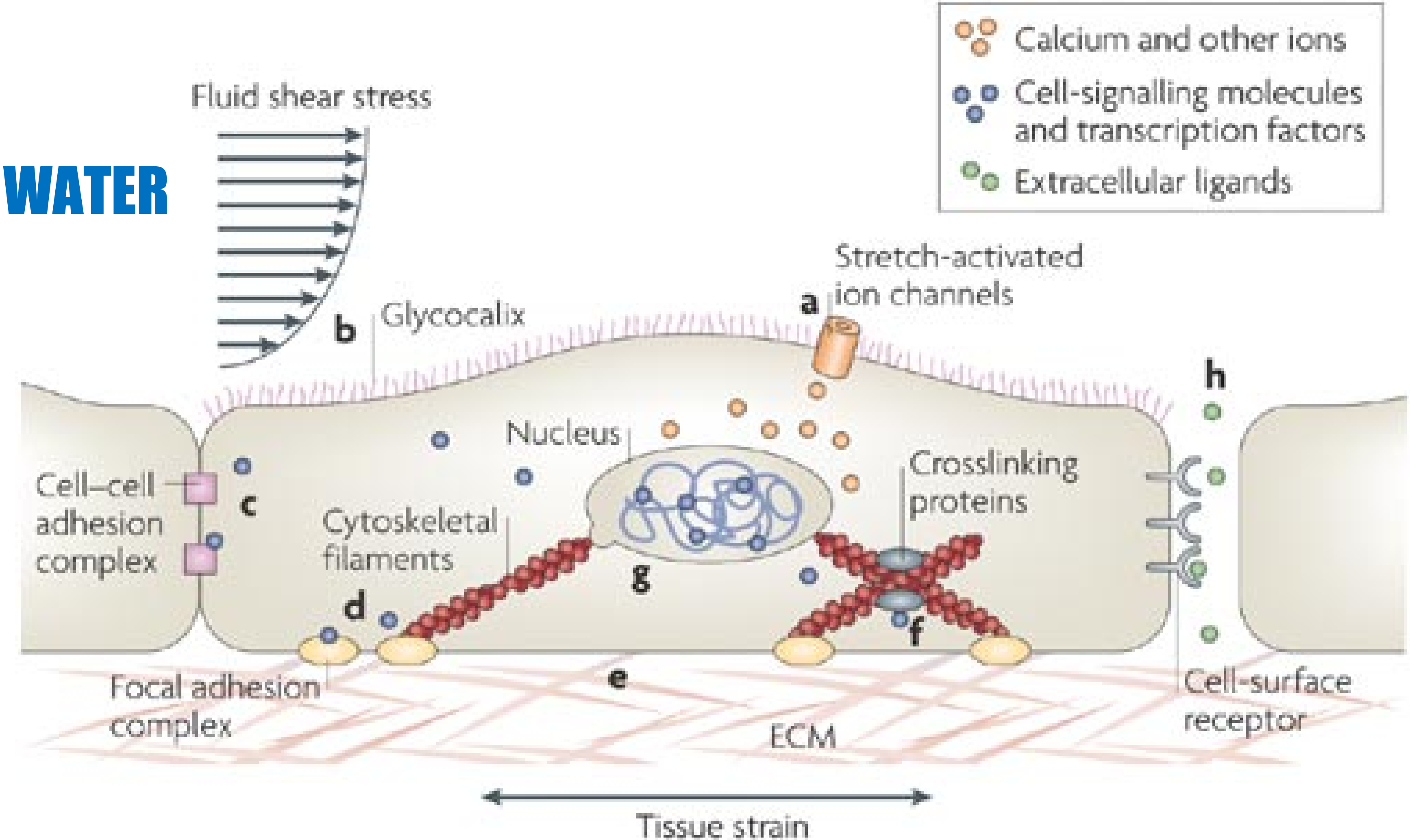
Shear stress



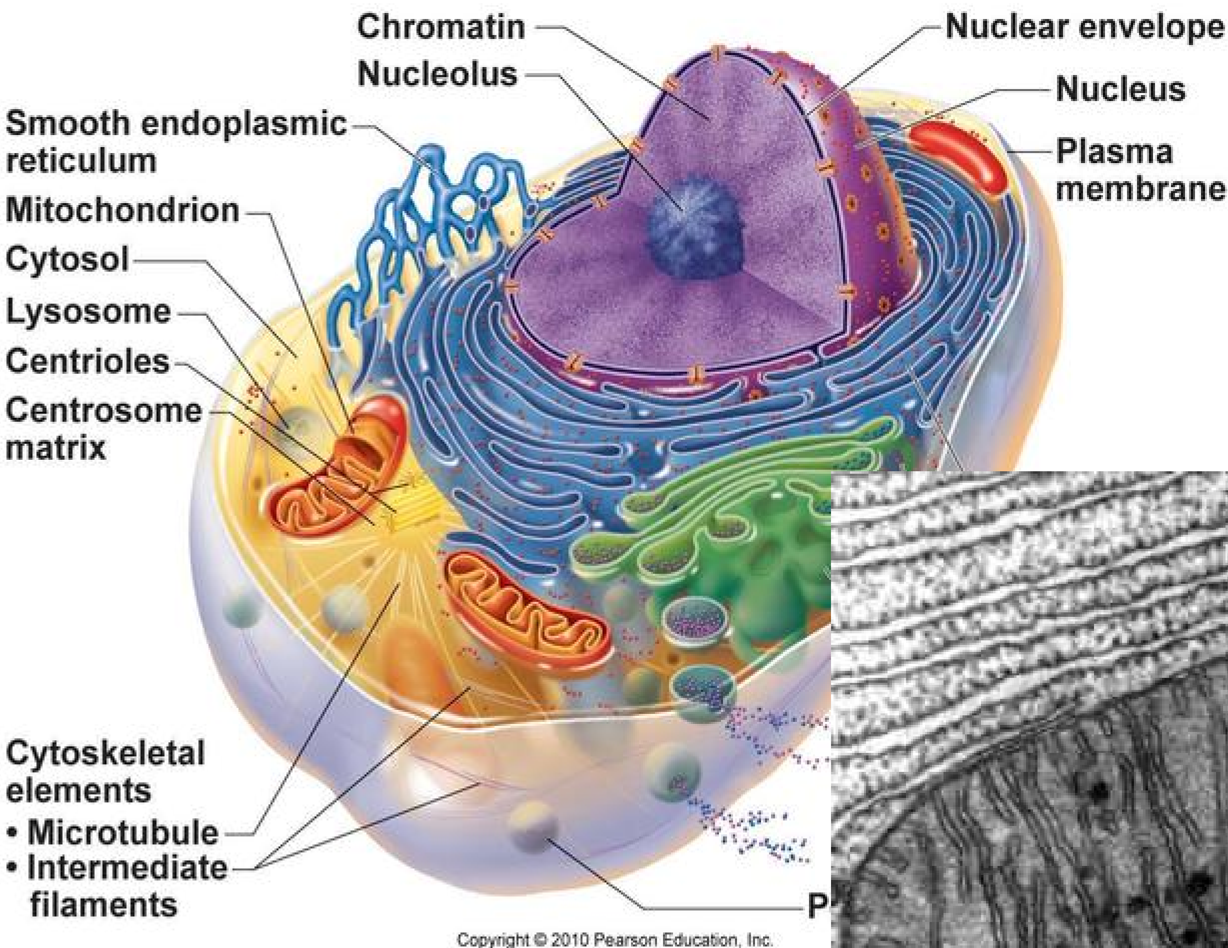


Mechanotransduction

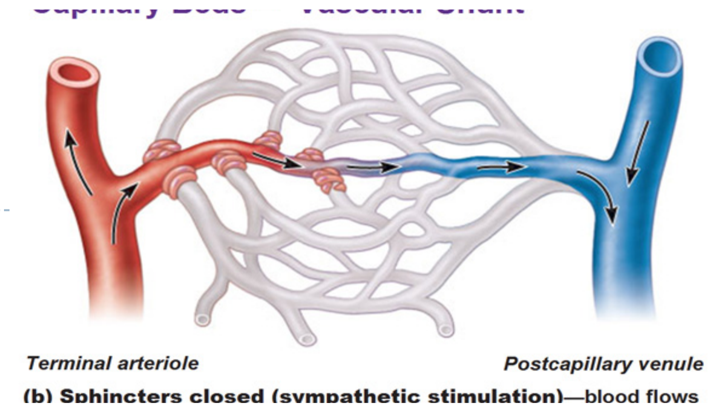
WATER



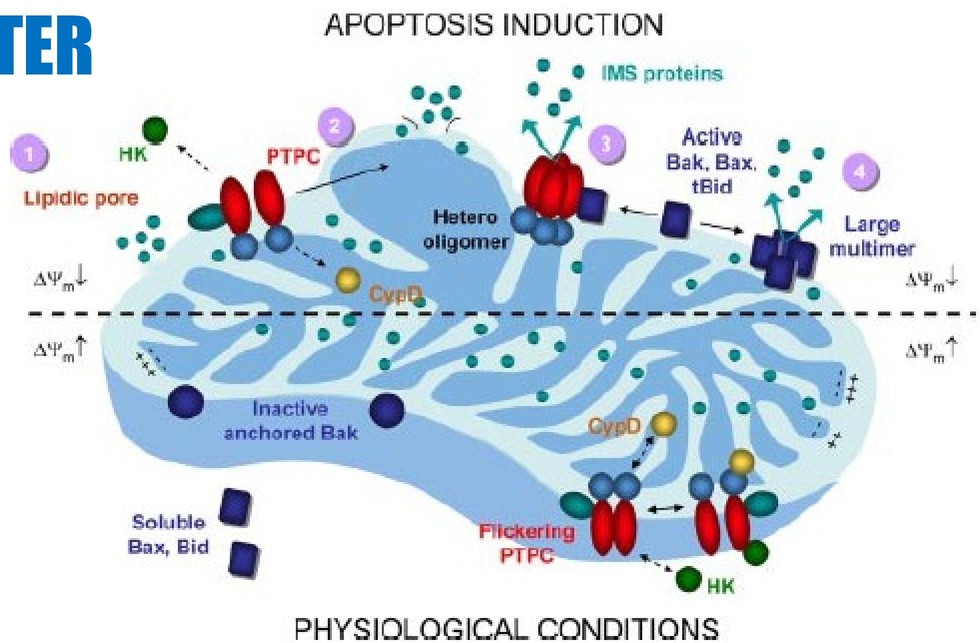
Mitochondrion



Mitochondial disaster



WATER



irreversible shock

reversible shock

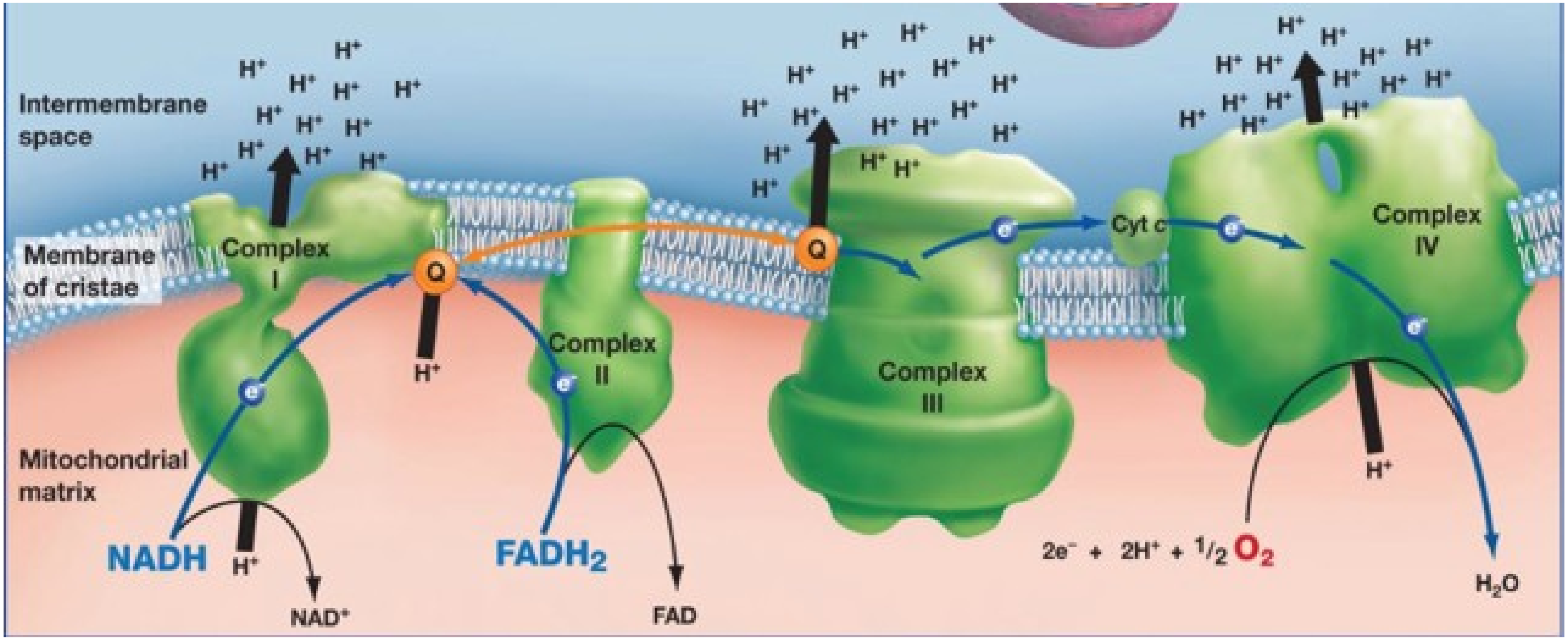
Mitochondrial Membrane Permeabilization in Cell Death

GUIDO KROEMER, LORENZO GALLUZZI, AND CATHERINE BRENNER

nstitut Gustave Roussy, Institut National de la Santé et de la Recherche Médicale Unit "Apoptosis, Cancer and mmunity," Université de Paris-Sud XI, Villejuif; and Centre National de la Recherche Scientifique UMR 8159, Université de Versailles/Saint-Quentin en Yvelines, Versailles, France

Mitochondrial phosphorylation

- Normal oxidative phosphorylation in mitochondria



WATER

Treatment of shock

FILL IN THE INTRAVASCULAR SPACE

All circulatory shock states **require quick and large-volume IV fluid replacement**, as does severe intravascular volume depletion (eg, due to diarrhea or heatstroke).
Intravascular volume deficiency is acutely compensated for by vasoconstriction, followed over hours by migration of fluid from the extravascular compartment to the intravascular compartment, maintaining circulating volume at the expense of total body water. However, this compensation is overwhelmed after major losses.

Goals in fluid resuscitation

BIG GOALS

MAP (Mean Arterial Pressure)
CVP (Central Venous Pressure),
ScvO2 (central venous oxygen saturation),
urine output

small GOALS

FCD (Functional Capillary Density)
DO_2 (tissue oxygen delivery),
numer of activated leukocytes

BOTH are DIFFICULT but
easier to acheive

Caring for the Critically Ill Patient

Effects of Fluid Resuscitation With Colloids vs Crystalloids on Mortality in Critically Ill Patients Presenting With Hypovolemic Shock: The CRISTAL Randomized Trial

Djillali Annane, MD, PhD[1]; Shidasp Siami, MD[2]; Samir Jaber, MD, PhD[3]; Claude Martin, MD, PhD[4]; Souheil Elatrous, MD[5]; Adrien Descorps Declère, MD[6]; Jean Charles Preiser, MD[7]; Hervé Outin, MD[8]; Gilles Troché, MD[9]; Claire Charpentier, MD[10]; Jean Louis Trouillet, MD[11]; Antoine Kimmoun, MD[12]; Xavier Forceville, MD, PhD[13]; Michael Darmon, MD[14]; Olivier Lesur, MD, PhD[15]; Jean Reignier, MD[16]; Fékri Abroug, MD[17]; Philippe Berger, MD[18]; Christophe Clec'h, MD, PhD[19]; Joël Cousson, MD[20]; Laure Thibault, MD[21]; Sylvie Chevret, MD, PhD[22]

JAMA 2013, 310 (6)

- 2857patients ICU
- France, Belgium, North Africa, and Canada

Colloids versus crystalloids for fluid resuscitation in critically ill patients (Review)

Perel P, Roberts I, Ker K

Cochrane Collaboration 2013

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THE QUESTION IS NOT TO GIVE FLUIDS OR NOT TO GIVE

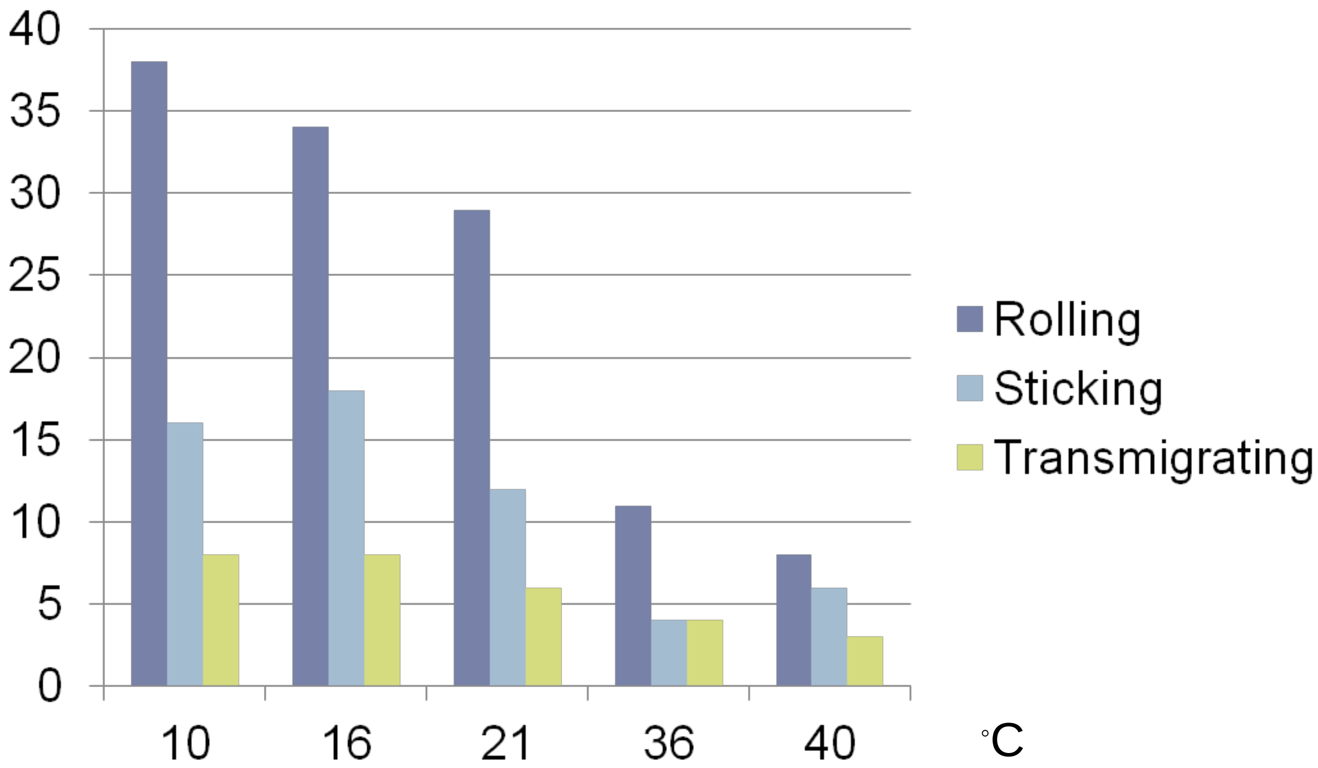
BUT HOW TO GIVE !

...crystalloids for fluid resuscitation in critically ill patients (Review)

Perel P, Roberts I, Ker K

Cochrane Collaboration 2013

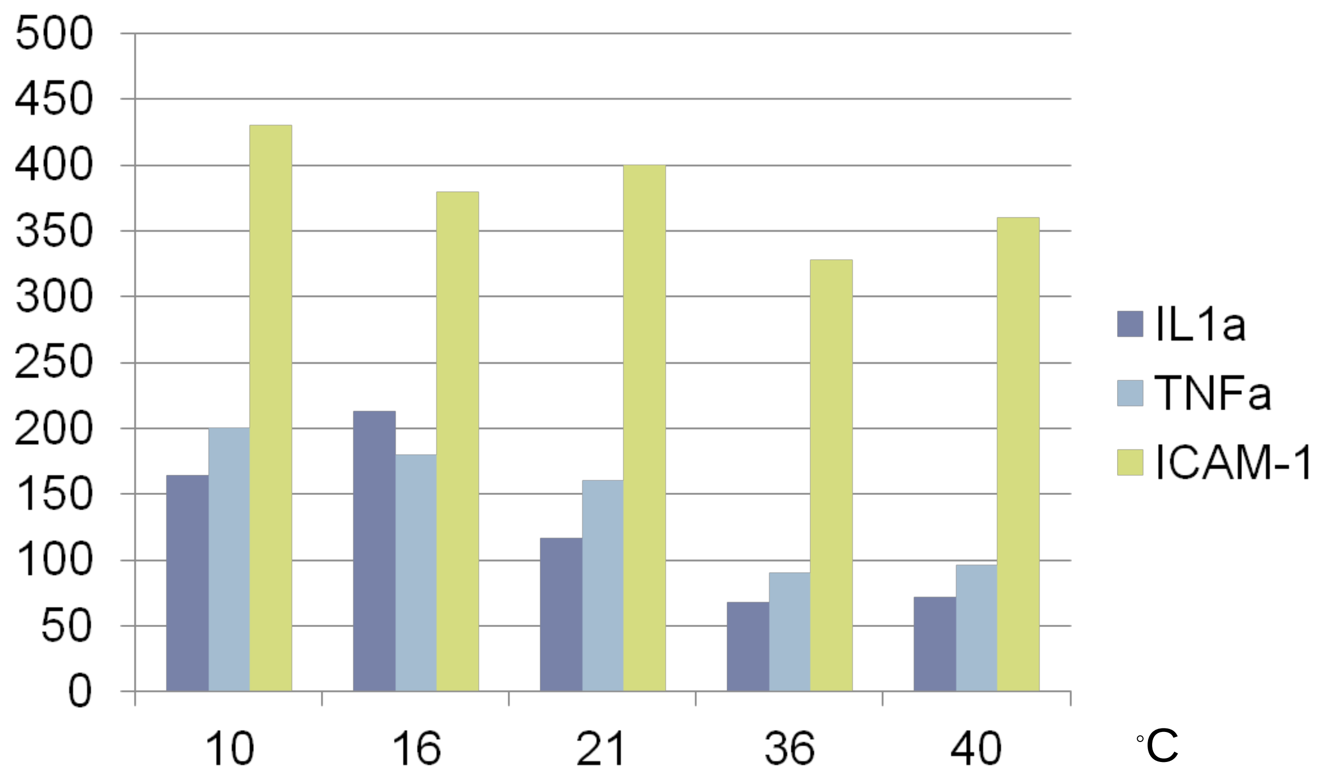
Cold vs. warm Ringer's lactate infussion



Number of activated leukocytes after fluid resuscitation with different temperatures

Szopinski J., Kusza K., Siemionow M., Cwykiel J., Ozturk C.
Microcirculatory response to fluid resuscitation with different temparature
In a rat cremaster model - data not published

Cold vs. warm Ringer's lactate infussion



Proinflamatory cytokines after fluid resuscitation with different temperatures

Szopinski J., Kusza K., Siemionow M., Cwykiel J., Ozturk C.
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