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Do colloids have a place in resuscitation?

Matthias Jacob
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University Hospital Munich

St.-Elisabeth-Hospital Straubing

Possible Conflicts of Interest

Lecture fees from and scientific cooperations with

Baxter
B. Braun
CSL Behring
Fresenius Kabi
Grifols
Serumwerk Bernburg

Further Conflicts of Interest

Further Conflicts of Interest

Oktober-fest

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DER UNIVERSITÄT MÜNCHEN

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1. Principal Considerations

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1. Principal Considerations

2. Physiology of the Microcirculation

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1. Principal Considerations

2. Physiology of the Microcirculation

3. Scientific Facts

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1. Principal Considerations

2. Physiology of the Microcirculation

3. Scientific Facts

4. Outcome-based Evidence

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1. Principal Considerations

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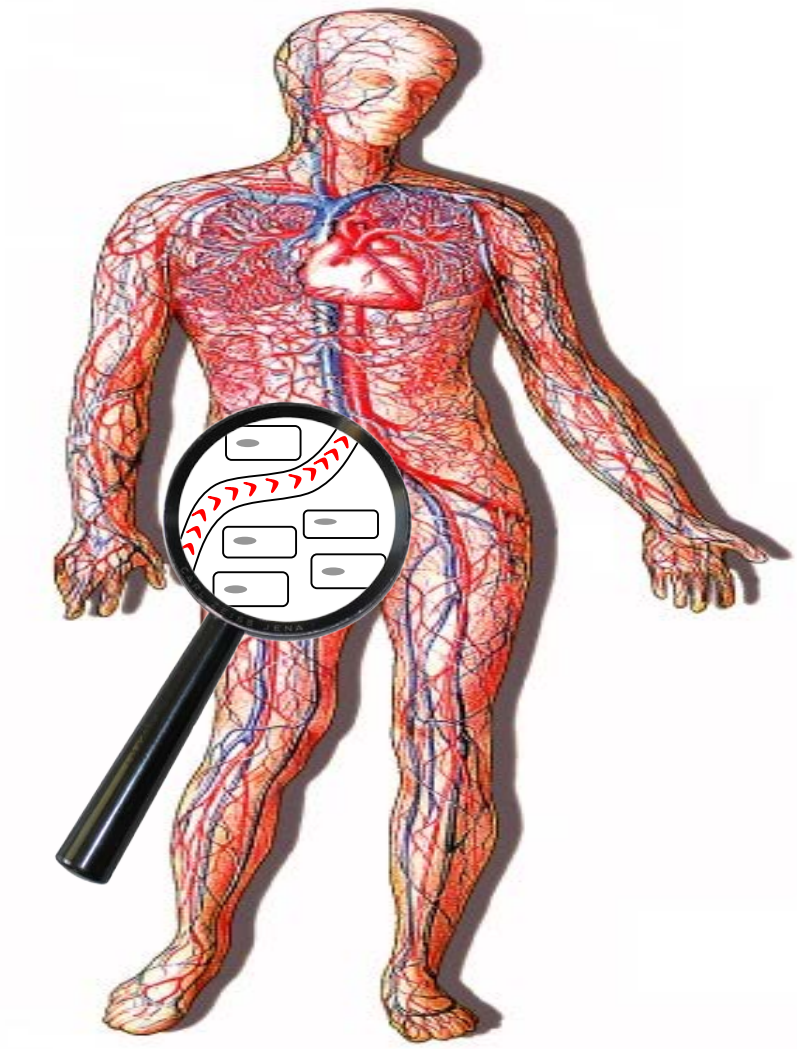
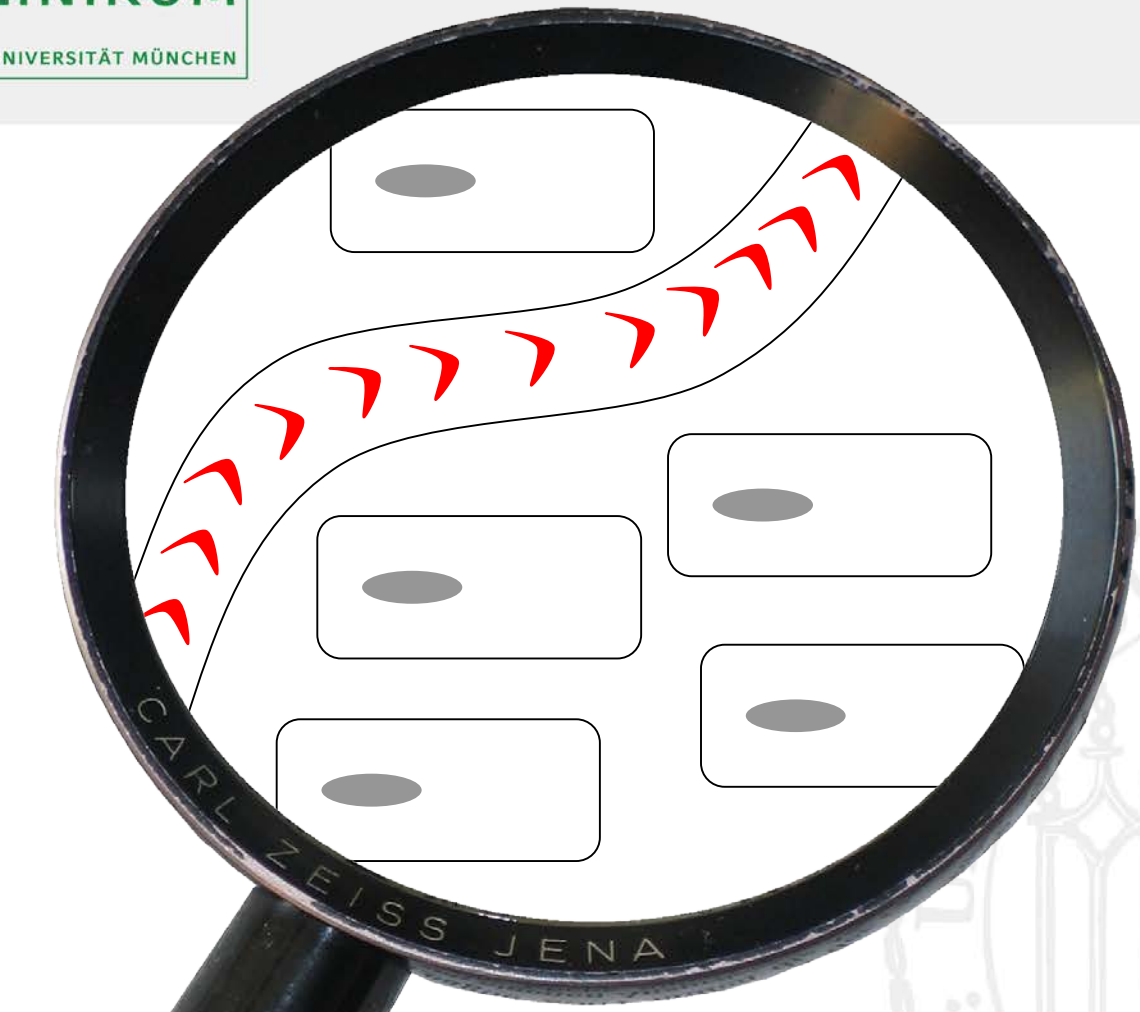
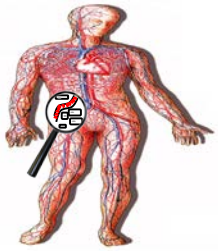
The Classical Principle



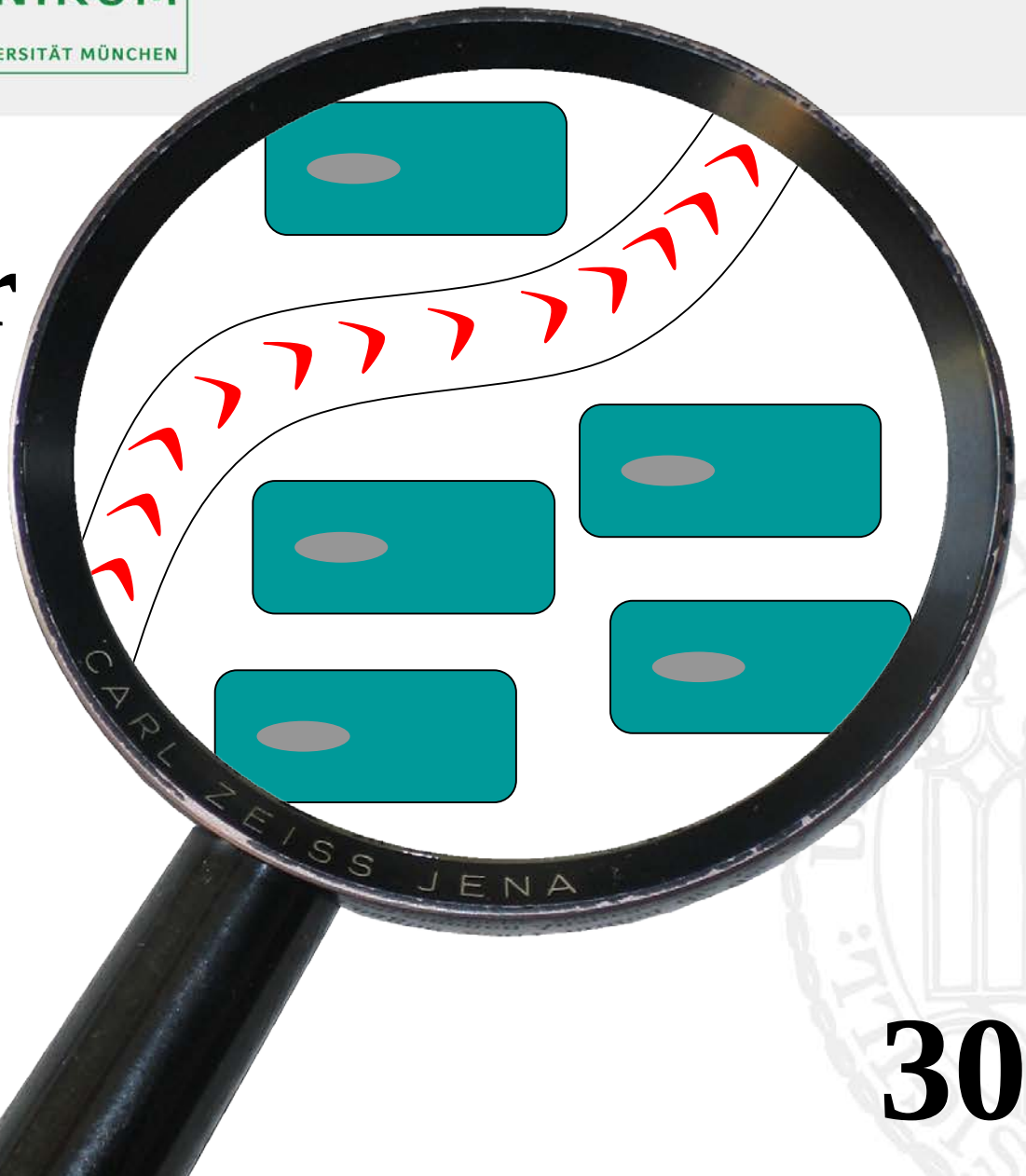
The Classical Principle

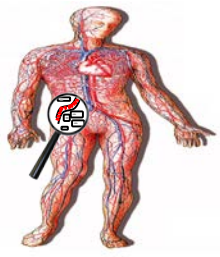




45 litres

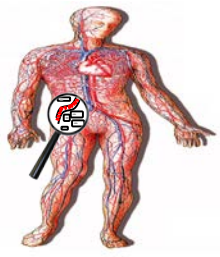
intra-cellular space





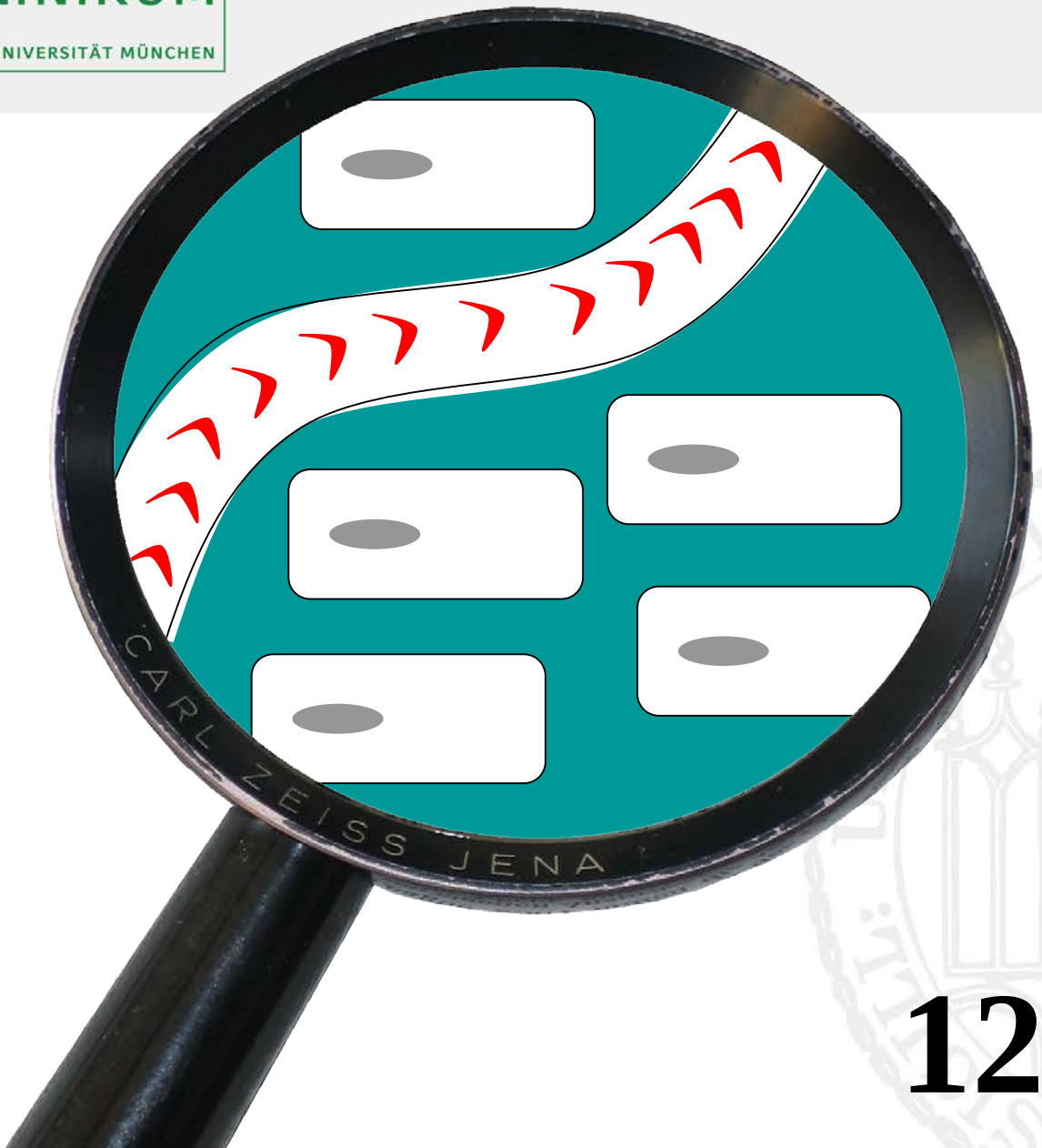
30 litres

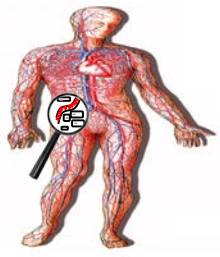
extra-cellular space



15 litres

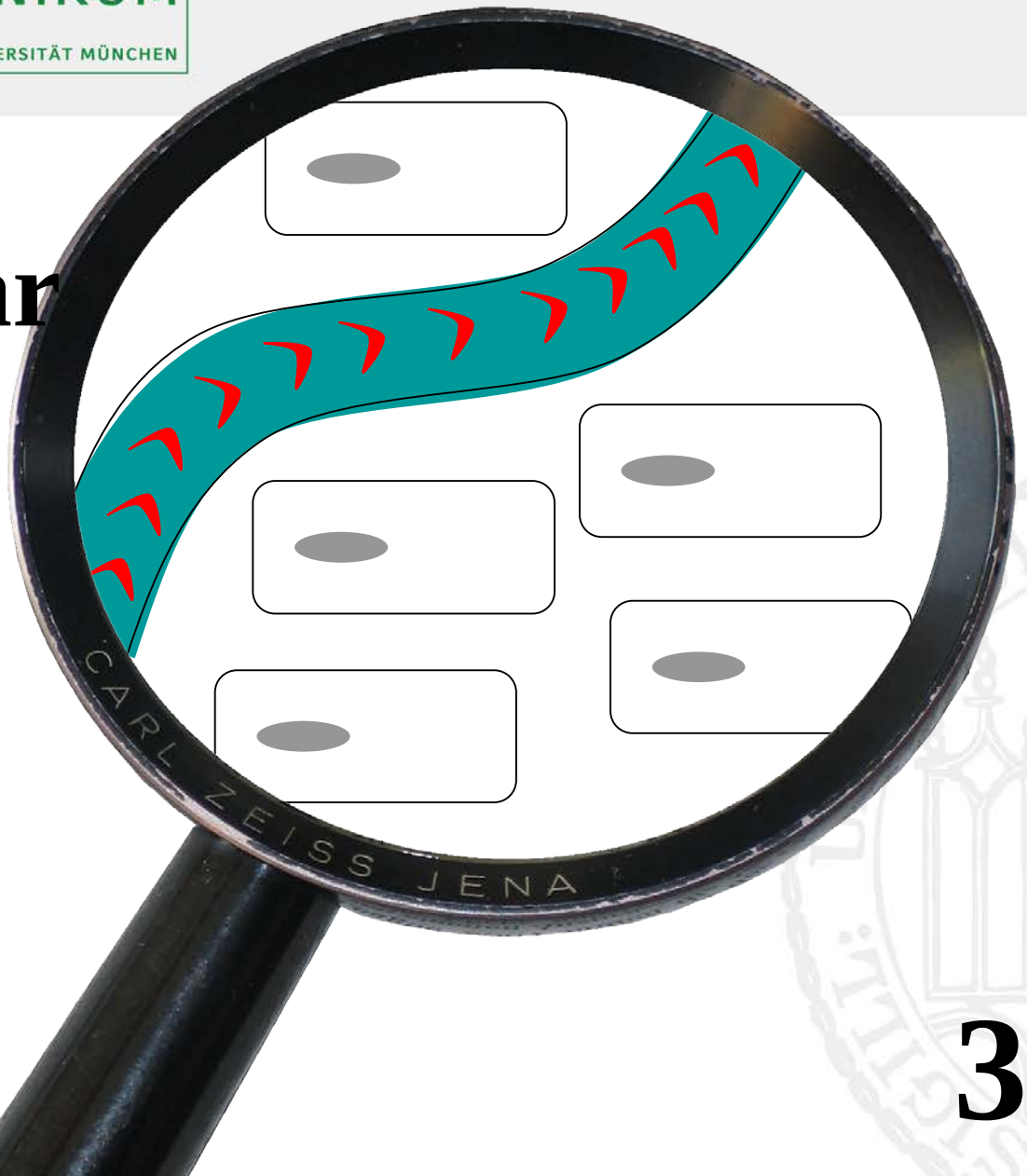
inter-stitial space

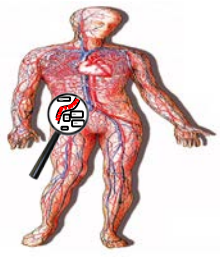




12 litres

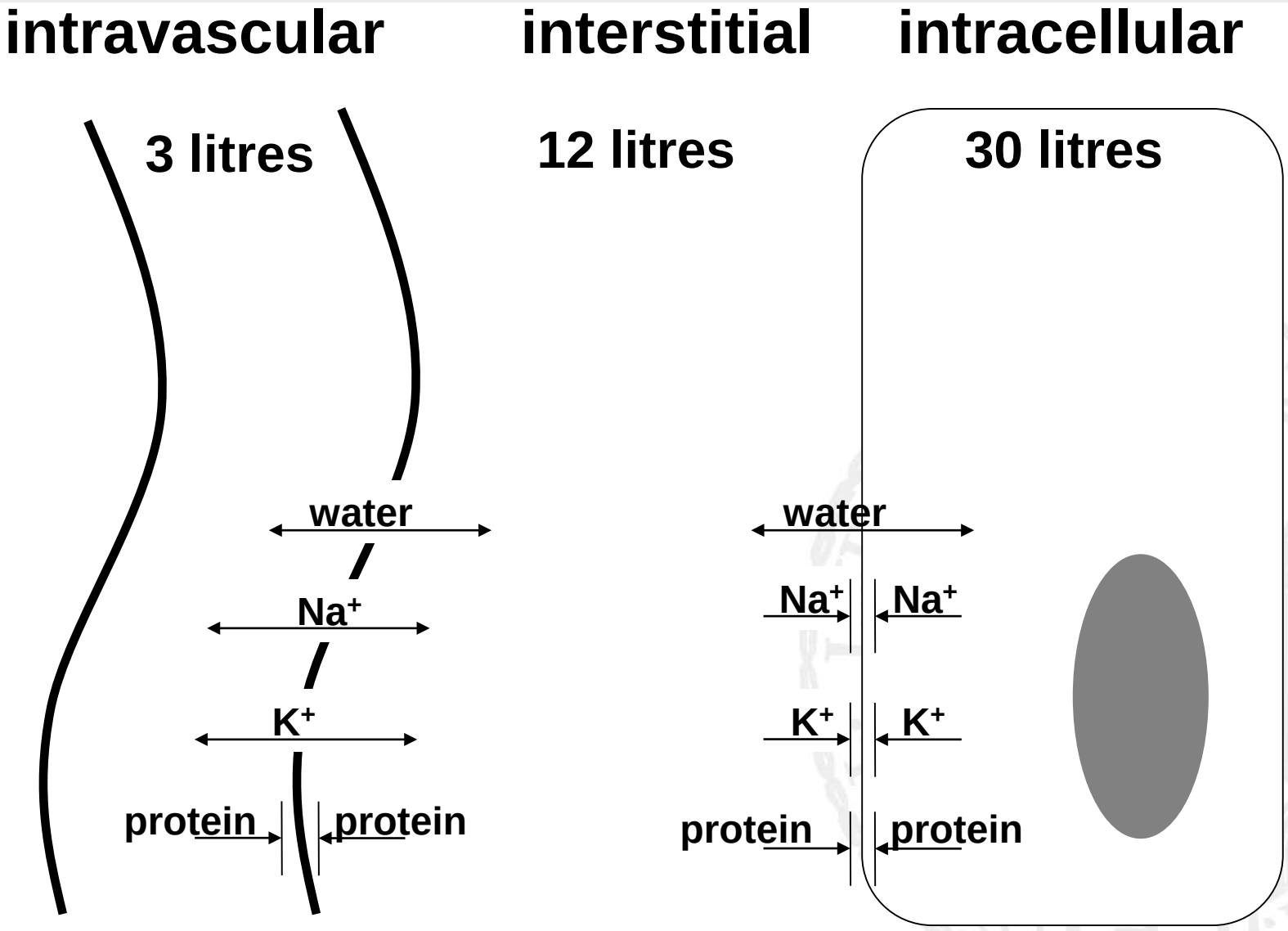
intra-vascular space





3 litres

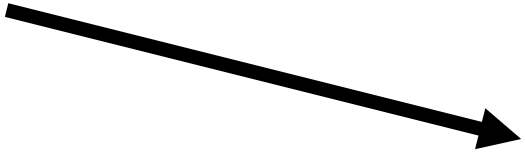
Intuition


intravascular
interstitial
intracellular
3 litres
12 litres
30 litres
water
Na+
K+
protein
protein
water
Na+
Na+
K+
K+
protein
protein

Intuition

Infusion Therapy

Fluid Substitution



Volume Replacement

Intuition

Infusion Therapy

Fluid Substitution

extracellular

Crystalloid

Volume Replacement

intravascular

Colloid / Protein

Colloid / Protein

Colloid / Protein

artificial or natural (isooncotic)

Colloid / Protein

artificial or natural (isooncotic)

if the patient needs preload

Colloid / Protein

artificial *or natural* ***(isooncotic)***

if the patient needs preload

and costs do matter

REALLY.....???

Consensus Statement of the ESICM Task Force on Colloid Volume Therapy in Critically Ill Patients

Reinhart K, Perner A, Sprung CL, Jaeschke R, Schortgen F, Groeneveld J, Beale R and Hartog C

Intensive Care Med 2012, 38:368-83

Consensus Statement of the ESICM Task Force on Colloid Volume Therapy in Critically Ill Patients

Reinhart K, Perner A, Sprung CL, Jaeschke R, Schortgen F, Groeneveld J, Beale R and Hartog C

(…) we suggest not to use 6% HES 130 (…)

Intensive Care Med 2012, 38:368-83

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Round Table Conference „Types of i.v.-Fluids“ ISICEM, 2012, Brussels

Chairmen: M Mythen and J Myburgh

S Finfer, G Martin, C Ince, M Jacob, J Bagshaw, J Kellum, R Bellomo, S Finney, J Wernerman, L McIntyre, C Martin, J Morgan, JL Vincent, A Shaw, L Gattinoni, L Kaplan, A Perner, K Reinhart, K Maitland

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„physiology is the only polar star we have…“

Luciano Gattinoni

D Bihari, S Bonfiglio, C Ince, M Jacob, J Bagshaw, J Kellum, R Bellomo, S Finney, J Wernerman, L McIntyre, C Martin, J Morgan, JL Vincent, A Shaw, L Gattinoni, L Kaplan, A Perner, K Reinhart, K Maitland

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D Chelazzi, C Ince, M Jacob, J Bagshaw, J Kellum, R Bellomo, S Finney, J Wernerman, [illegible], A Kaplan, A Perner, K Reinhart, K Maitland

„I do not care about physiology, I care about outcome-based evidence!“
Konrad Reinhart

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Evidence-Based Medicine In Fluid and Volume Handling – A Problem?

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Three Principles of Evidence-Based Medicine

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Three Principles of Evidence-Based Medicine

1. Absence of Evidence is not Evidence of Absence

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Three Principles of Evidence-Based Medicine

2. Present Evidence is Evidently Present

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Three Principles of Evidence-Based Medicine

3. Evidence for Harm due to Drug Misuse Might be Related

1) to the Drug or

2) to the Misuse

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Infusion Therapy and Outcome-based Evidence

The History

The New England Journal of Medicine

EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

EMANUEL RIVERS, M.D., M.P.H., BRYANT NGUYEN, M.D., SUZANNE HAVSTAD, M.A., JULIE RESSLER, B.S., ALEXANDRIA MUZZIN, B.S., BERNHARD KNOBLICH, M.D., EDWARD PETERSON, PH.D., AND MICHAEL TOMLANOVICH, M.D., FOR THE EARLY GOAL-DIRECTED THERAPY COLLABORATIVE GROUP*

Conclusions Early goal-directed therapy provides significant benefits with respect to outcome in patients with severe sepsis and septic shock. (N Engl J Med 2001;345:1368-77.)

Rivers E et al. N Engl J Med 2001; 345 (19): 1368-77

beyond that, **evidence** concerning volume replacement therapy is **unreliable** and **incomplete**

Jacob M et al. Anesthesiology 2011, 114:483-4

Bunggaard-Nielssen et al. Acta Anaesthesiol Scand 2009, 53:843-51

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Creating Evidence (Ideal Case)

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Creating Evidence (Ideal Case)

Causal Therapy

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Creating Evidence (Ideal Case)

Standard

Creating Evidence (Ideal Case)

Standard

New Idea

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Creating Evidence (Ideal Case)

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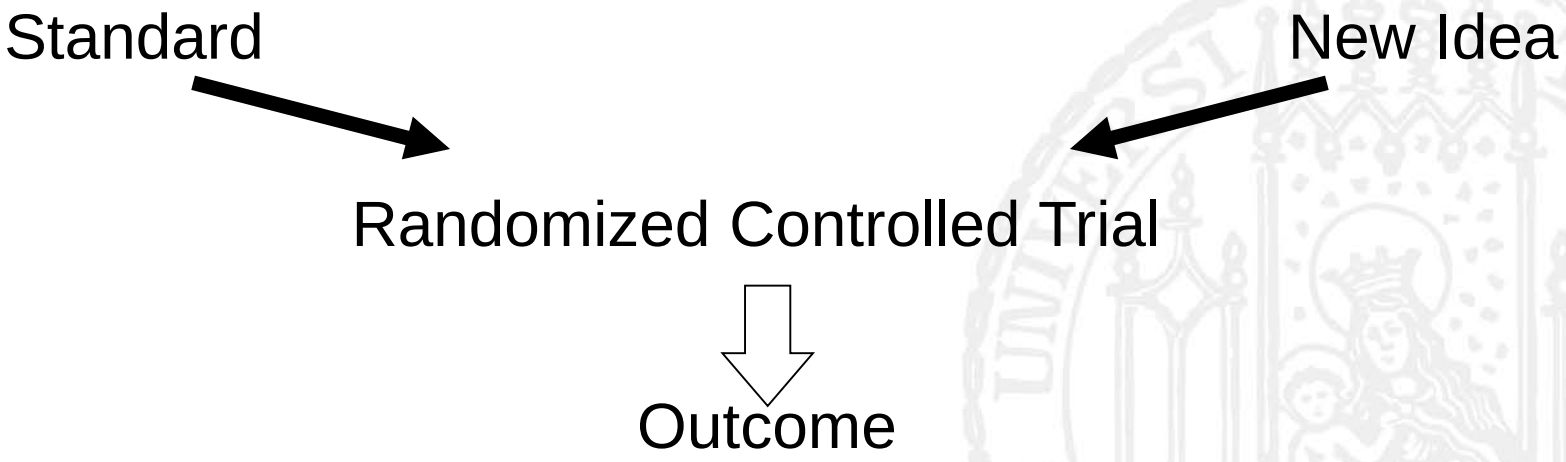
Creating Evidence (Ideal Case)



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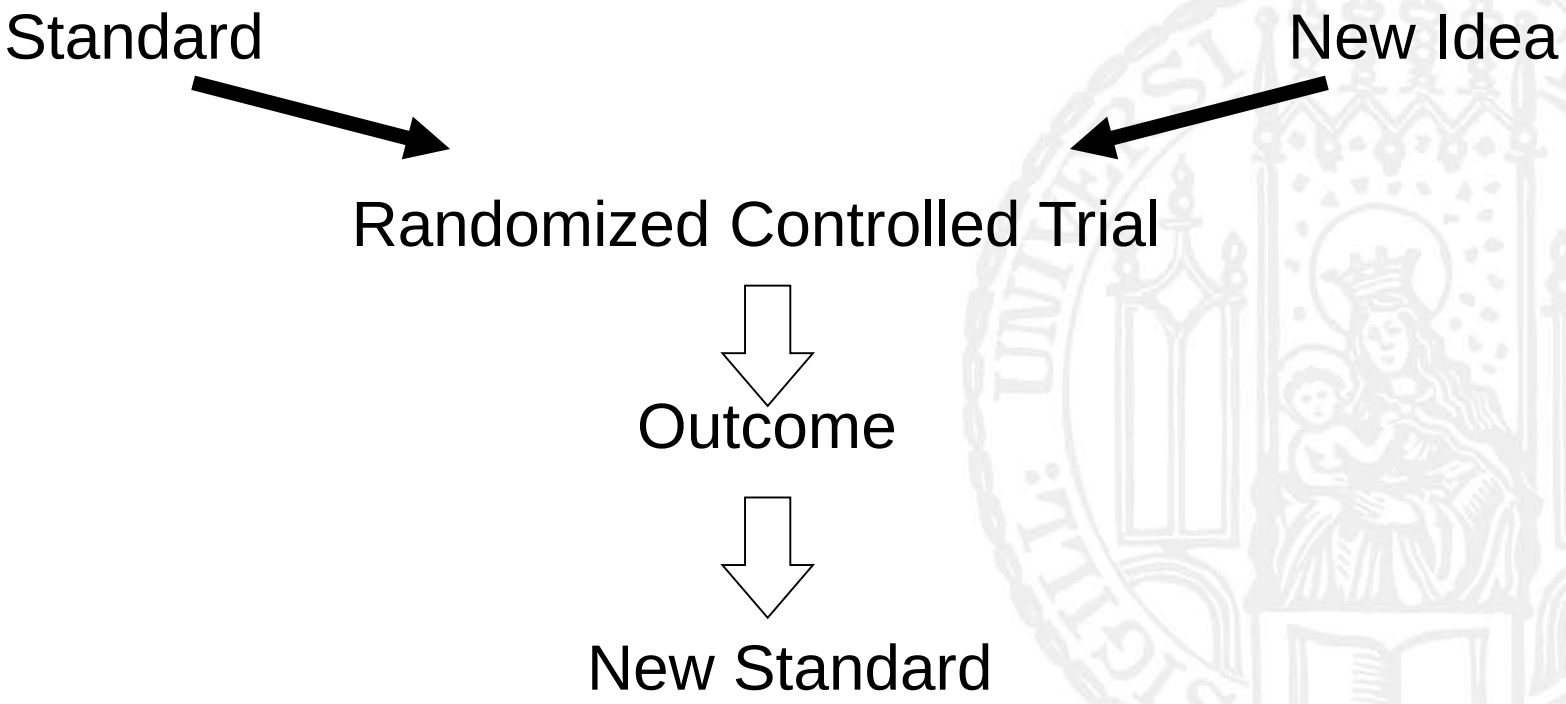
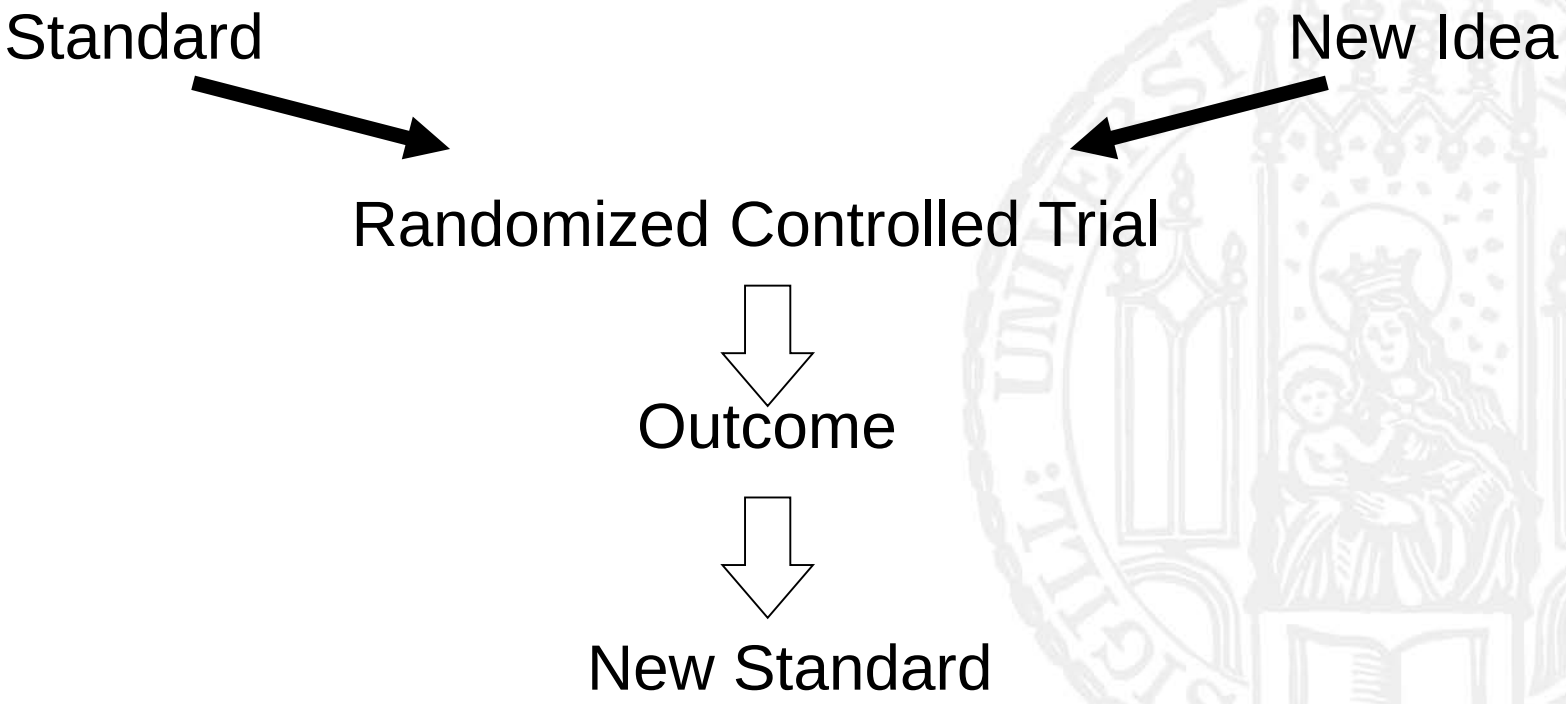


Creating Evidence (Volume Replacement Therapy)



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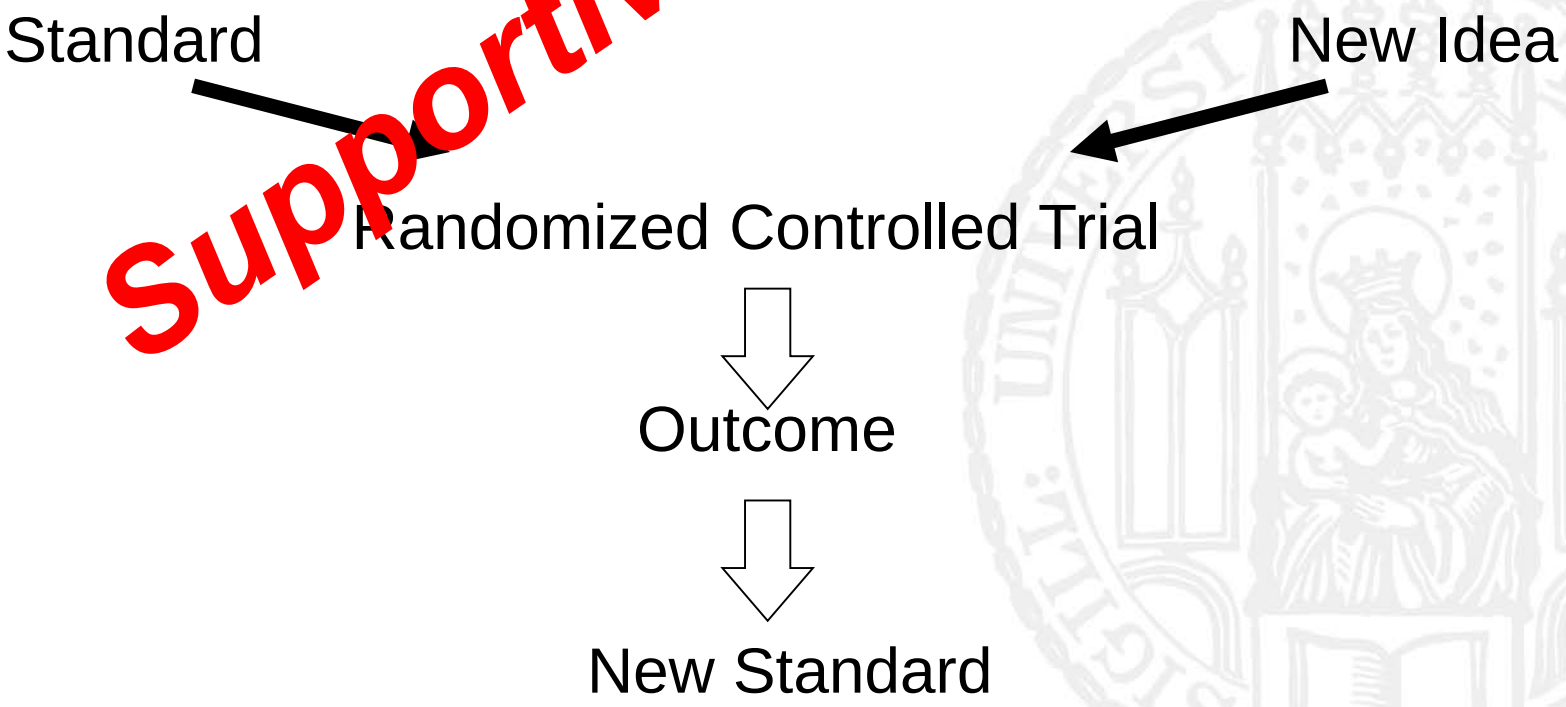
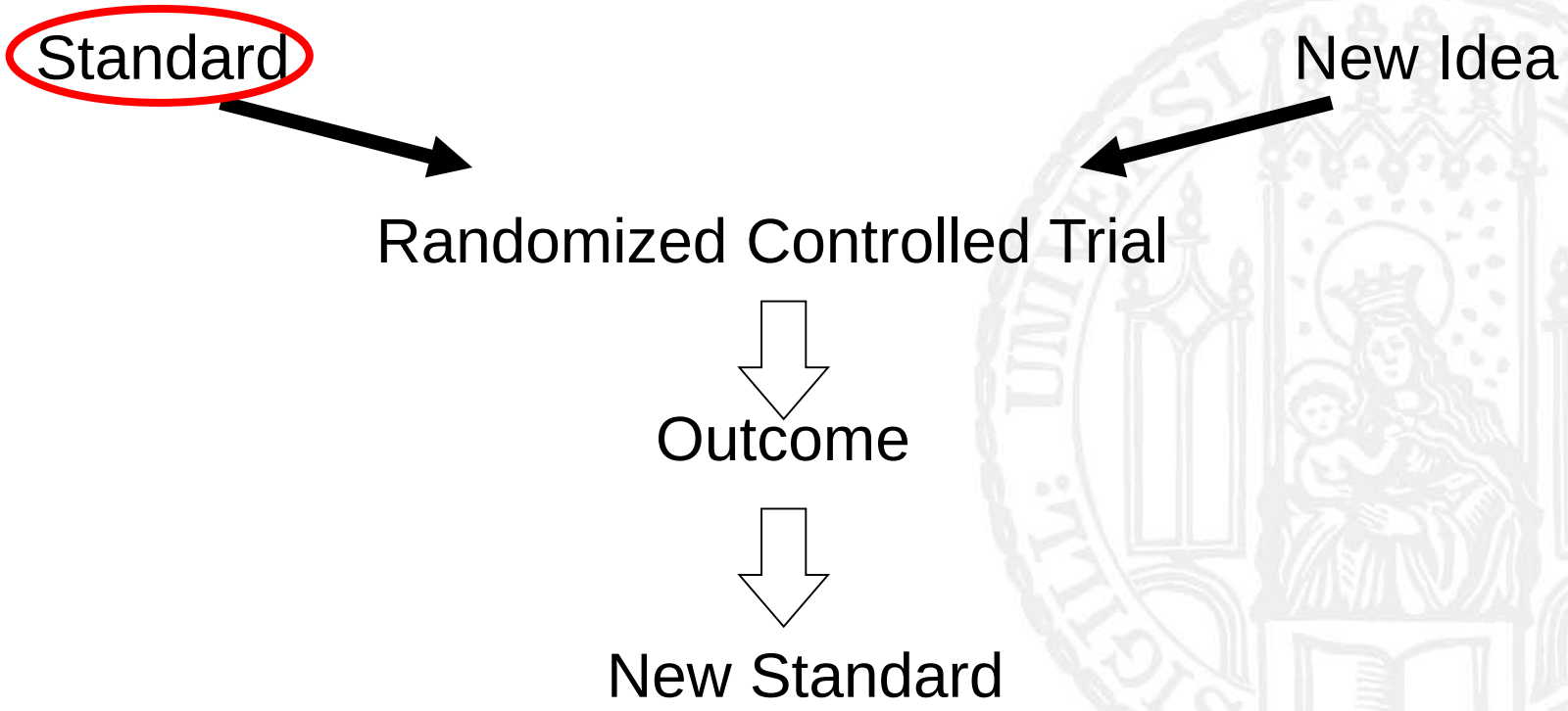
Creating Evidence (Volume Replacement Therapy)

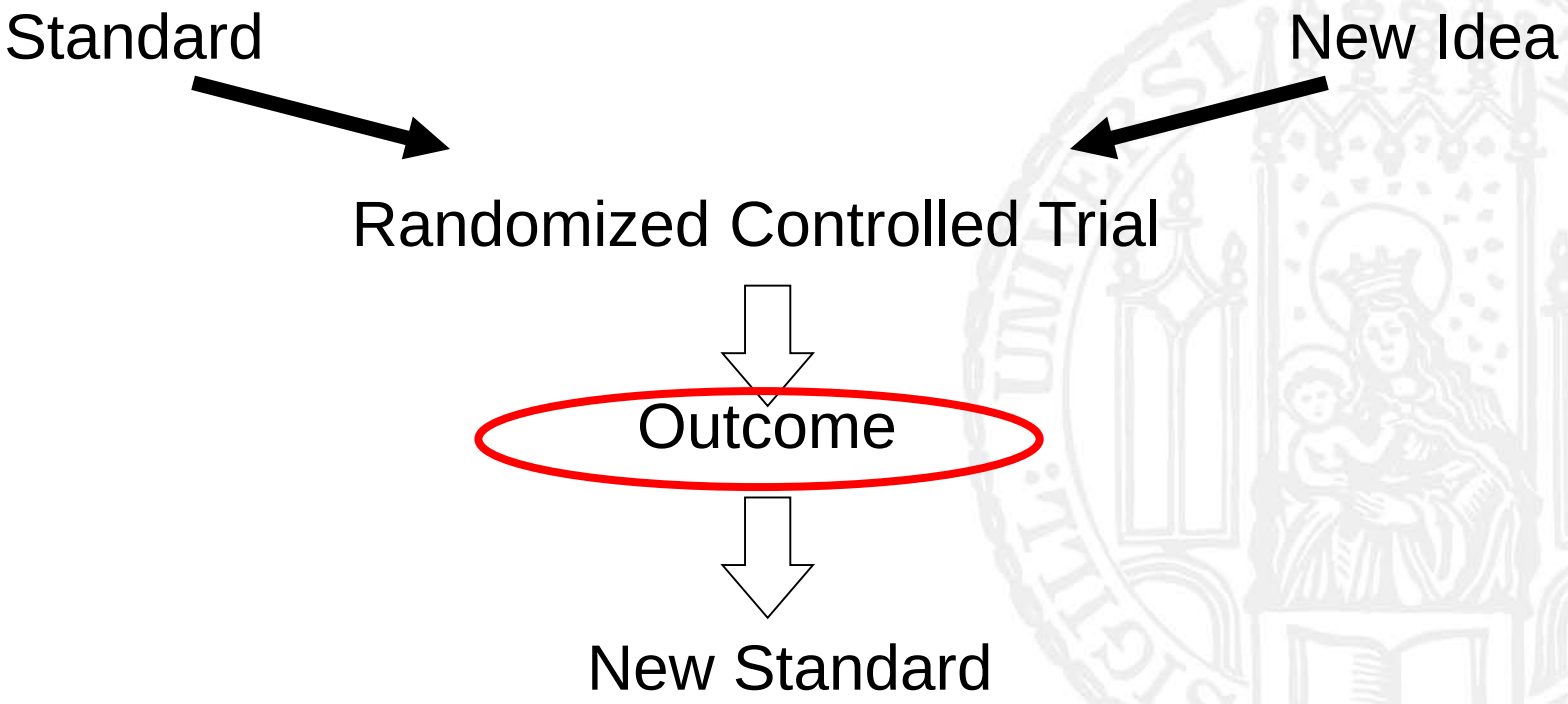
Supportive Measure



Creating Evidence (Volume Replacement Therapy)



Creating Evidence (Volume Replacement Therapy)



until today, it is impossible to formulate **outcome-based** recommendations on volume replacement therapy

Jacob M et al. Anesthesiology 2011, 114:483-4

Bunggaard-Nielssen et al. Acta Anaesthesiol Scand 2009, 53:843-51

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„Body of Evidence“ concerning Infusion Therapy

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„Body of Evidence“ concerning Infusion Therapy

↓

Outcome

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Physiology and Pathophysiology

↖

„Body of Evidence“ concerning Infusion Therapy

↓

Outcome

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Physiology and Pathophysiology

Scientific Facts

„Body of Evidence“ concerning Infusion Therapy

Outcome

in 2015 it is possible **and reasonable** to formulate **rational** recommendations on volume replacement therapy

Jacob M et al. Anesthesiology 2011, 114:483-4

Bunggaard-Nielssen et al. Acta Anaesthesiol Scand 2009, 53:843-51

Volume Replacement Therapy

Van Aken et al. Anaesth Intensivmed 2010, 51:211-18

Jacob M et al. Anesthesiology 2011, 114:483-4

Volume Replacement Therapy

Based on
Facts and
Physiology

Supported by
Outcome-based
Evidence

Van Aken et al. Anaesth Intensivmed 2010, 51:211-18

Jacob M et al. Anesthesiology 2011, 114:483-4

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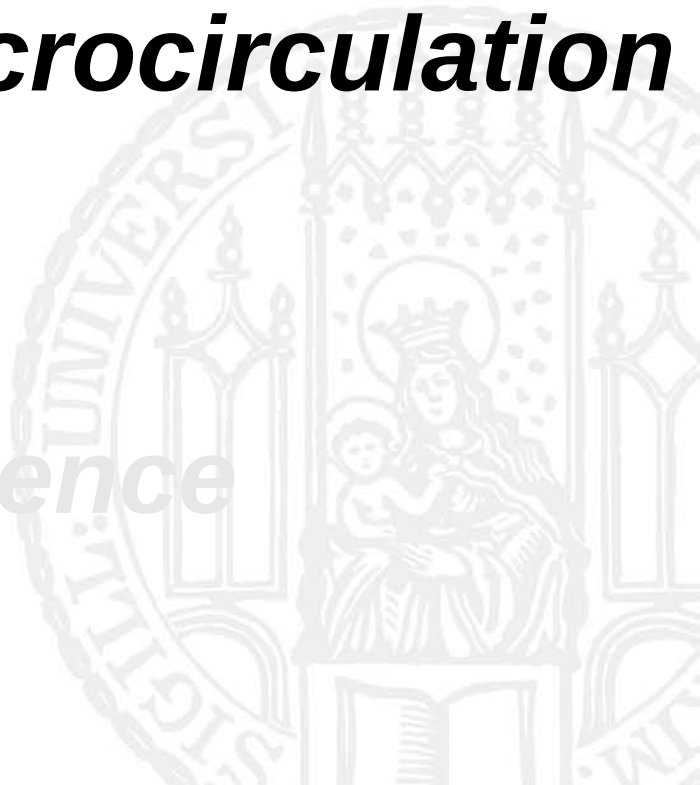
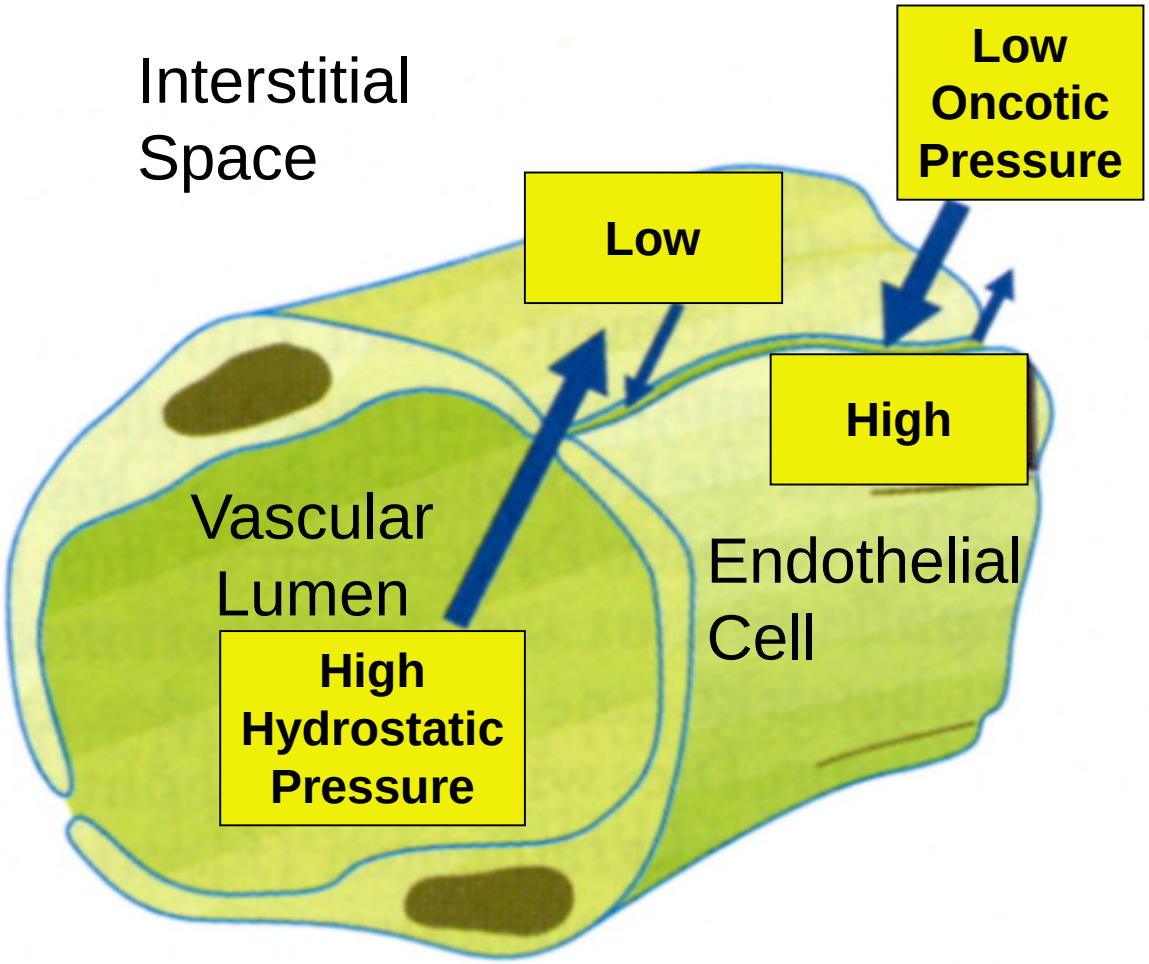
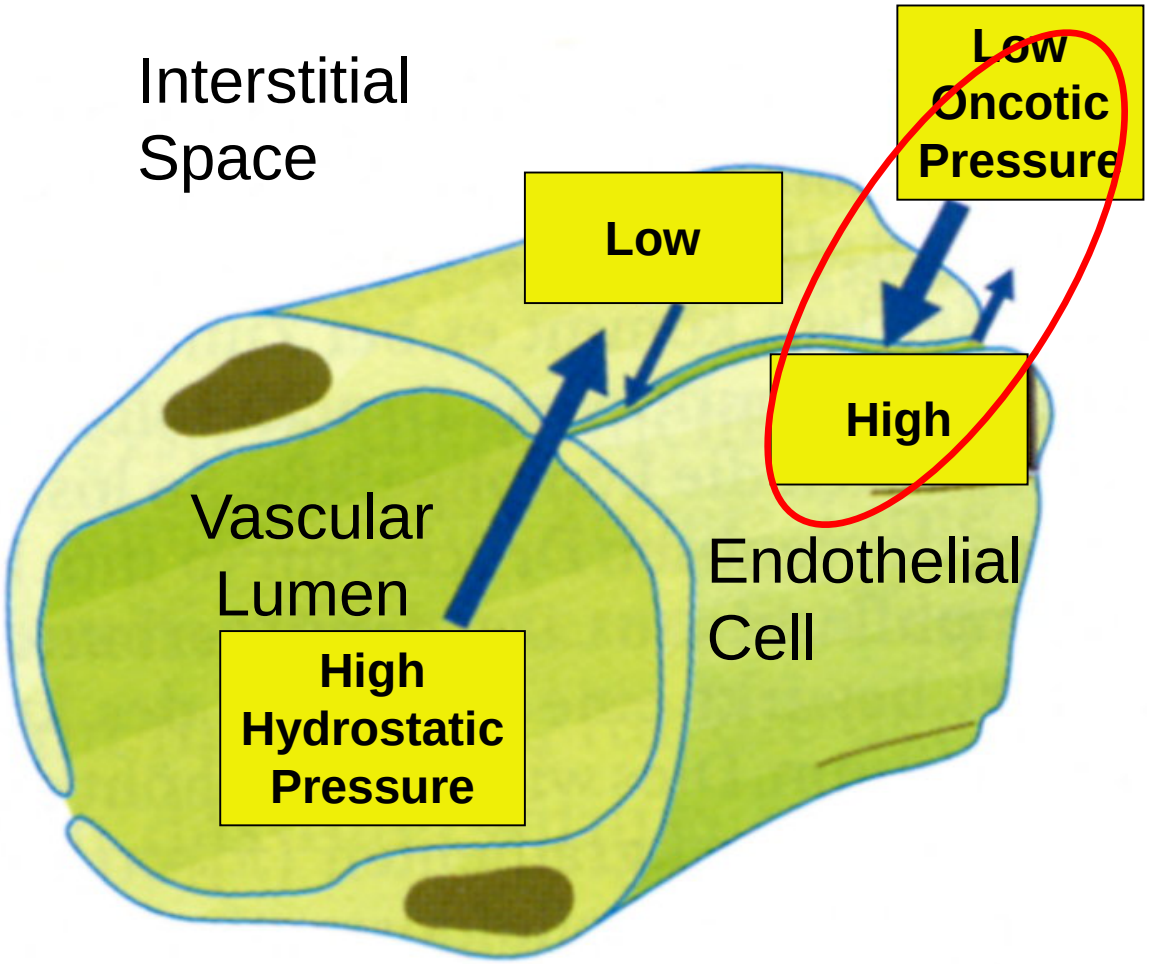




Ernest Starling
1866 - 1927

J Physiol 1896, 19: 312-26.



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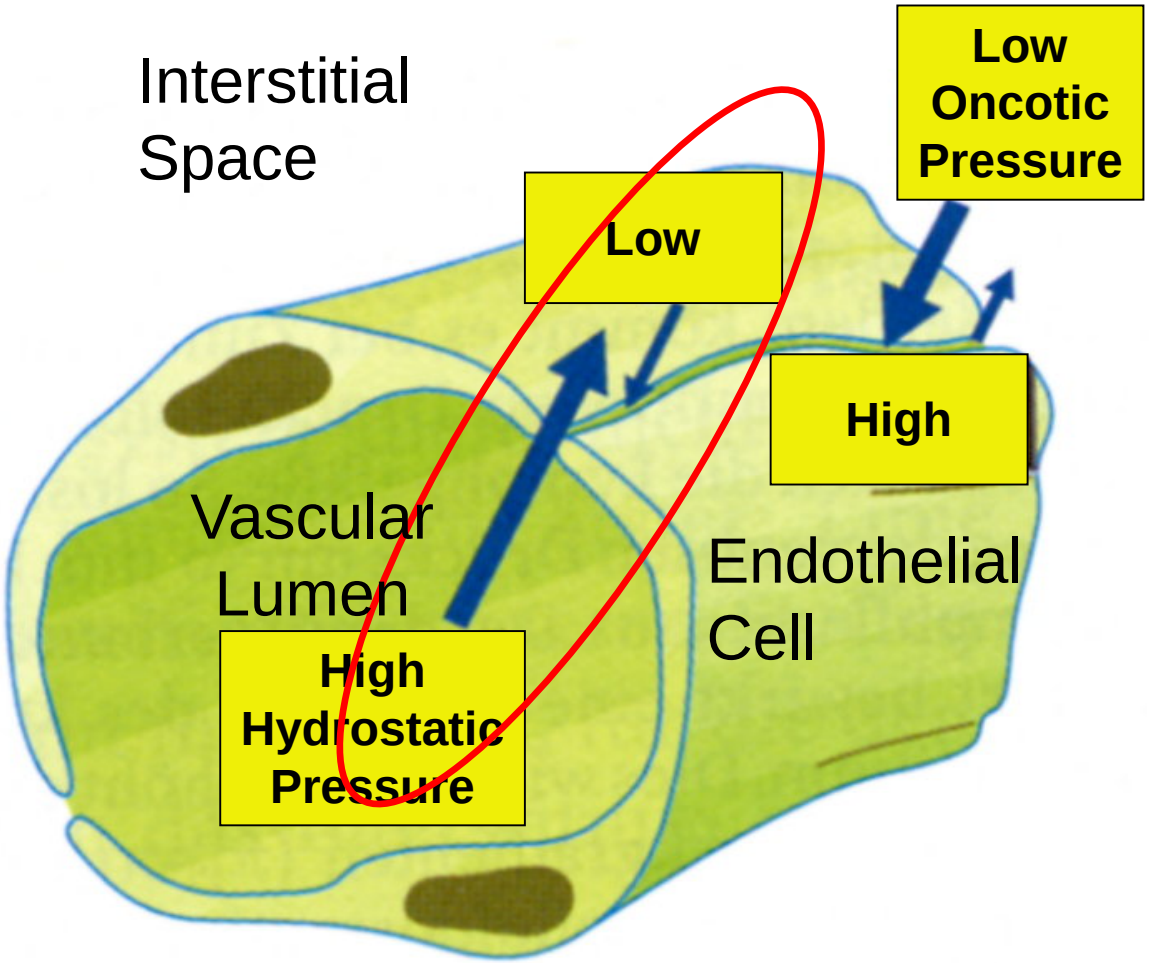

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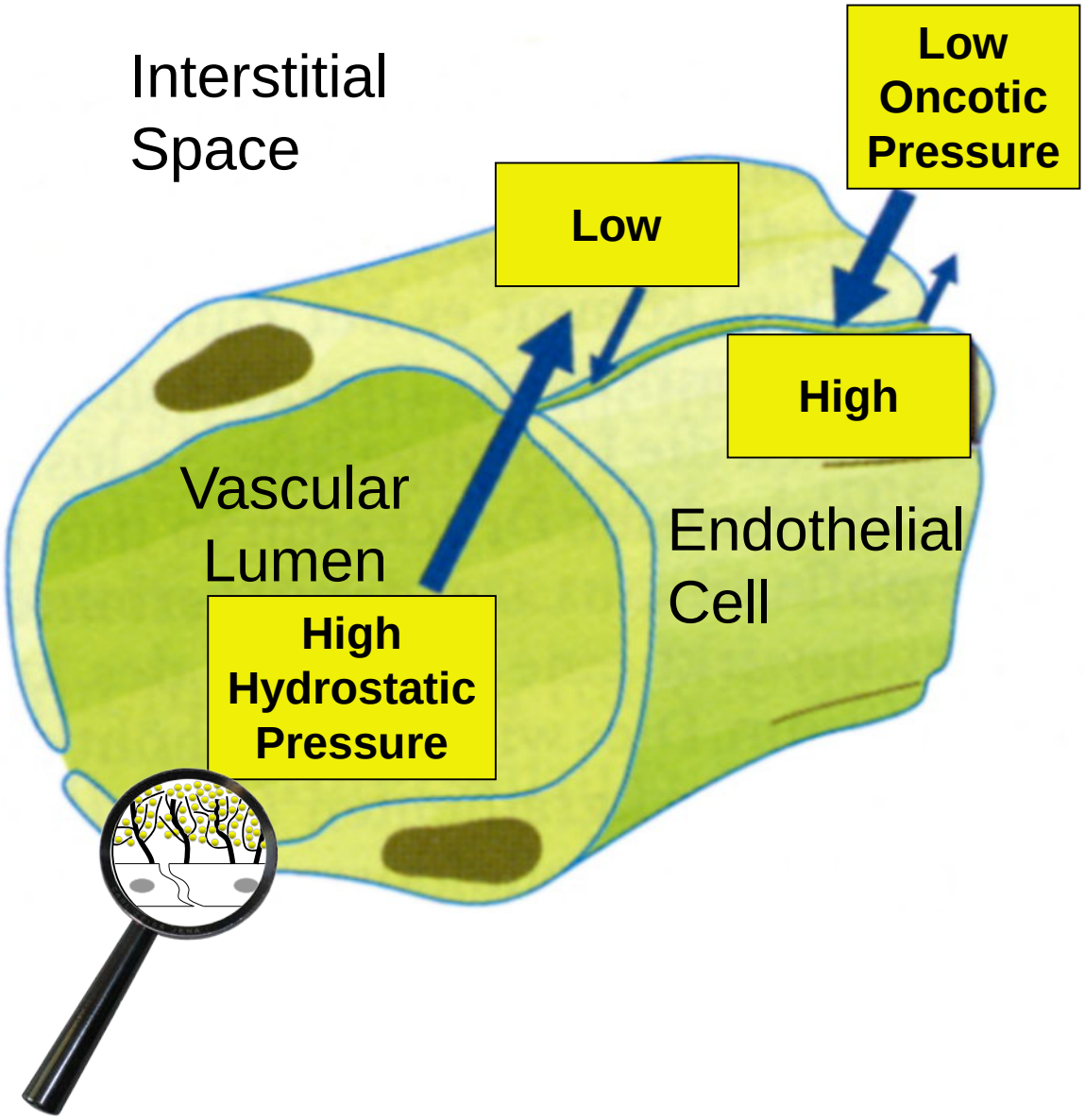

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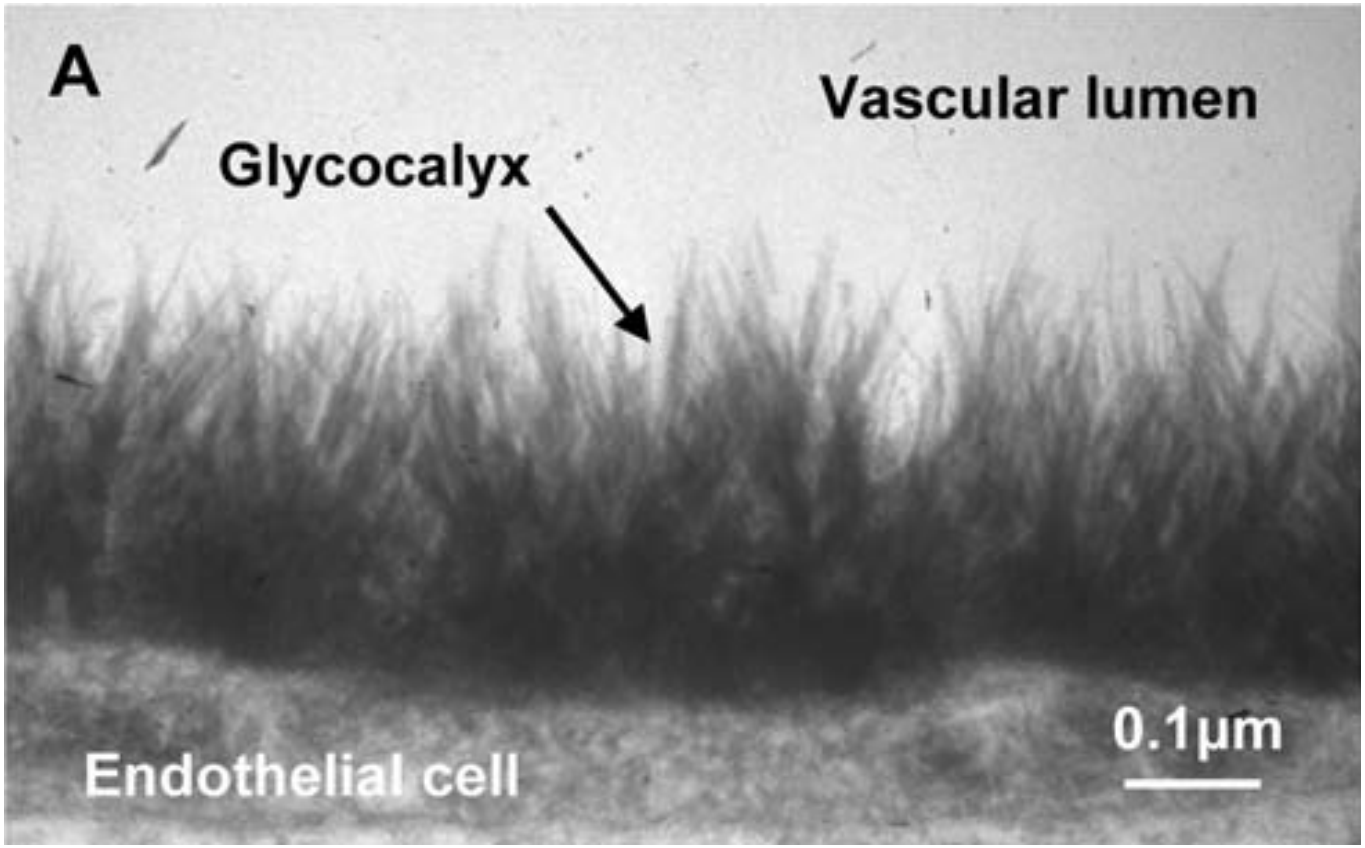
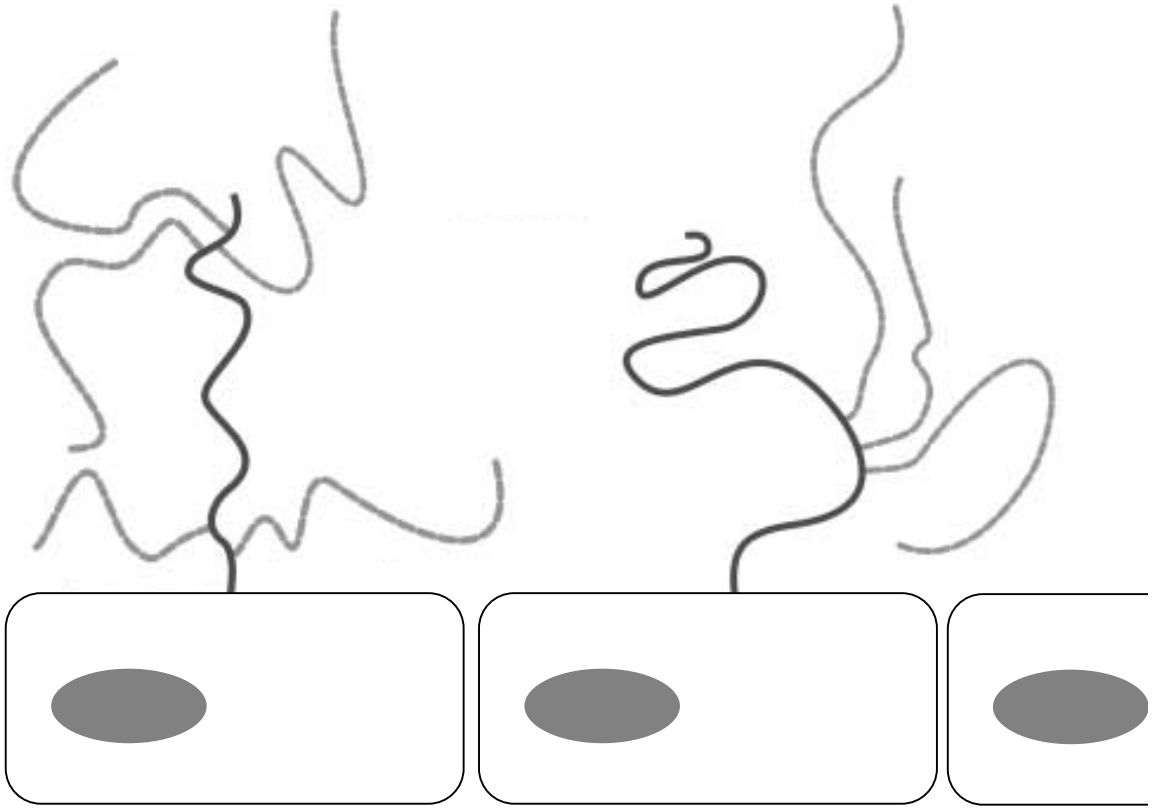
endothelial glycocalyx



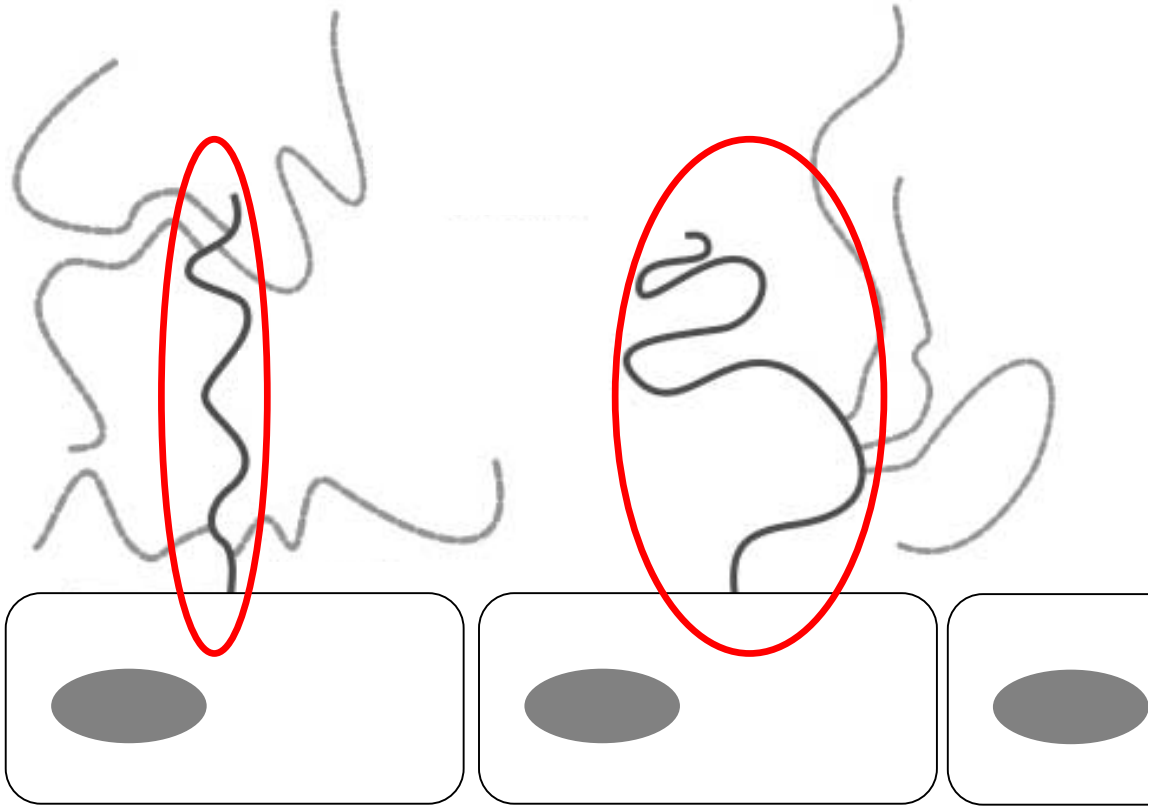
Chappell D and Jacob M et al. (2009) Circ Res 83:388-96

Jacob M et al. (2007) J Appl Physiol 102: 1235-42

endothelial glycocalyx



endothelial glycocalyx



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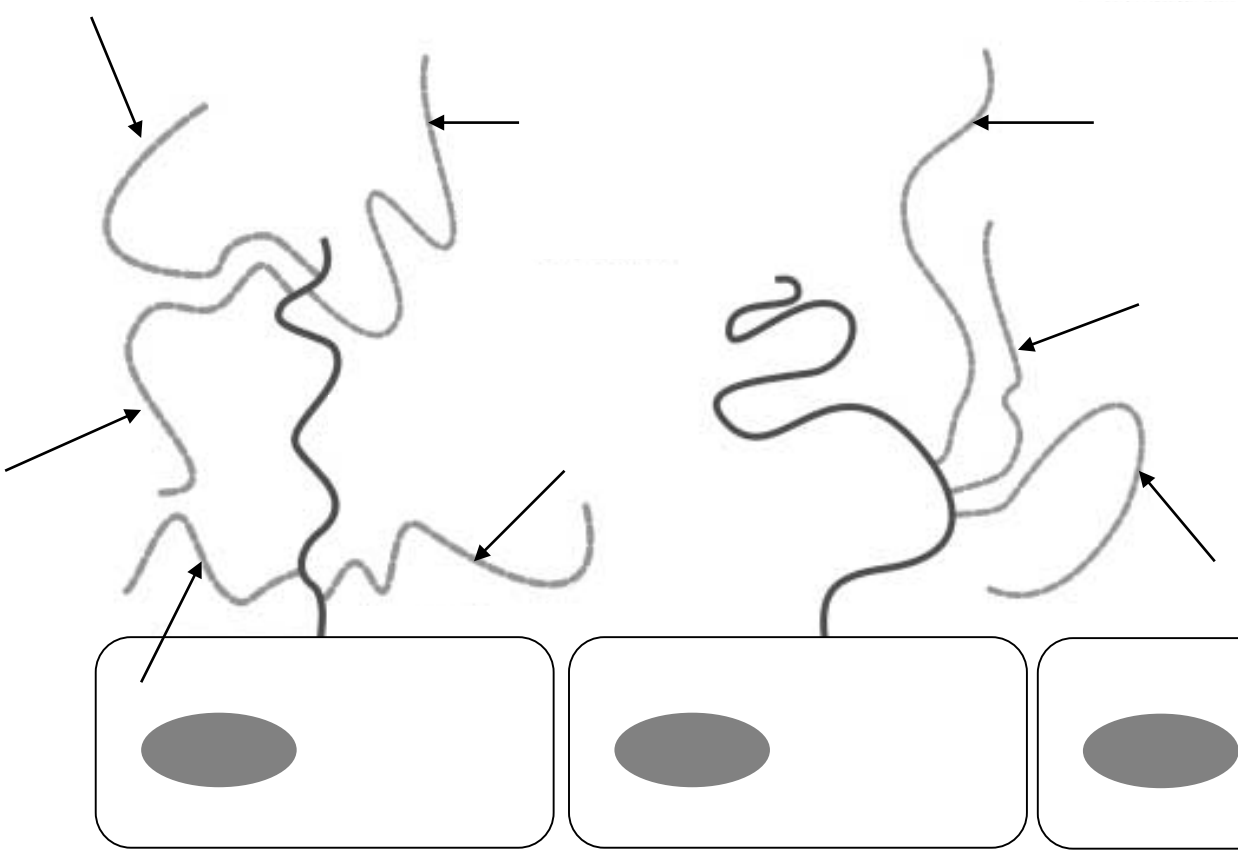
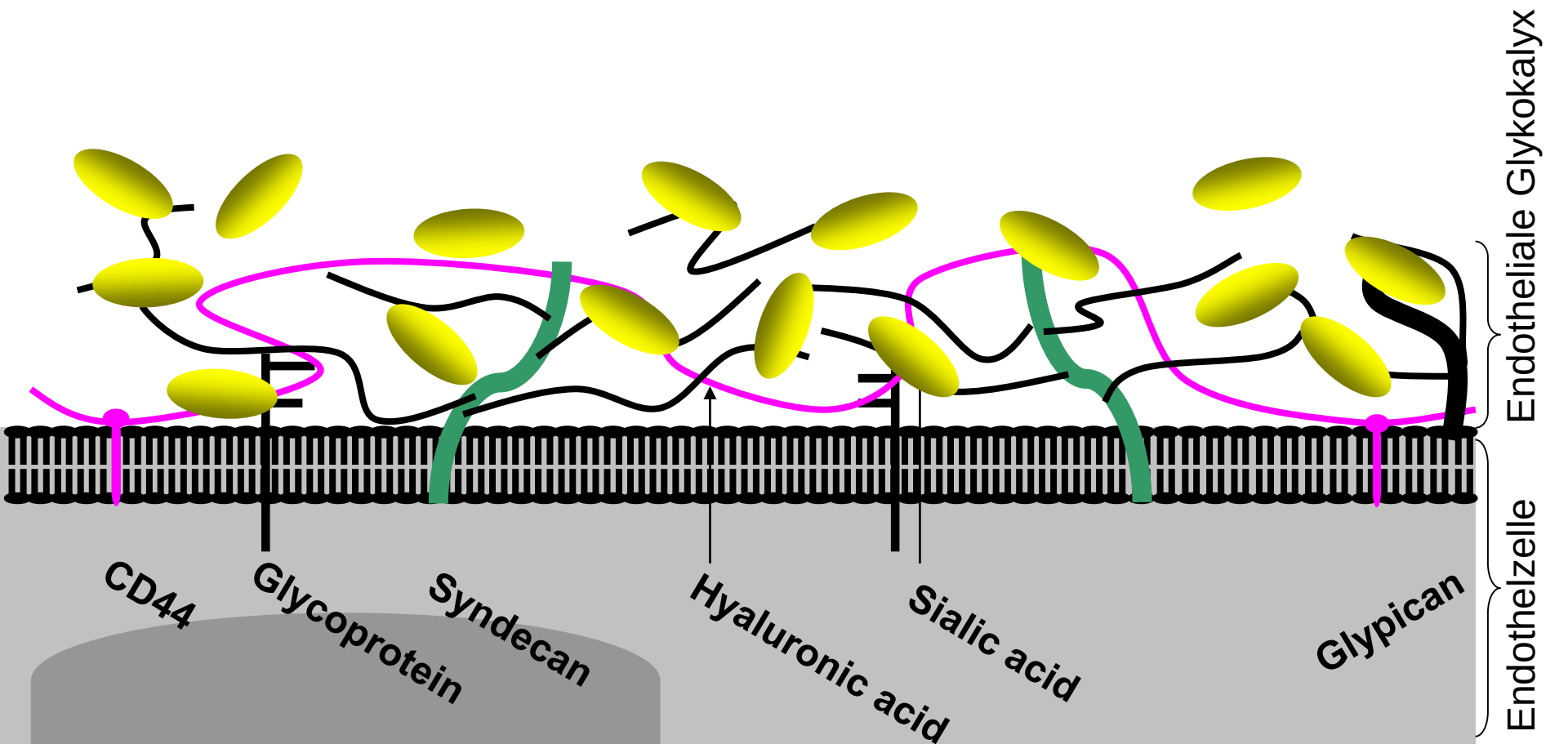
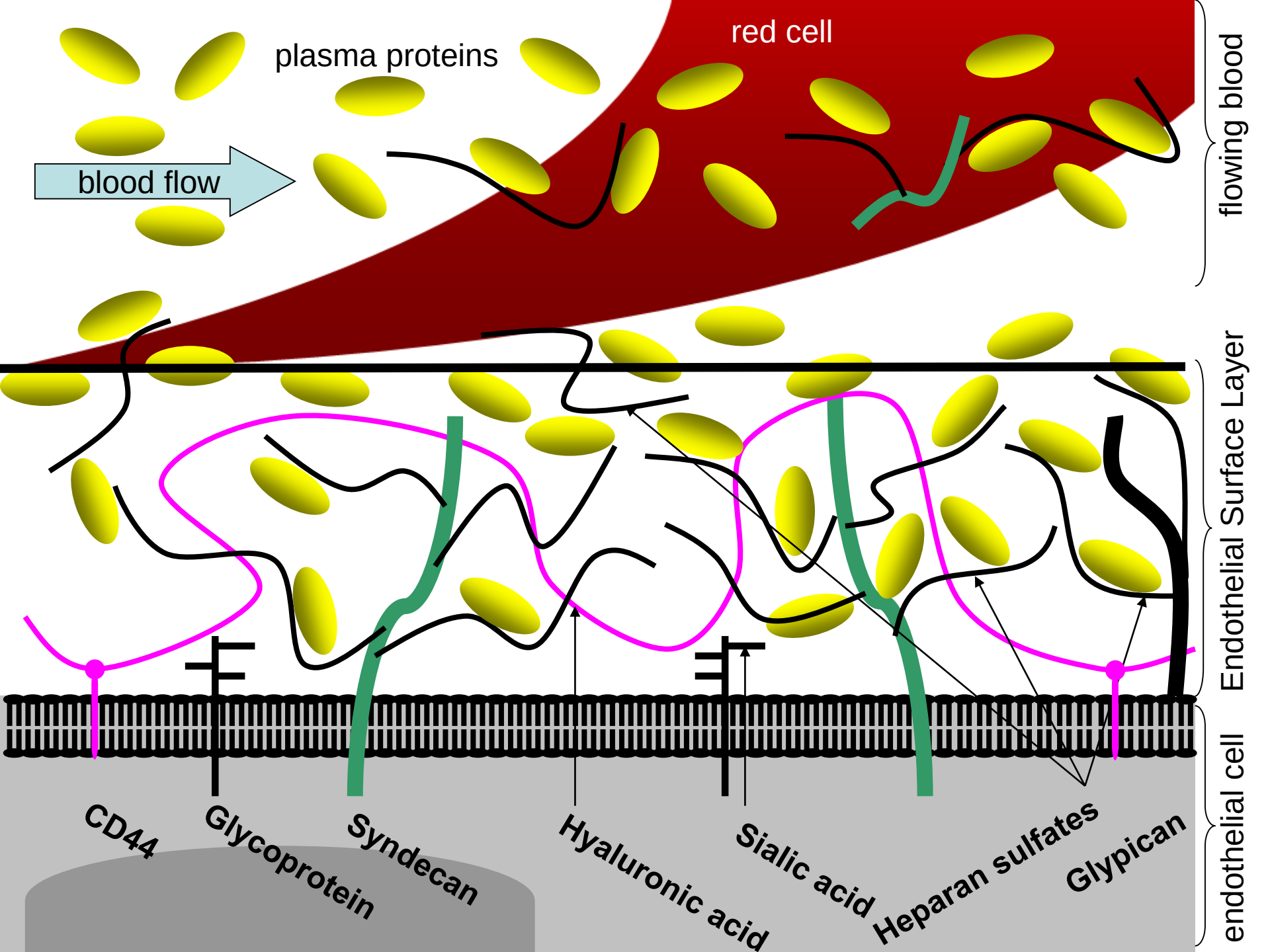
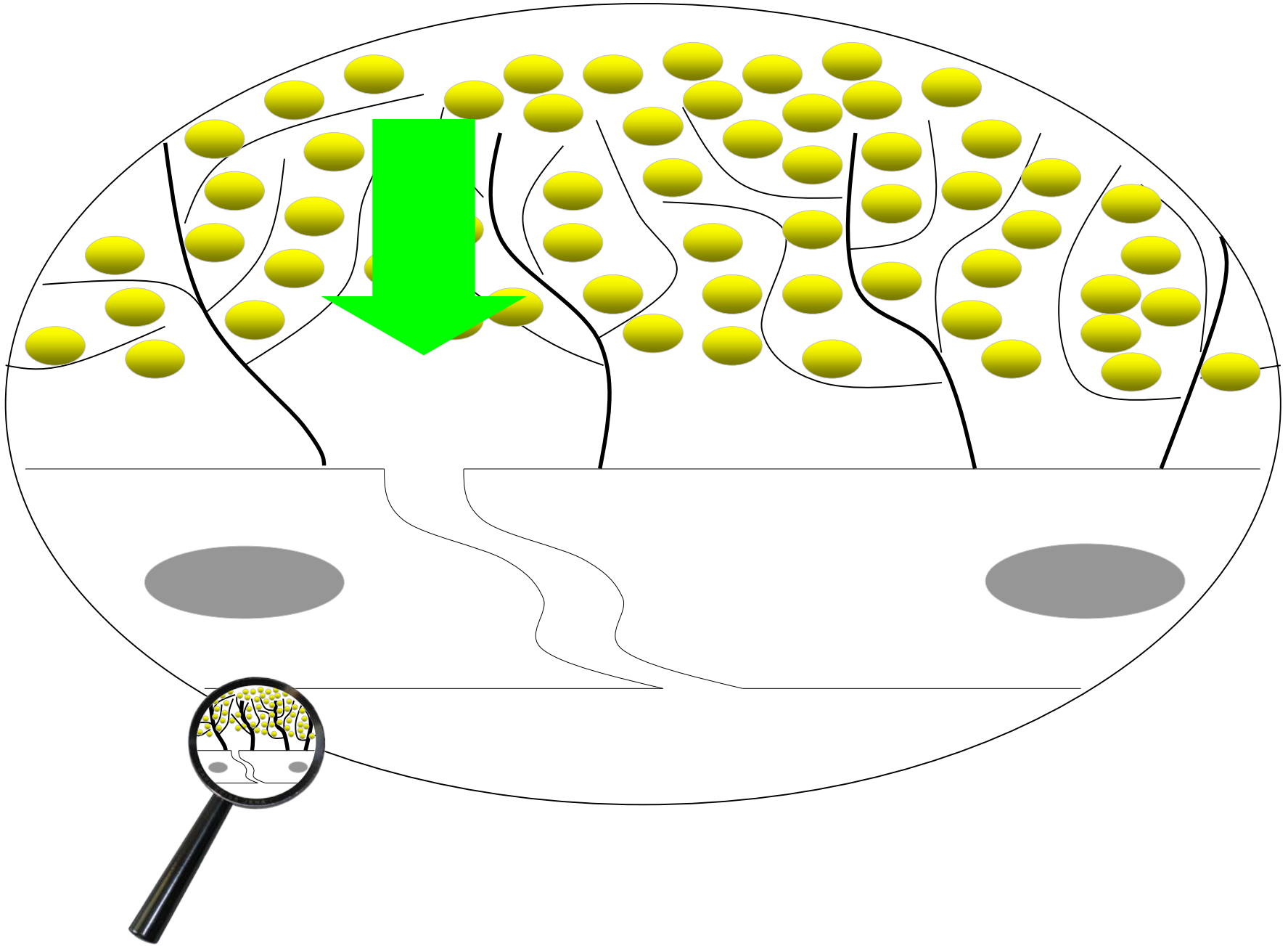


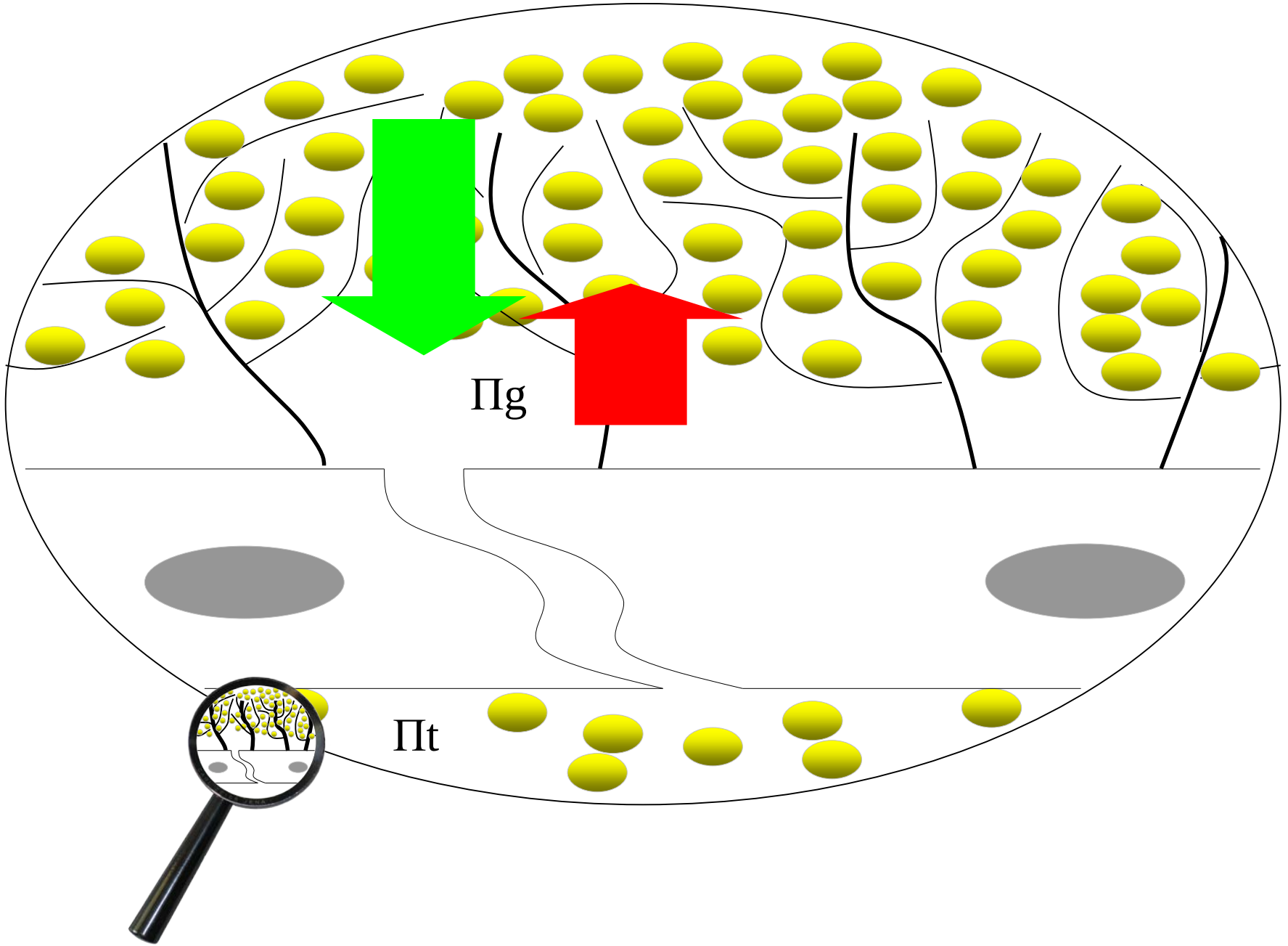
endothelial glycocalyx




plasma proteins
red cell
blood flow
flowing blood
Endothelial Surface Layer
endothelial cell
CD44
Glycoprotein
Syndecan
Hyaluronic acid
Sialic acid
Heparan sulfates
Glypican



Jacob M et al. (2007) Cardiovasc Res 73: 575-586
Adamson RH et al. (2004) J Physiol 557:889-907



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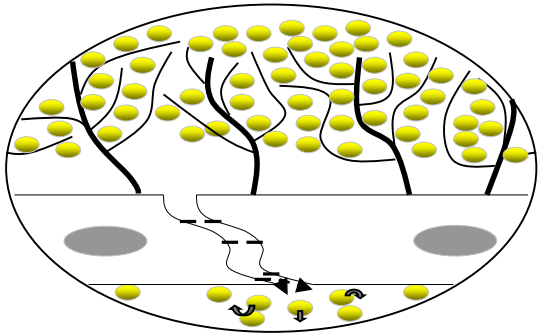
hypervolemia

ischemia / reperfusion



heparanase

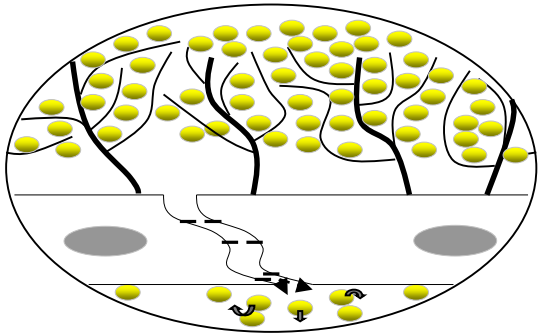
inflammatory mediators

hyperglycemia

Marechal X et al. Shock. 2008;29:572-6
Nieuwdorp M et al. Diabetes 2006;55:480-486
Rehm M et al. Circulation 2007; 116:1896-1906
Vlodavsky I et al. Thromb Res 2007; 120 Suppl 2:S112-S120

hypervolemia

ischemia / reperfusion



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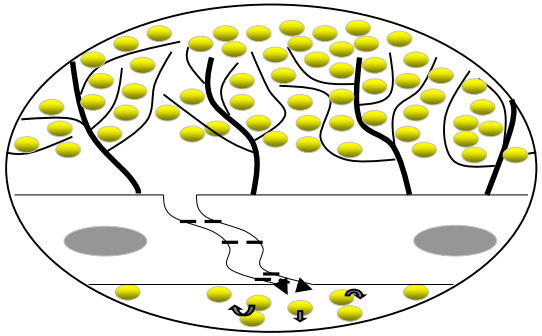

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Vlodavsky I et al. Thromb Res 2007; 120 Suppl 2:S112-S120

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Volume Replacement Therapy

- Physiology✓
- Facts
- Outcome-based Evidence

The Endothelial Surface Layer is an important and fragile part of the vascular barrier

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The Endothelial Surface Layer is an important and fragile part of the vascular barrier

1. Principal Considerations

2. Physiology of the Microcirculation

3. Scientific Facts

4. Outcome-based Evidence

Target:

Target:

Normovolemia

Indication for Volume Therapy:

Indication for Volume Therapy:

Intravascular Hypovolemia

Command Variable:

Command Variable:

Blood Volume

the central pharmacokinetic property of volume preparations

Volume Effect

the central pharmacokinetic property of volume preparations

Volume Effect

that part of the infused amount

Volume Effect

that part of the infused amount -remaining within the circulatory compartment

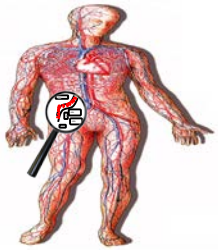
Volume Effect

that part of the infused amount
-remaining within the circulatory compartment
-not causing interstitial edema

Volume Replacement Therapy

Volume Effect

isotonic crystalloid



Ringer`s Lactate

Jacob M et al. Crit Care 2012, 16: R86

Ringer`s Lactate

ANH, n = 10, healthy preoperative patients

Jacob M et al. Crit Care 2012, 16: R86

Ringer`s Lactate

ANH, n = 10, healthy preoperative patients

Blood Loss: 1097 ± 285 mL

Crystalloid Infusion: 3430 ± 806 mL

Jacob M et al. Crit Care 2012, 16: R86

Ringer`s Lactate

ANH, n = 10, healthy preoperative patients

Blood Loss: 1097 ± 285 mL

Crystalloid Infusion: 3430 ± 806 mL

Blood Volume: 3959 ± 387 → 3501 ± 499 mL

Jacob M et al. Crit Care 2012, 16: R86

Ringer`s Lactate

ANH, n = 10, healthy preoperative patients

Blood Loss: 1097 ± 285 mL

Crystalloid Infusion: 3430 ± 806 mL

Blood Volume: 3959 ± 387 → 3501 ± 499 mL

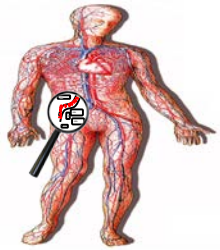
Volume Effect: 17 ± 10%

Jacob M et al. Crit Care 2012, 16: R86

Volume Replacement Therapy

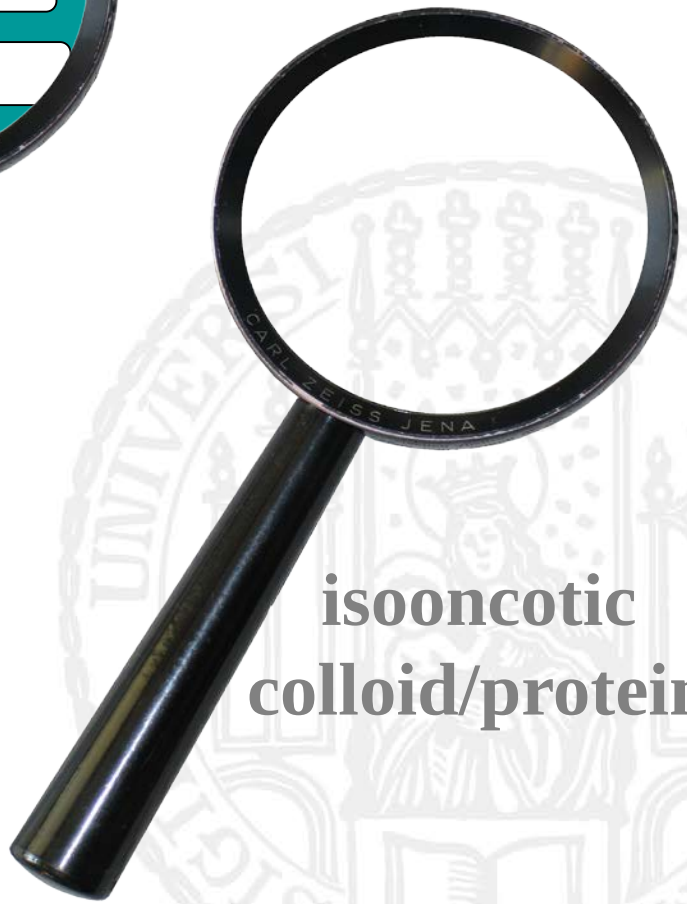
Volume Effect

isotonic crystalloid

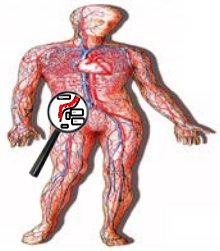


Volume Replacement Therapy

Volume Effect



isooncotic
colloid/protein



6% HES 130/0.4

Jacob M et al., Anaesthesist 2003, 52:896-904

6% HES 130/0.4

ANH, n = 10, healthy preoperative patients

Jacob M et al., Anaesthesist 2003, 52:896-904

6% HES 130/0.4

ANH, n = 10, healthy preoperative patients

Blood Loss: 1431 ± 388 mL

Colloid Infusion: 1686 ± 437 mL

Jacob M et al., Anaesthesist 2003, 52:896-904

6% HES 130/0.4

ANH, n = 10, healthy preoperative patients

Blood Loss: 1431 ± 388 mL

Colloid Infusion: 1686 ± 437 mL

Blood Volume: 4142 ± 986 → 4360 ± 1083 mL

Jacob M et al., Anaesthesist 2003, 52:896-904

6% HES 130/0.4

ANH, n = 10, healthy preoperative patients

Blood Loss: 1431 ± 388 mL

Colloid Infusion: 1686 ± 437 mL

Blood Volume: 4142 ± 986 → 4360 ± 1083 mL

Volume Effect: 98 ± 12%

Jacob M et al., Anaesthesist 2003, 52:896-904

Volume Replacement Therapy

Directly Measured Volume Effects

Directly Measured Volume Effects in Literature

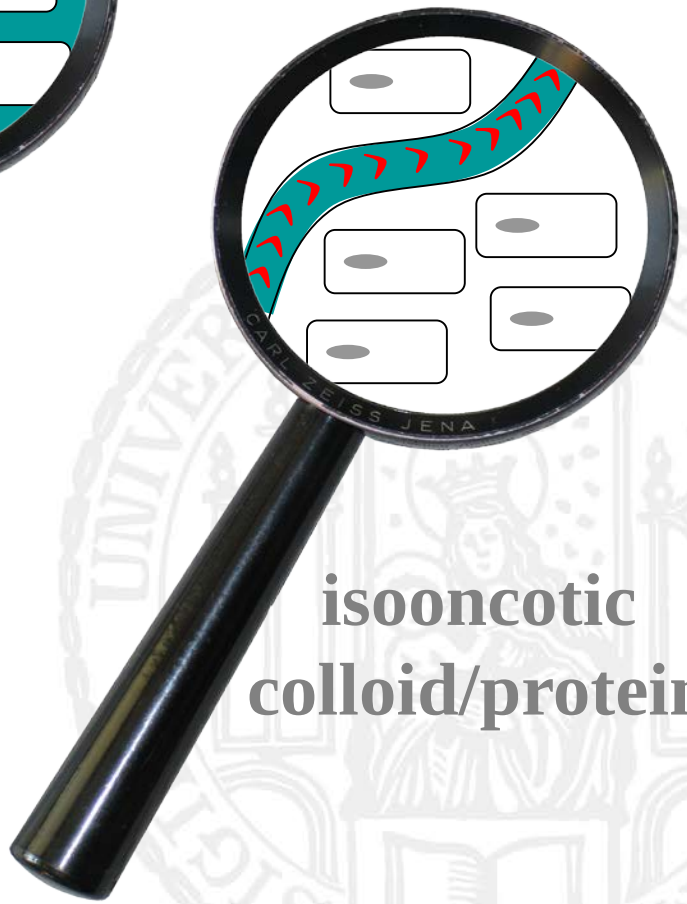
Preparation	Model	Volume Effect [%]	n	Reference
5% Human Albumin	ANH	85 ± 16	10	ANAESTHESIST 2001
	ANH	87 ± 14	15	ANESTHESIOLOGY 2000
6% HES 200/0.5	ANH	90 ± 18	10	ANAESTHESIST 2001
6% HES 130/0.4	ANH	98 ± 12	10	ANAESTHESIST 2003

Isooncotic Colloids – Normovolemia

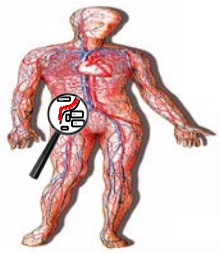
Values are mean ± SD.
n = number of patientients;ANH = actue normovolemic hemodilution;
VL = volume loading; TH = therapeutical infusion in the face of a decreased blood volume; HES = hydroxyethyl starch
*case report
#intended, but not reached

Volume Replacement Therapy

Volume Effect



isooncotic
colloid/protein



5% Human Albumin

Rehm M et al., Anesthesiology 2001, 95:849-56

5% Human Albumin

VL, n = 10, healthy preoperative patients

Rehm M et al., Anesthesiology 2001, 95:849-56

5% Human Albumin

VL, n = 10, healthy preoperative patients

Blood Loss: ---

Colloid Infusion: 1379 ± 128 mL

Rehm M et al., Anesthesiology 2001, 95:849-56

5% Human Albumin

VL, n = 10, healthy preoperative patients

Blood Loss: ---

Colloid Infusion: 1379 ± 128 mL

Blood Volume: 4189 ± 769 → 4713 ± 868 mL

Rehm M et al., Anesthesiology 2001, 95:849-56

5% Human Albumin

VL, n = 10, healthy preoperative patients

Blood Loss: ---

Colloid Infusion: 1379 ± 128 mL

Blood Volume: 4189 ± 769 → 4713 ± 868 mL

Volume Effect: 38 ± 21%

Rehm M et al., Anesthesiology 2001, 95:849-56

Volume Replacement Therapy

Directly Measured Volume Effects

Directly Measured Volume Effects in Literature

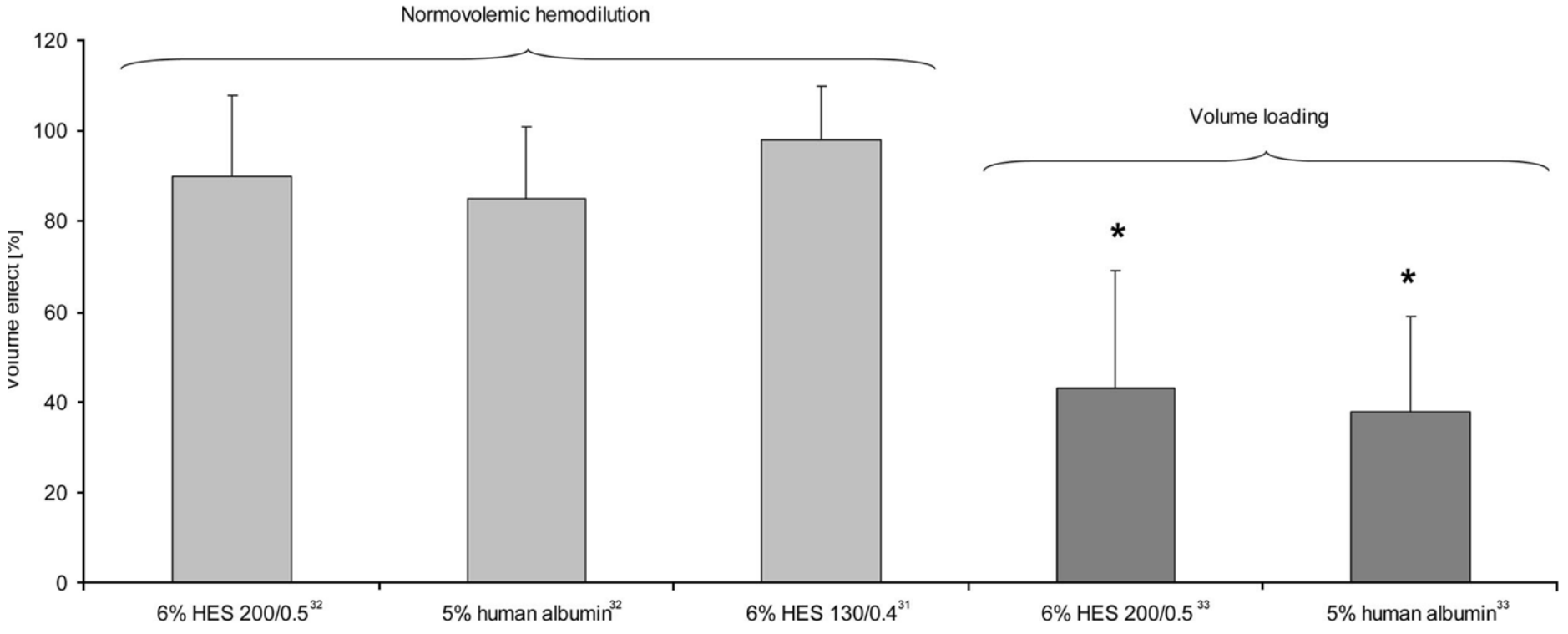
Preparation	Model	Volume Effect [%]	n	Reference
5% Human Albumin				
	VL	38 ± 21	10	ANESTHESIOLOGY 2001
6% HES 200/0.5				
	VL	43 ± 26	10	ANESTHESIOLOGY 2001

Isooncotic Colloids – Hypervolemia

Values are mean ± SD.
n = number of patientients;ANH = actue normovolemic hemodilution;
VL = volume loading; TH = therapeutical infusion in the face of a decreased blood volume; HES = hydroxyethyl starch
*case report
#intended, but not reached

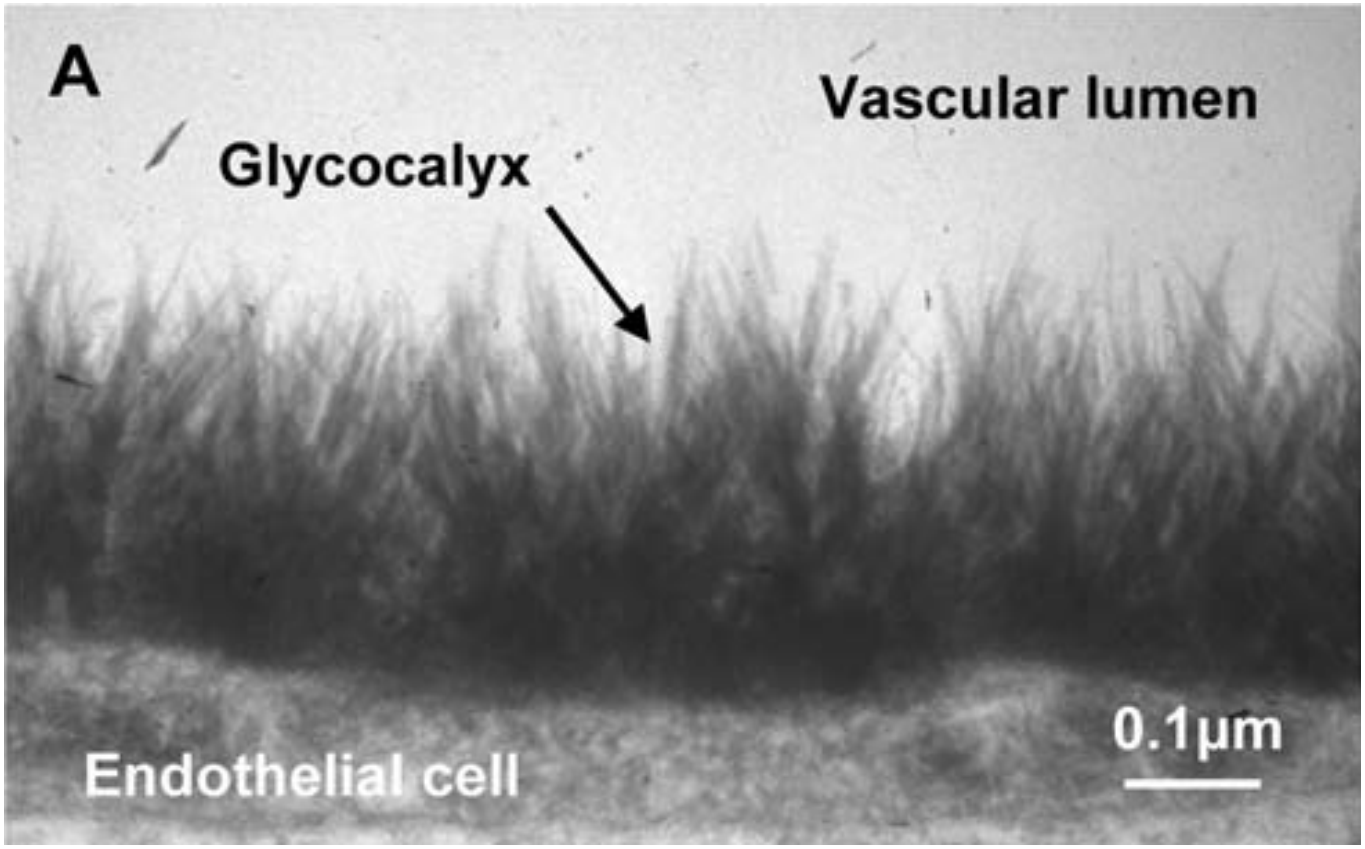
Volume Replacement Therapy

Directly Measured Volume Effects



colloideal volume-effects are context-sensitive

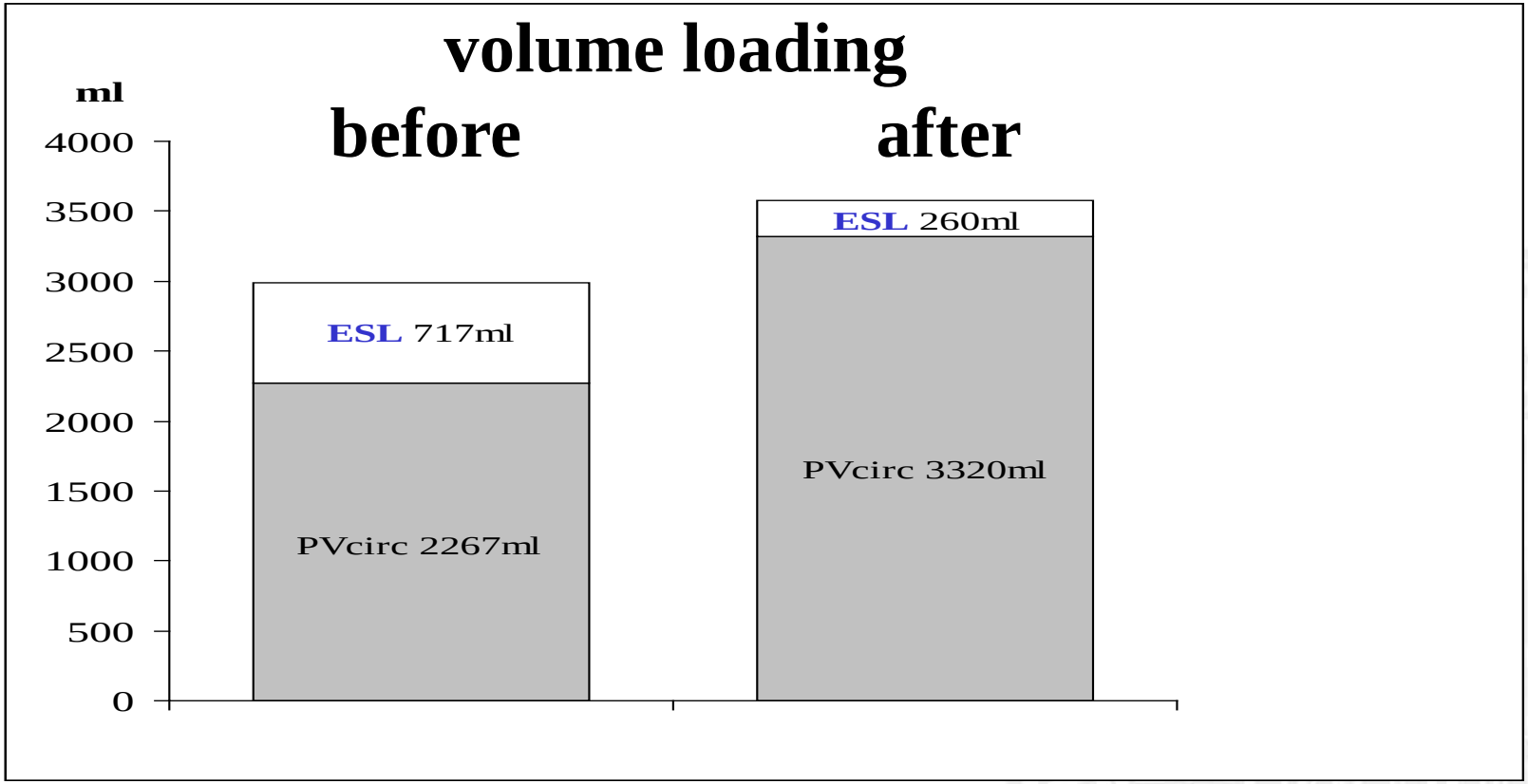
Jacob M et al., Lancet 2007, 369: 1984-6



Chappell D and Jacob M et al. (2009) Circ Res 83:388-96

Volume Replacement Therapy

Directly Measured Volume Effects



Rehm M et al., Anesthesiology 2001, 95:849-56

shift towards the interstitial space

Chappell D & Jacob M et al. (2008)
Anesthesiology 109: 723-40

shift towards the interstitial space

Type I ***Type II***

Chappell D & Jacob M et al. (2008)
Anesthesiology 109: 723-40

shift towards the interstitial space

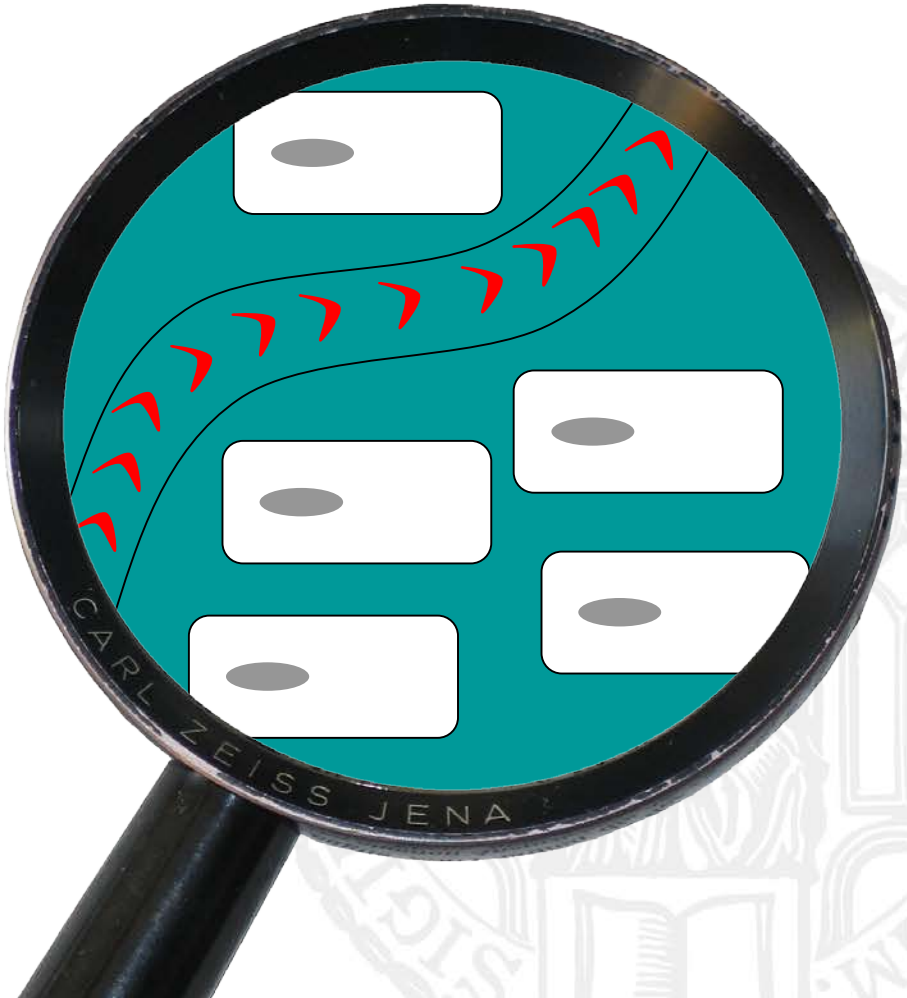
Type I

Chappell D & Jacob M et al. (2008)
Anesthesiology 109: 723-40

shift towards the interstitial space

Type I

→ predictible



Chappell D & Jacob M et al. (2008)
Anesthesiology 109: 723-40

shift towards the interstitial space

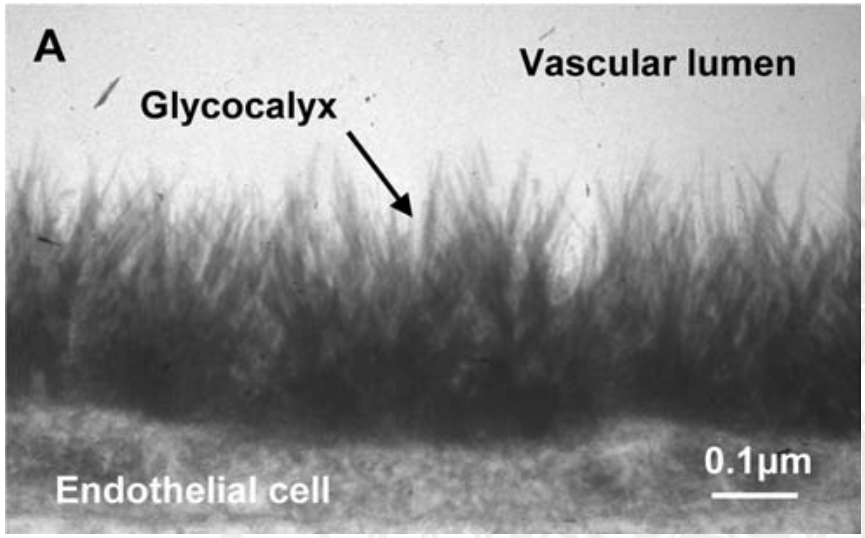
Type II

Chappell D & Jacob M et al. (2008)
Anesthesiology 109: 723-40

shift towards the interstitial space

Type II

→ inconstant



Chappell D & Jacob M et al. (2008)
Anesthesiology 109: 723-40

shift towards the interstitial space

Type I ***Type II***

→ at least in part avoidable

Chappell D & Jacob M et al. (2008)
Anesthesiology 109: 723-40

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Volume Replacement Therapy

- Physiology✓
- Facts
- Outcome-based Evidence

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Volume Replacement Therapy

- Physiology✓
- Facts✓
- Outcome-based Evidence

The Volume Effect of an Isotonic Crystalloid is Much Smaller than that of an Isooncotic Colloid

Avoiding Intravascular Hypervolemia Protects the Vascular Barrier

A Differentiating Indication of Crystalloids and Colloids helps to maintain Tissue Fluid Balance

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1. Principal Considerations

2. Physiology of the Microcirculation

3. Scientific Facts

4. Outcome-based Evidence

ICU ⟷ SURGERY

ICU

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

14 June 2013
EMA/349341/2013

PRAC recommends suspending marketing authorisations for infusion solutions containing hydroxyethyl-starch

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[3] Myburgh, J.A. *et al.* Hydroxyethyl starch or saline for fluid resuscitation in intensive care; N Engl J Med 2012; 367(20):1901-11.

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Fluidhandling: Principle options

Initial Stabilisation

Maintenance

Fluidhandling: Principle options

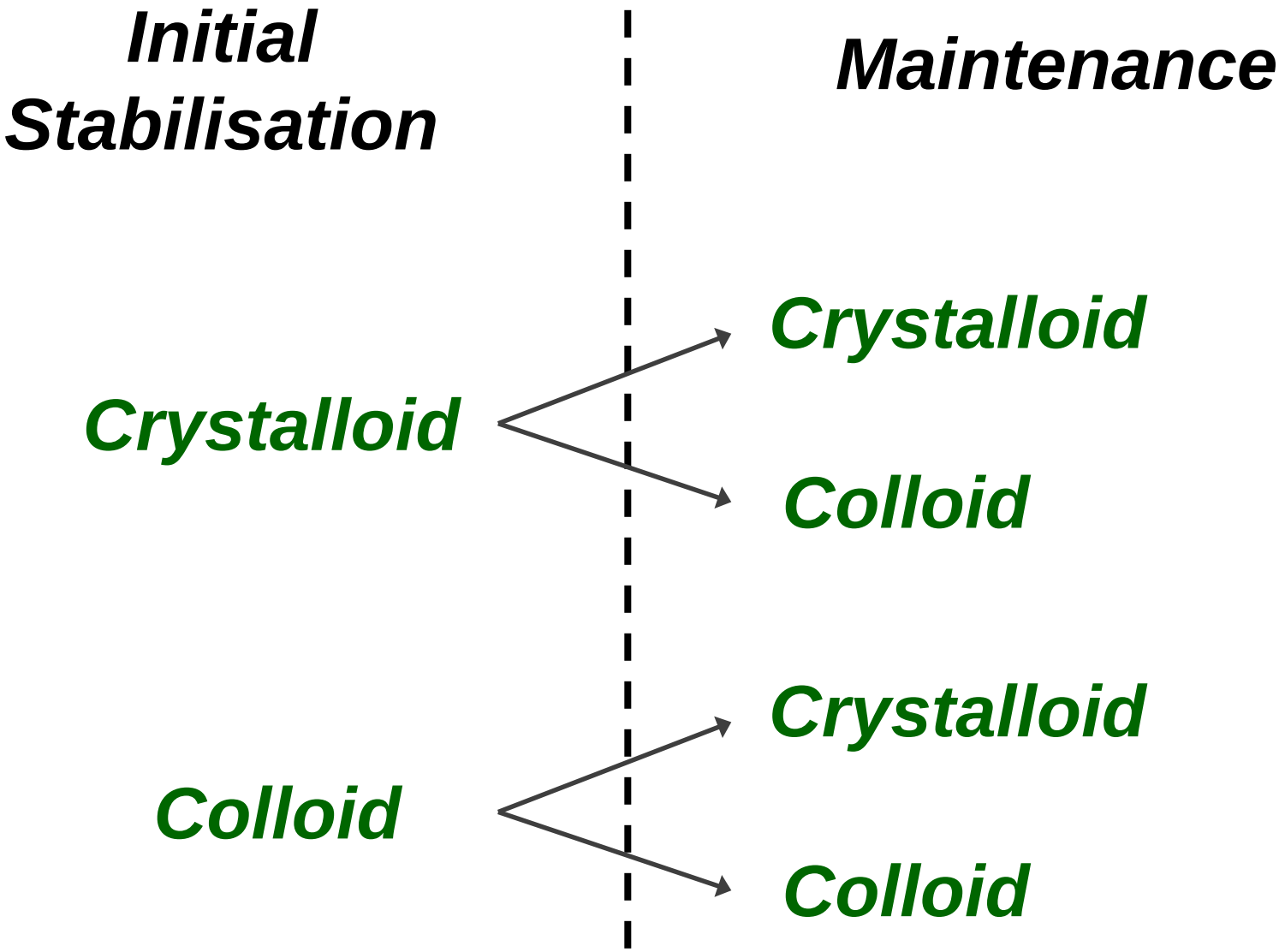
Initial Stabilisation

Crystalloid

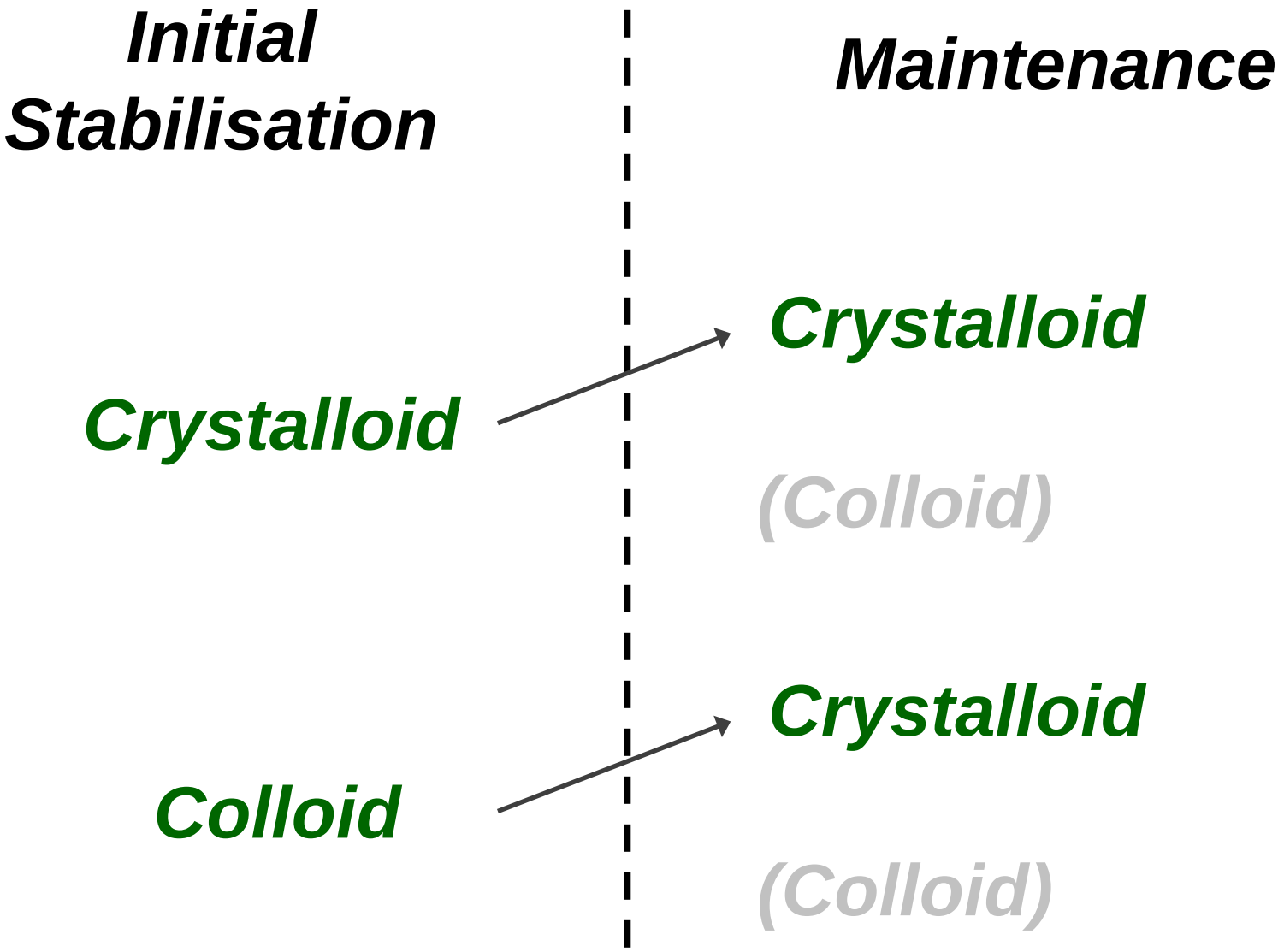
Colloid

Maintenance

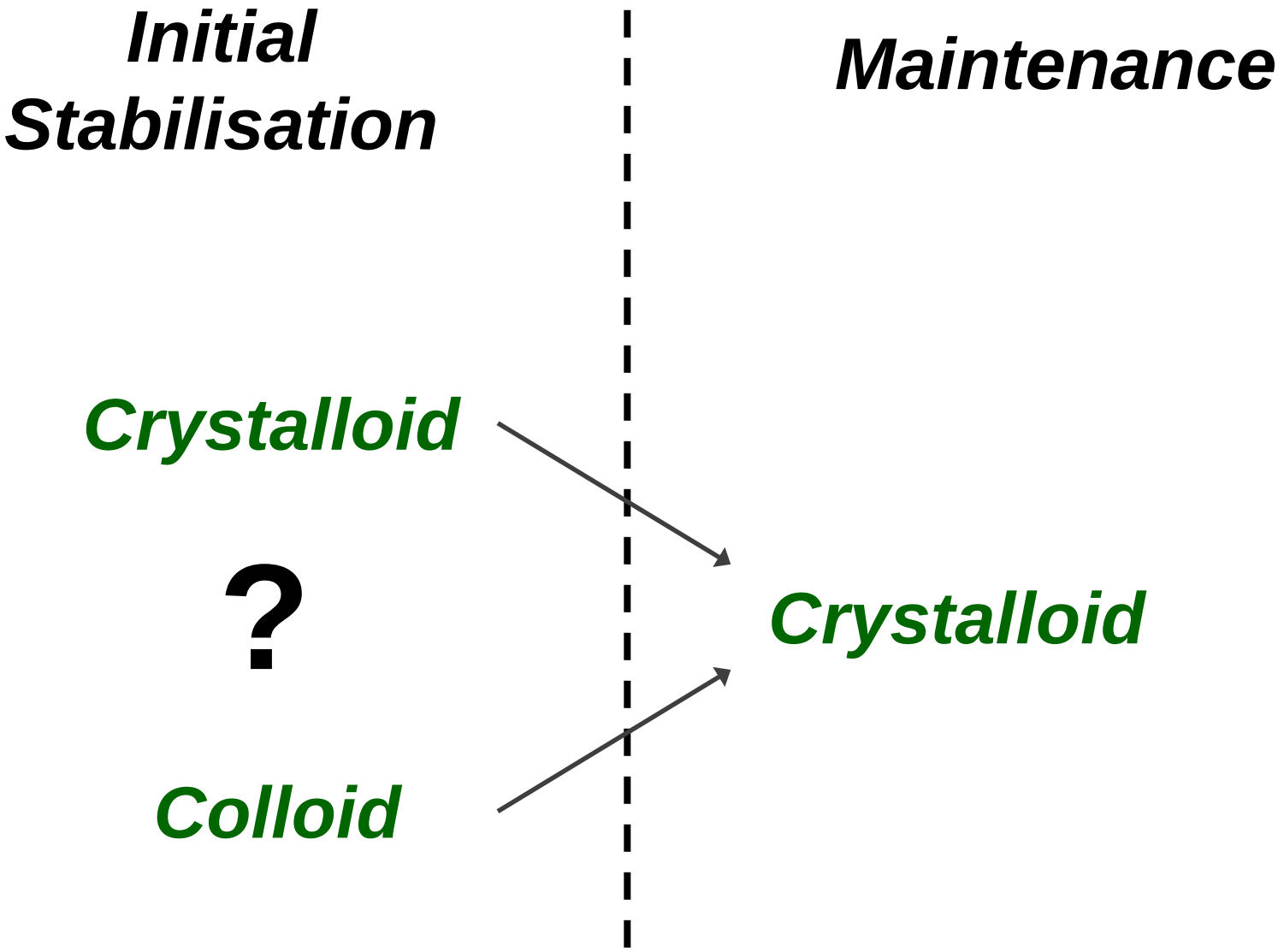
Fluidhandling: Principle options



Fluidhandling: Principle options



What we want to know:



The VISEP-Trial

N Engl J Med 2008, 358: 125-39

The VISEP-Trial

600 patients with severe sepsis

N Engl J Med 2008, 358: 125-39

The VISEP-Trial

600 patients with severe sepsis
Ringer´s lactate vs. 10% HES 200

N Engl J Med 2008, 358: 125-39

The VISEP-Trial

600 patients with severe sepsis
Ringer´s lactate vs. 10% HES 200
→hyperoncotic solutions without proper indication do harm

N Engl J Med 2008, 358: 125-39

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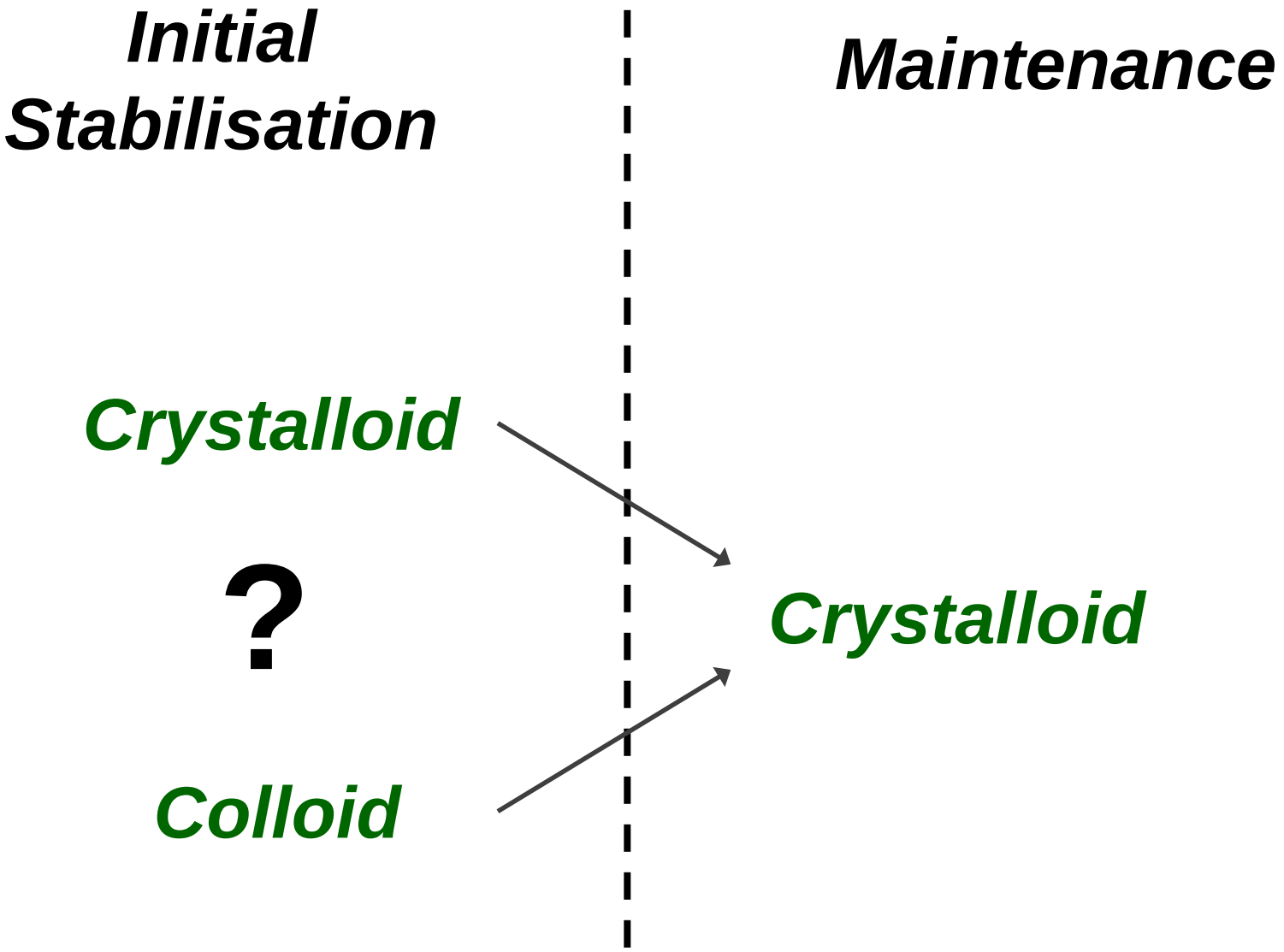
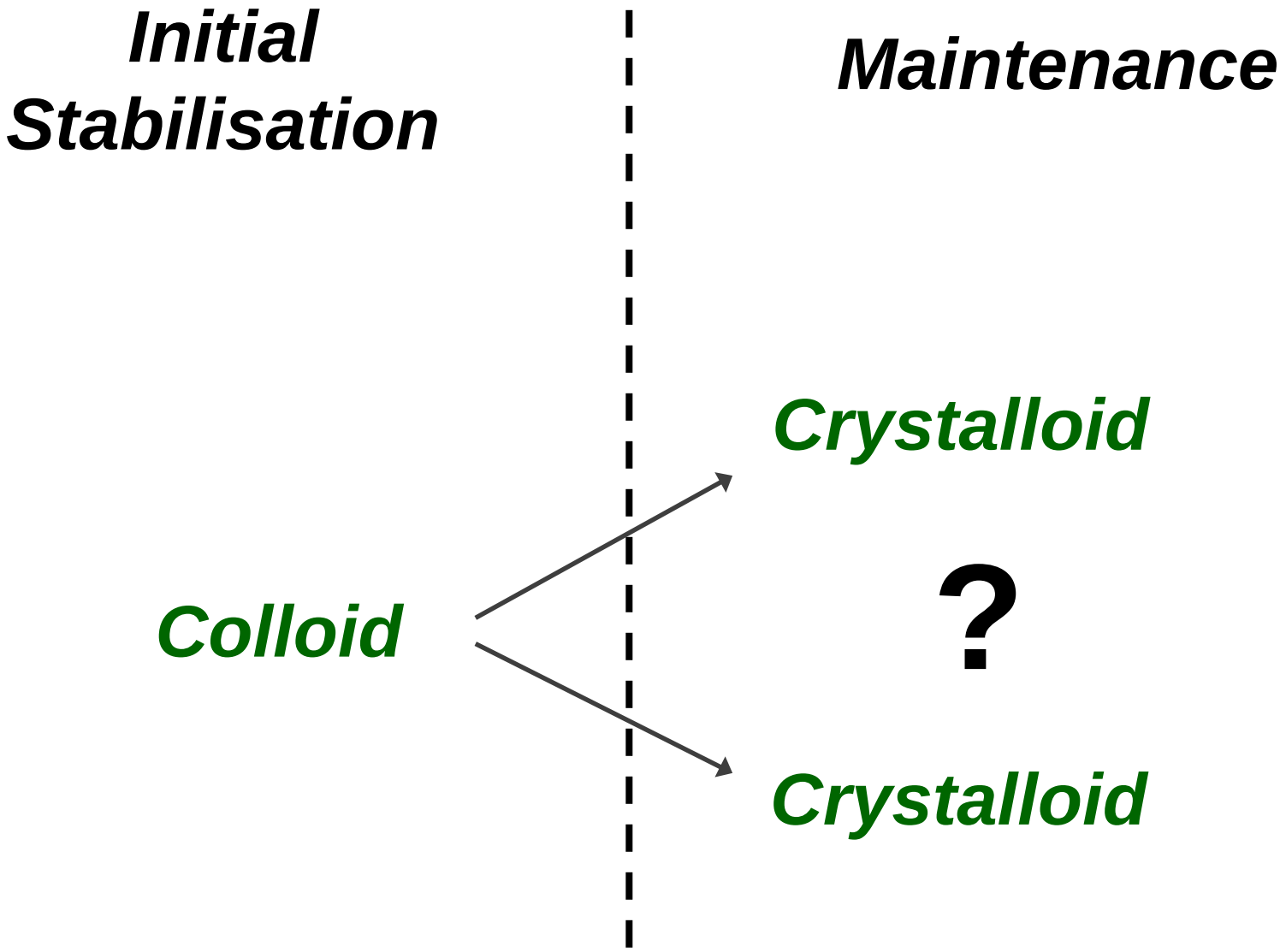


What VISEP evaluated:



The VISEP-Trial

600 patients with severe sepsis
Ringer´s lactate vs. 10% HES 200

→hyperoncotic solutions without proper indication do harm

This was not the Question

N Engl J Med 2008, 358: 125-39

The 6S-Study

N Engl J Med 2012, 367:124-34

The 6S-Study

800 patients with severe sepsis
Ringer`s acetate vs. 6% HES 130
→increase in mortality with HES

N Engl J Med 2012, 367:124-34

The 6S-Study

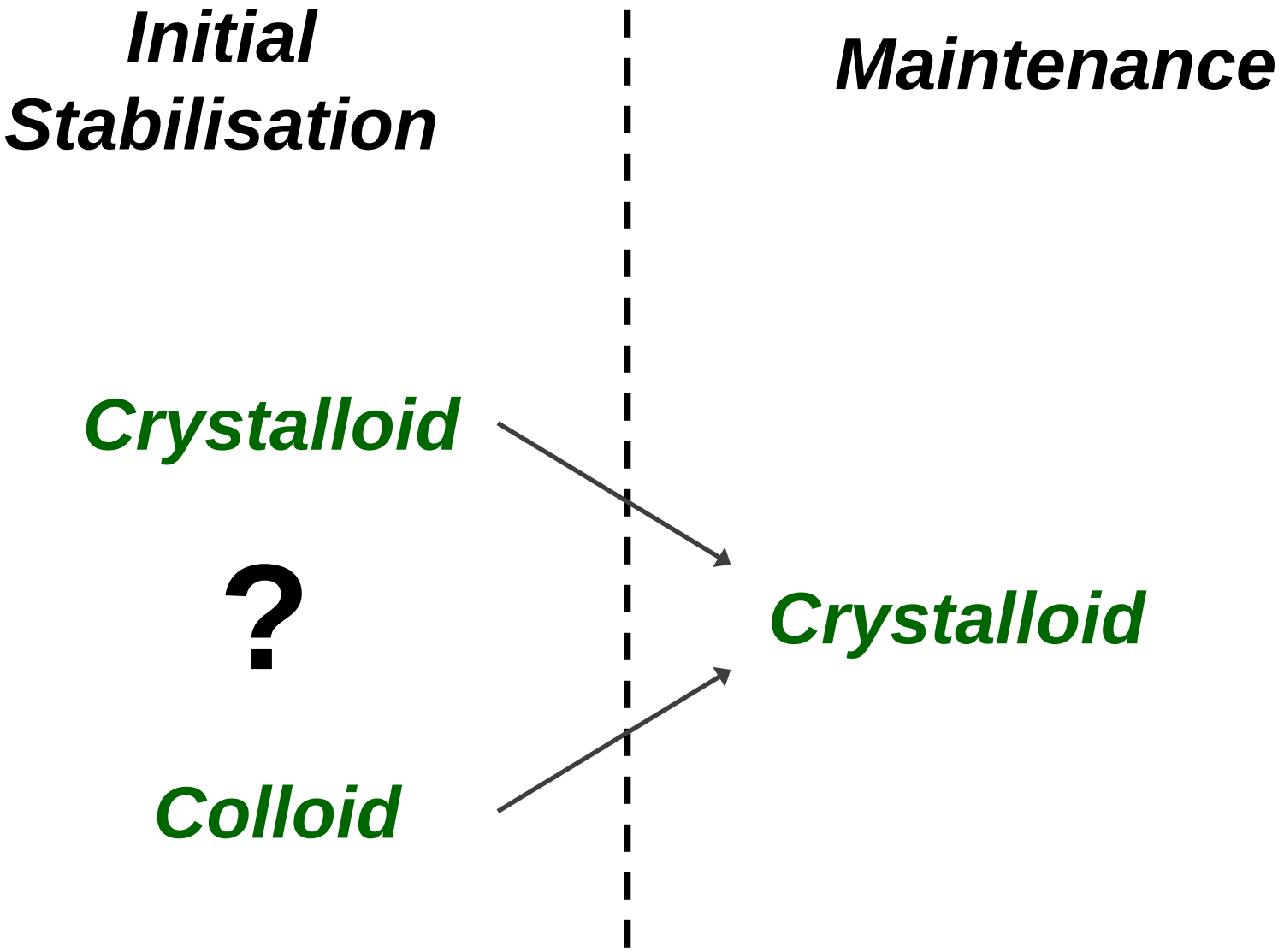
BUT:

→Patients in both groups again hemodynamically stable when included

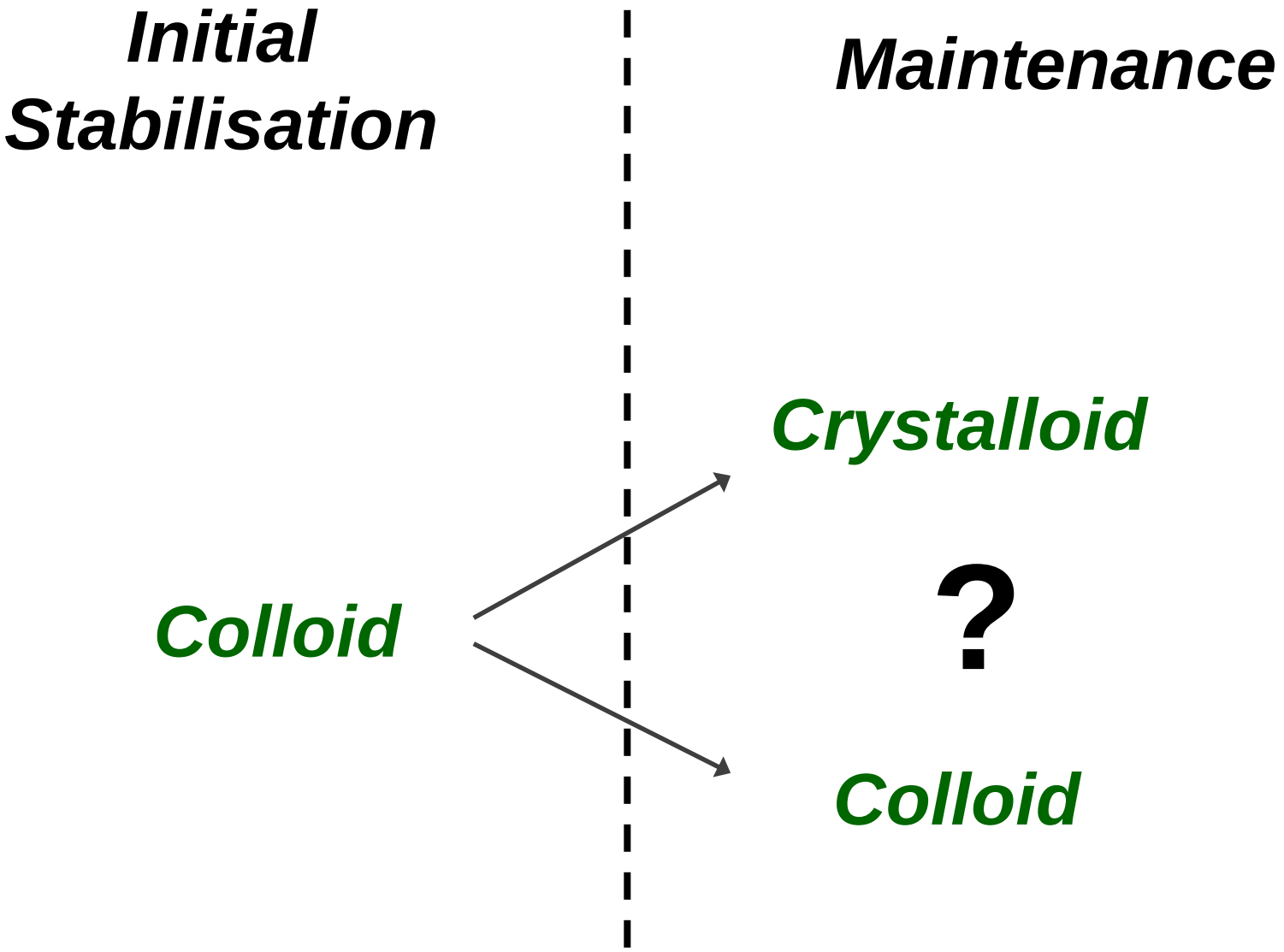
Chappell D and Jacob M
Letter to the editor
N Engl J Med 2012

N Engl J Med 2012, 367:124-34

What we wanted to know:



What 6S evaluated:



The 6S-Study

BUT:

→Patients in both groups again hemodynamically stable when included

This was not the Question

Chappell D and Jacob M
Letter to the editor
N Engl J Med 2012

N Engl J Med 2012, 367:124-24

The CHEST-Study

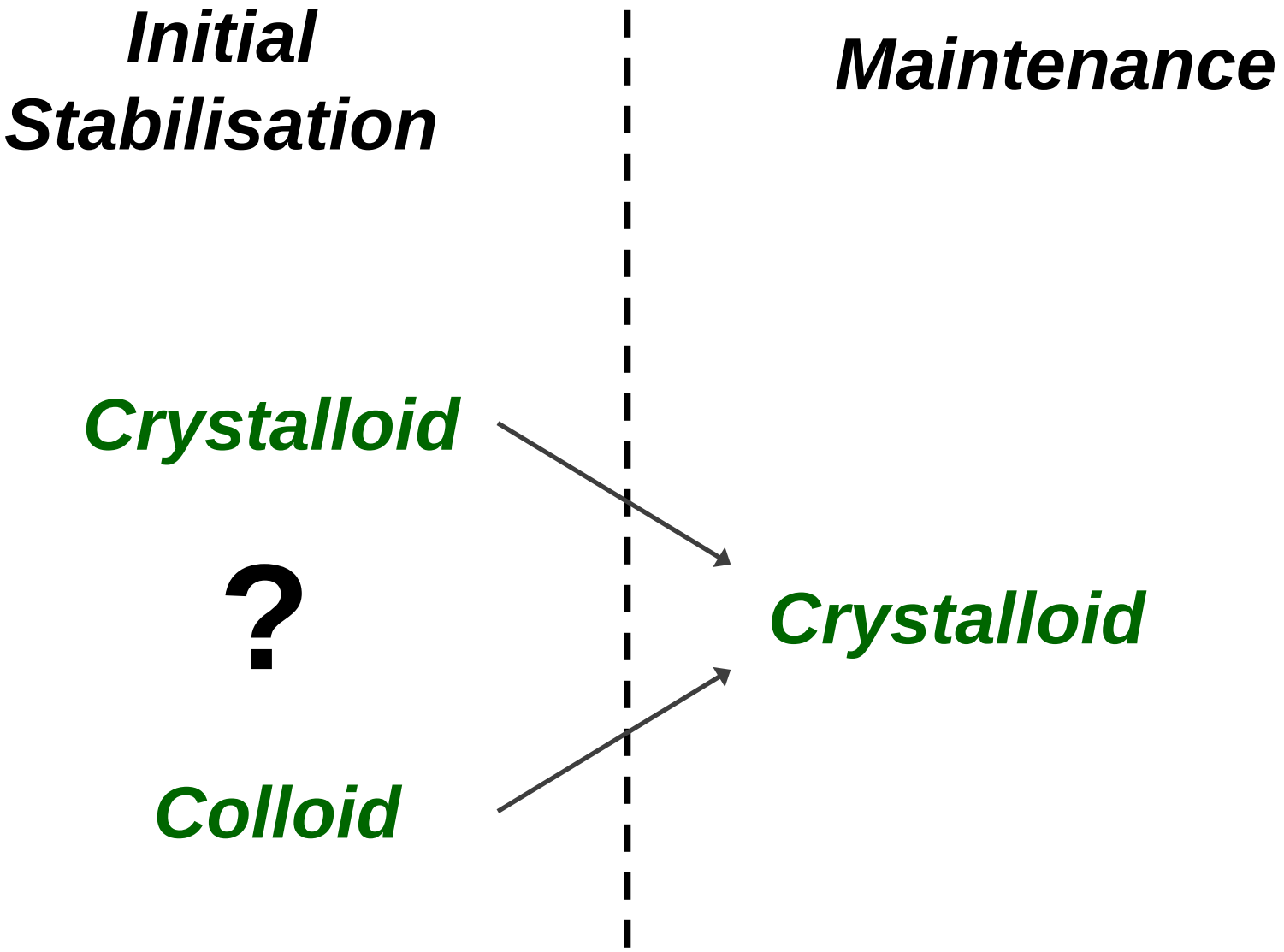
N Engl J Med 2012, 367:1901-11

The CHEST-Study

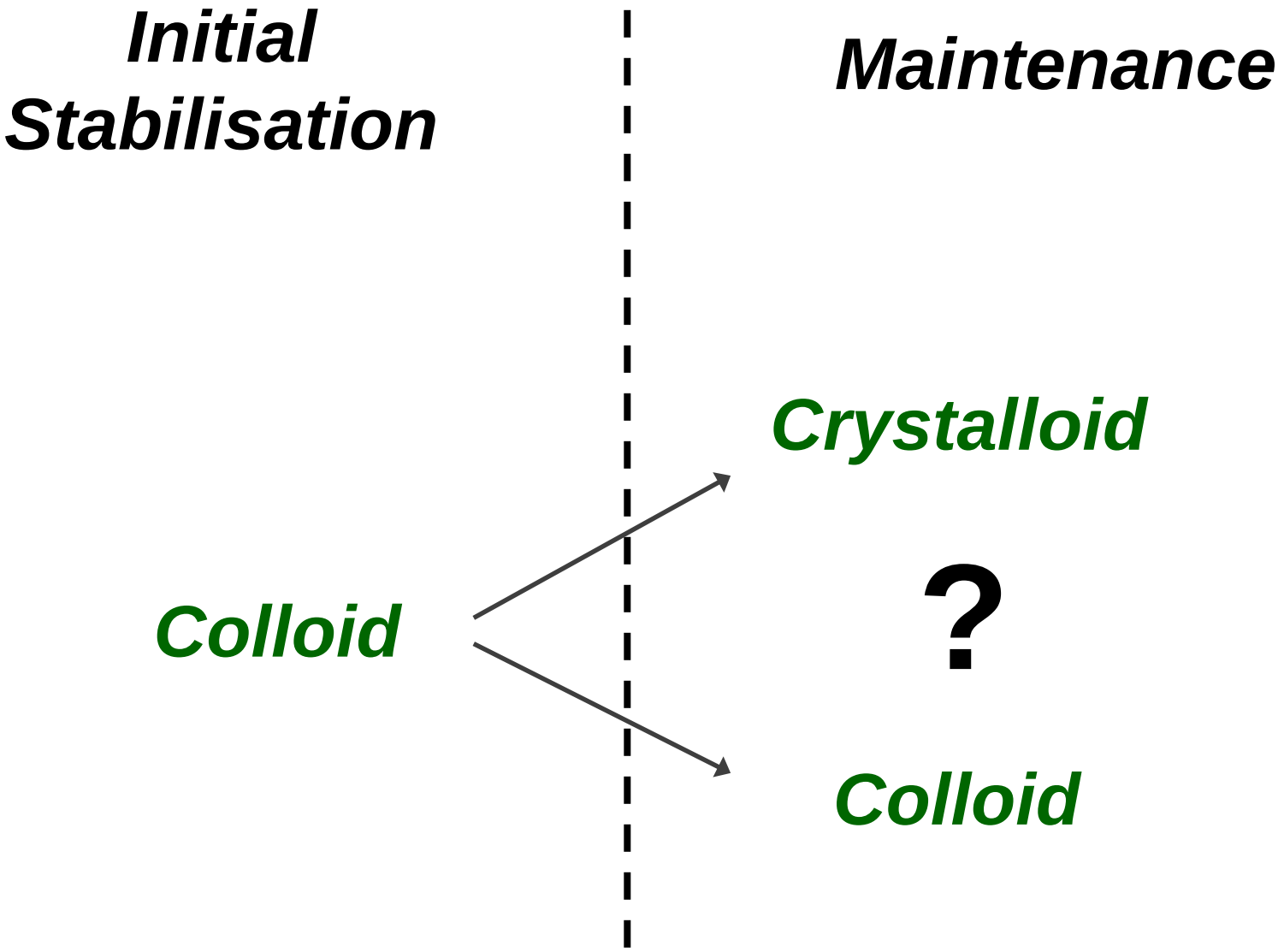
7000 ICU-patients (2000 sepsis)
saline vs. 6% HES 130
→no clinically relevant differences

N Engl J Med 2012, 367:1901-11

What we wanted to know:



What CHEST evaluated:



The CHEST-Study

7000 ICU-patients (~600 sepsis)

saline vs. 6% HES 130

→no clinically relevant differences

Starches are „Safe“ (?)

N Engl J Med 2012, 367:1901-11

Fluidhandling: Principle options

Initial Stabilisation

not part of the interventional period of

- **VISEP**
- **6S**
- **CHEST**

Maintenance

Fluidhandling: Principle options

Initial Stabilisation

not part of the interventional period of

- VISEP
- 6S
- CHEST

Colloid

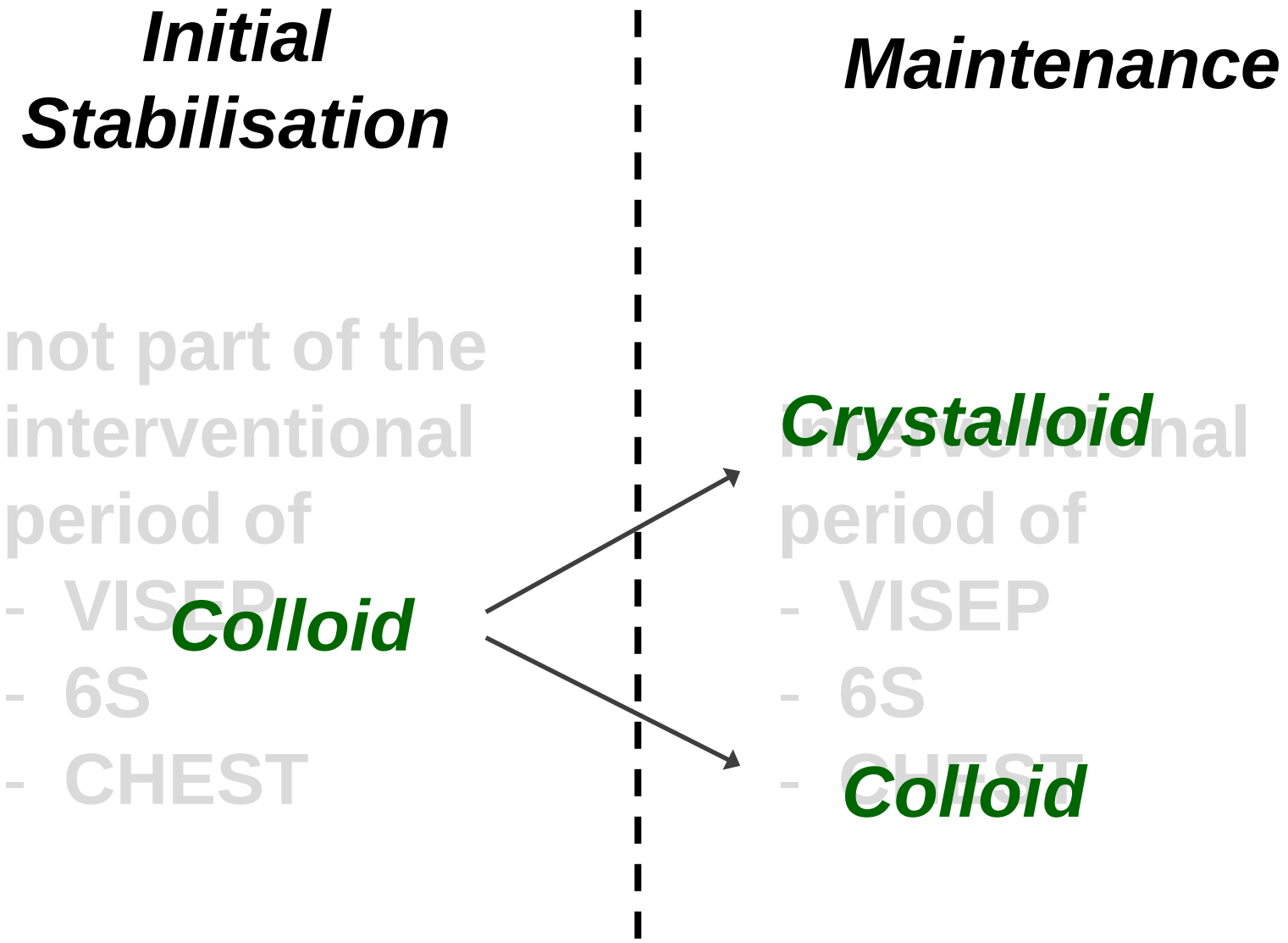
Maintenance

Fluidhandling: Principle options

Initial Stabilisation	***Maintenance***
not part of the interventional period of - VISEP - 6S - CHEST	**interventional period of** **- VISEP** **- 6S** **- CHEST**

Colloid

Fluidhandling: Principle options



Fluidhandling: Principle options

Initial Stabilisation

Maintenance

not part of the interventional period of
- VISEP
- 6S
- CHEST

Colloid

Crystalloid

interventional period of
- VISEP
- 6S
- CHEST

Colloid

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The 3rd Principle of Evidence-Based Medicine

Do You Remember?

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The 3rd Principle of Evidence-Based Medicine

Evidence for Harm due to Drug Misuse Might be Related

1) to the Drug or

2) to the Misuse

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The 3rd Principle of Evidence-Based Medicine

Evidence for Harm due to Drug Misuse Might be Related

1) to the Drug or

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Fluidhandling: Principle options

Initial Stabilisation

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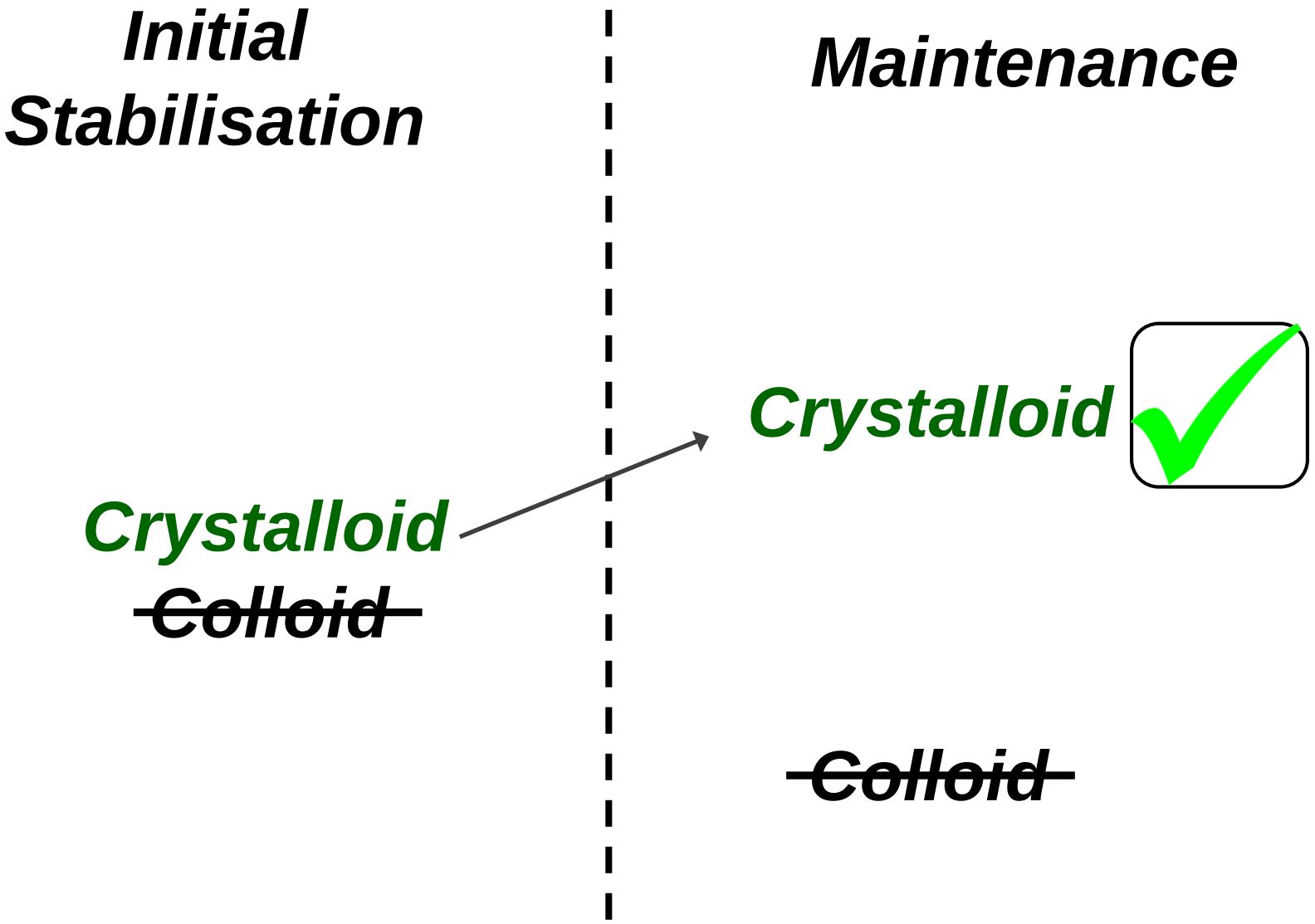
Colloid

Crystalloid

Colloid

Fluidhandling: Principle options



Lesson Learned:

Lesson Learned:

do not use political decisions in scientific discussions

Lesson Learned:

do not use political decisions in scientific discussions,
even if it is done in Europe!!

Scientific conclusion for ***proper*** HES use in septic patients from literature:

Scientific conclusion for ***proper*** HES use in septic patients from literature:

NONE!

Scientific conclusion for the bleeding surgical patient from ICU literature:

Scientific conclusion for the bleeding surgical patient from ICU literature:

NONE!

Scientific conclusion for the bleeding surgical patient from ICU literature:

NONE!

→ Do not extrapolate!

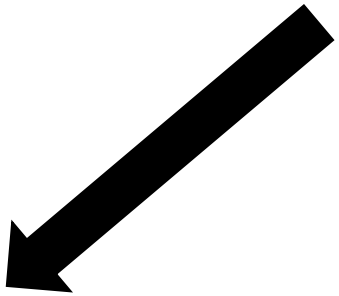
ICU ⟷ SURGERY

SURGERY

HES Use in SURGERY

HES Use in

SURGERY



Volume Effectiveness

Safety

Benefit

HES Use in

SURGERY

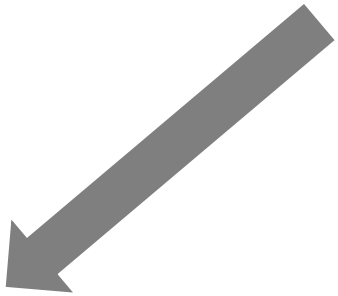
Volume ✓
Effectiveness

Safety

Benefit

HES Use in

SURGERY



Volume ✓
Effectiveness

Safety

Benefit

HES Use in

SURGERY

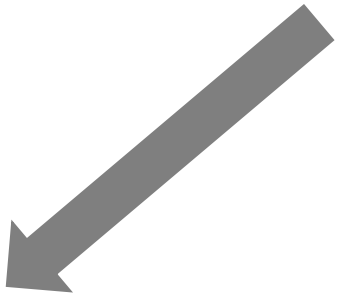
Volume ✓
Effectiveness

Safety ?

Benefit

HES Use in

SURGERY



Volume ✓
Effectiveness

Safety ?

Benefit

Studies evaluating peri-operative individualised GDT with HES

Studies evaluating peri-operative individualised GDT with HES

Device

Studies evaluating peri-operative individualised GDT with HES

Device + HES

Studies evaluating peri-operative individualised GDT with HES

Device + HES + Algorithm

Studies evaluating peri-operative individualised GDT with HES

Device + HES + Algorithm

 Improved Outcome

Studies evaluating peri-operative individualised GDT with HES

- **Mythen** MG, Webb AR. Perioperative plasma volume expansion reduces the incidence of gut mucosal hypoperfusion during cardiac surgery. **Arch Surg 1995; 130: 423–9.**
- **Sinclair** S, James S, Singer M. Intraoperative intravascular volume optimisation and length of hospital stay after repair of proximal femoral fracture: randomised controlled trial. **Br Med J 1997; 315: 909–12.**
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- **Gan** TJ, Soppitt A, Maroof M et al. Goal-directed intraoperative fluid administration reduces length of hospital stay after major surgery. **Anesthesiology 2002; 97: 820–6.**
- **Moretti** EW, Robertson KM, El-Moalem H, Gan TJ. Intraoperative colloid administration reduces postoperative nausea and vomiting and improves postoperative outcomes compared with crystalloid administration**. Anesth Analg 2003; 96:611-617**
- **Benes** J, Chytra I, Altmann P. et al. Intraoperative fluid optimisation using stroke volume variation in high risk surgical patients: results of prospective randomised trial. **Crit Care 2010; 14:R118**
- **Feldheiser** A. Pavlova V, Bonomo T. et al. Balanced crystalloid compared with balanced colloid solution using a goal-directed hemodynamic algorithm. BJA 2013; 110 (2):231-240.

Studies evaluating peri-operative individualised GDT with HES

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Intraoperative fluid optimization using stroke volume variation in high risk surgical patients: results of prospective randomized study

Jan Benes*, Ivan Chytra, Pavel Altmann, Marek Hluchy, Eduard Kasal, Roman Svitak, Richard Pradl and Martin Stepan

Study characteristics

- 120 patients
- Major abdominal surgery
- Estimated blood loss >1000 ml
- **Control** vs. **GDT (Vigileo System)**
- Intraoperative Treatment:
  - crystalloideal maintenance (both groups):

    8 ml/kg/h crystalloids
  - colloids (HES 130):
    - "at the descretion of the anesthesiologist" (Control)
    - 3 ml/kg colloid solution if SVV > 10% (Vigileo)

Benes et al, Crit Care 2010; 14; R118

Difference between groups in morbidity and complications

Parameters	Vigileo group	Control group	*P* value
Number of patients			
ITT analysis	60	60	
Per protocol analysis	51	54	
Morbidity (day 30)			
Patients with complications			
ITT	**18 (30%)**	**35 (58.3%)**	**0.0033**
Per protocol	**16 (31.37%)**	**32 (59.26%)**	**0.0076**
Patient with severe complication(*)			
ITT	**7 (11.7%)**	**22 (36.6%)**	**0.0028**
Per protocol	**6 (11.76%)**	**19 (35.19%)**	**0.0097**
Complications (day 30)			
Per protocol	**32**	**73**	**0.0141**
Severe complications (day 30) (*)			
ITT	**13**	**41**	**0.0132**
Per protocol	**12**	**38**	**0.0274**

Benes et al, Crit Care 2010; 14; R118

Difference between groups in morbidity and complications

Parameters	Vigileo group	Control group	*P* value
Number of patients			
ITT analysis	60	60	
Per protocol analysis	51	54	
Morbidity (day 30)			
Patients with complications			
ITT	**18 (30%)**	**35 (58.3%)**	**0.0033**
Per protocol	**16 (31.37%)**	**32 (59.26%)**	**0.0076**
Patient with severe complication(*)			
ITT	**7 (11.7%)**	**22 (36.6%)**	**0.0028**
Per protocol	**6 (11.76%)**	**19 (35.19%)**	**0.0097**
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Determinants of Long-Term Survival After Major Surgery and the Adverse Effect of Postoperative Complications

Shukri F. Khuri, MD,†‡ William G. Henderson, PhD,§ Ralph G. DePalma, MD,¶ Cecilia Mosca, MSPH,§ Nancy A. Healey, BS,* Dharam J. Kumbhani, MD, SM,* and the Participants in the VA National Surgical Quality Improvement Program*

Objective: The objective of this study was to identify the determinants of 30-day postoperative mortality and long-term survival after major surgery as exemplified by 8 common operations.

Summary Background Data: The National Surgical Quality Improvement Program (NSQIP) database contains pre-, intra-, and 30-day postoperative data, prospectively collected in a standardized fashion by a dedicated nurse reviewer, on major surgery in the Veterans Administration (VA). The Beneficiary Identification and Records Locator Subsystem (BIRLS) is a VA file that depicts the vital status of U.S. veterans with 87% to 95% accuracy.

Methods: NSQIP data were merged with BIRLS to determine the vital status of 105,951 patients who underwent 8 types of operations performed between 1991 and 1999, providing an average follow up of 8 years. Logistic and Cox regression analyses were performed to identify the predictors of 30-day mortality and long-term survival, respectively.

Results: The most important determinant of decreased postoperative survival was the occurrence, within 30 days postoperatively, of any one of 22 types of complications collected in the NSQIP. *Independent of preoperative patient risk*, the occurrence of a 30-day complication in the total patient group reduced median patient survival by 69%. The adverse effect of a complication on patient survival was also influenced by the operation type and was sustained even when patients who did not survive for 30 days were excluded from the analyses.

Conclusions: The occurrence of a 30-day postoperative complication is more important than preoperative patient risk and intraoperative factors in determining the survival after major surgery in the

Khuri et al, Ann Surg 2005; 242: 326-343

Results:

- The most important determinant of **decreased postoperative survival** was the

  ⇒ **occurrence of complications within 30 days after surgery**

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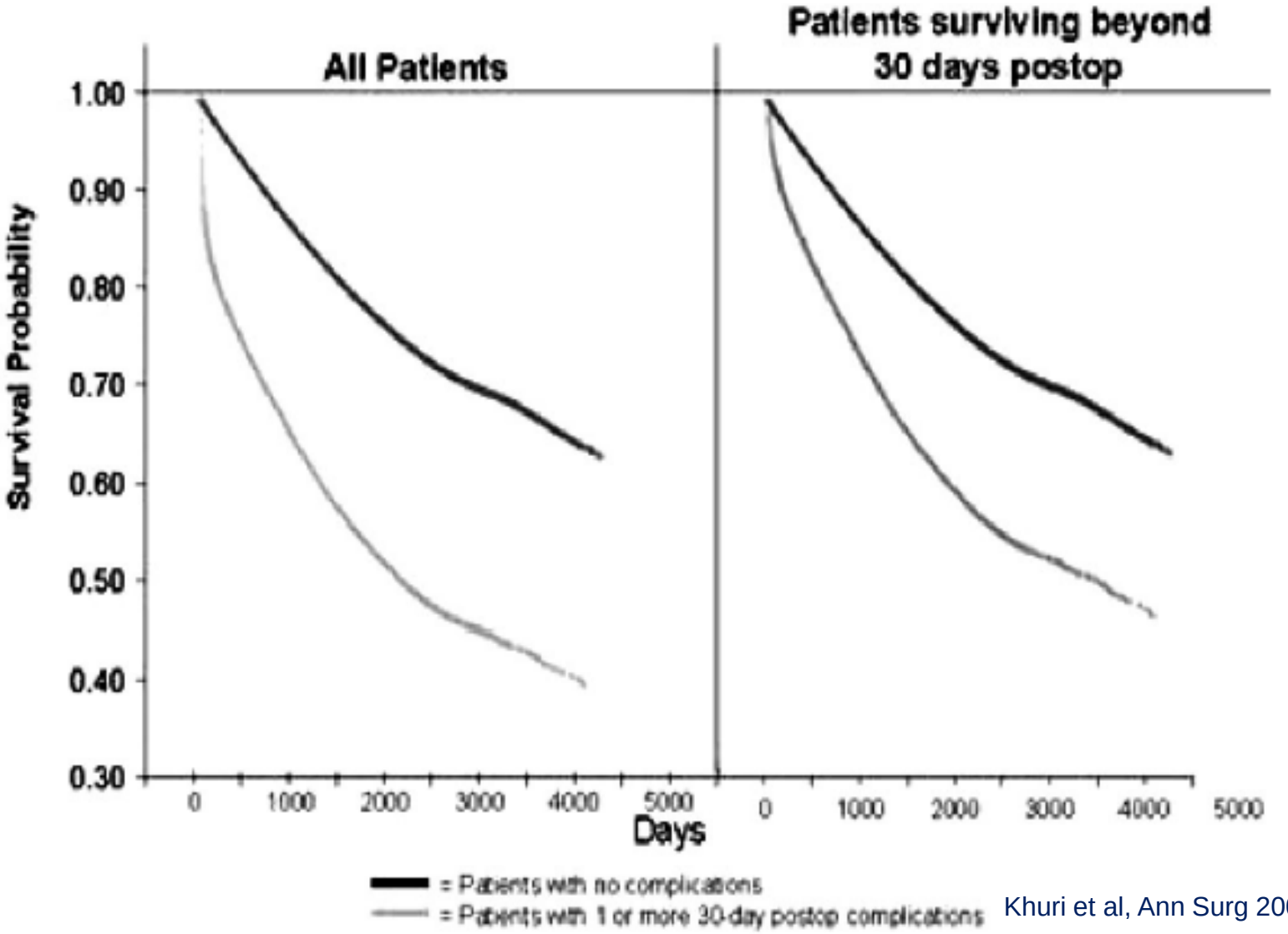

Khuri et al, Ann Surg 2005; 242: 326-343

My very Personal Combined Conclusion:

- It can be assumed that

  ⇒a **reduction in complication** rate

  by the use of HES for goal directed volume resuscitation may result in

  ⇒**a reduced mortality rate after major surgery**

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Volume Replacement Therapy

- Physiology✓
- Facts✓
- Outcome-based Evidence✓

Colloids require a proper indication

Colloids require a proper indication

The indication is: Hypovolemia

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Not over days in high dosage

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Not over days in high dosage

Only isooncotic preparations

Colloids require a proper indication

The indication is: Hypovolemia

Not over days in high dosage

Only isooncotic preparations

Until today no sepsis-study challenging the use of HES reflects the very initial stabilisation in shock

The indication-based preclinical and perioperative use of colloids can currently not seriously be questioned

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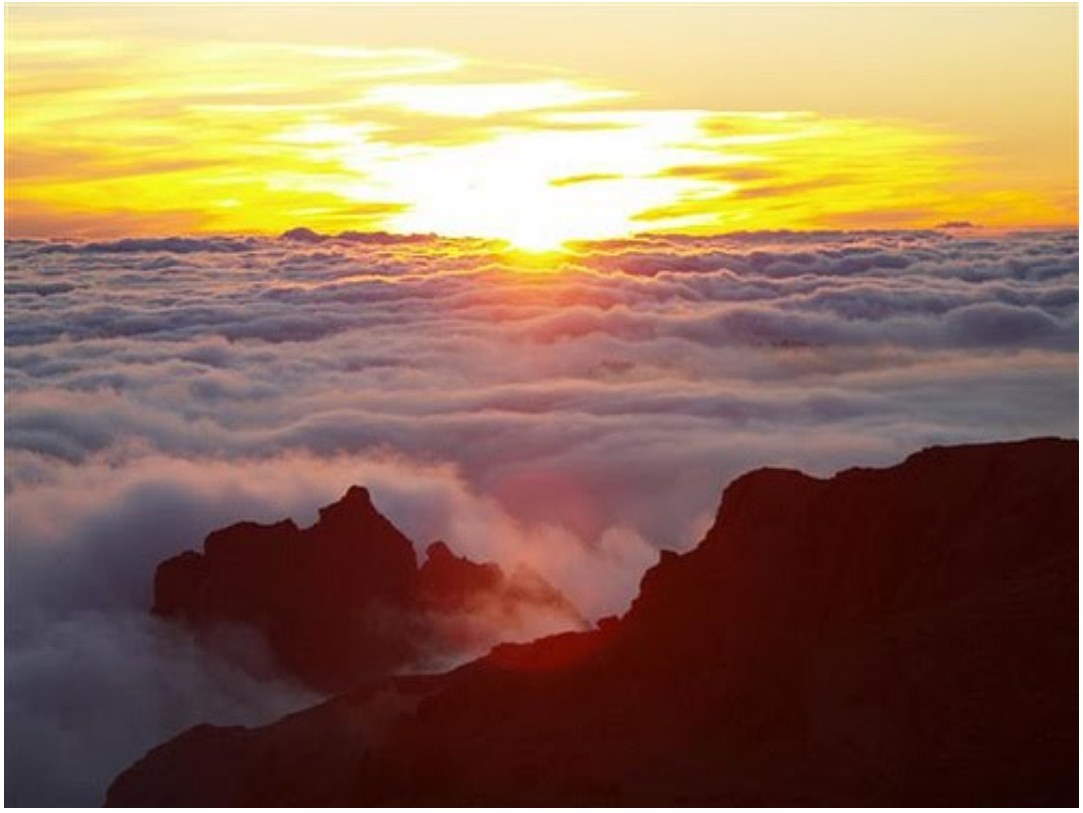
Conclusion



Do colloids have a place in resuscitation?

Do colloids have a place in resuscitation?

Yes, WHERE ELSE??

Do colloids have a place in resuscitation?

Yes, WHERE ELSE??

It Clearly Makes a Difference

What, and How Much, You Give!

Do colloids have a place in resuscitation?

Yes, WHERE ELSE??

It Clearly Makes a Difference

What, and How Much, You Give!

Perioperative Infusion Therapy

Perioperative Infusion Therapy

Target:

Steady State of the Compartments

Perioperative Infusion Therapy

Fluid Substitution

↓

extracellular

Crystalloid

Volume Replacement

↓

intravascular

Colloid / Protein

Perioperative Infusion Therapy

Fluid Substitution

↓

extracellular

Crystalloid

Volume Replacement

↓

intravascular

→ Crystalloid ←

↓

Type I Shifting

Do colloids have a place in resuscitation?

Yes, WHERE ELSE??

It Clearly Makes a Difference

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Fluid Substitution

↓

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Crystalloid

Volume Replacement

↓

intravascular

Colloid / Protein

Perioperative Infusion Therapy

Fluid Substitution

- extracellular
- Crystalloid

Volume Loading / Volume Preemptive

- Type II Shifting

Volume Replacement

- intravascular
- Colloid / Protein

Perioperative Infusion Therapy

Steady State of the Compartments

An Important Perioperative Target?

Perioperative Infusion Therapy

Steady State of the Compartments

An Important Perioperative Target?

→ *Yes, presuming* ***Rapid Stabilisation*** *and* ***Edema Prevention*** *are considered Important Targets*

In Which Patients can we expect a Benefit from Using Colloids?

In Which Patients can we expect a Benefit from Using Colloids Instead of Crystalloids?

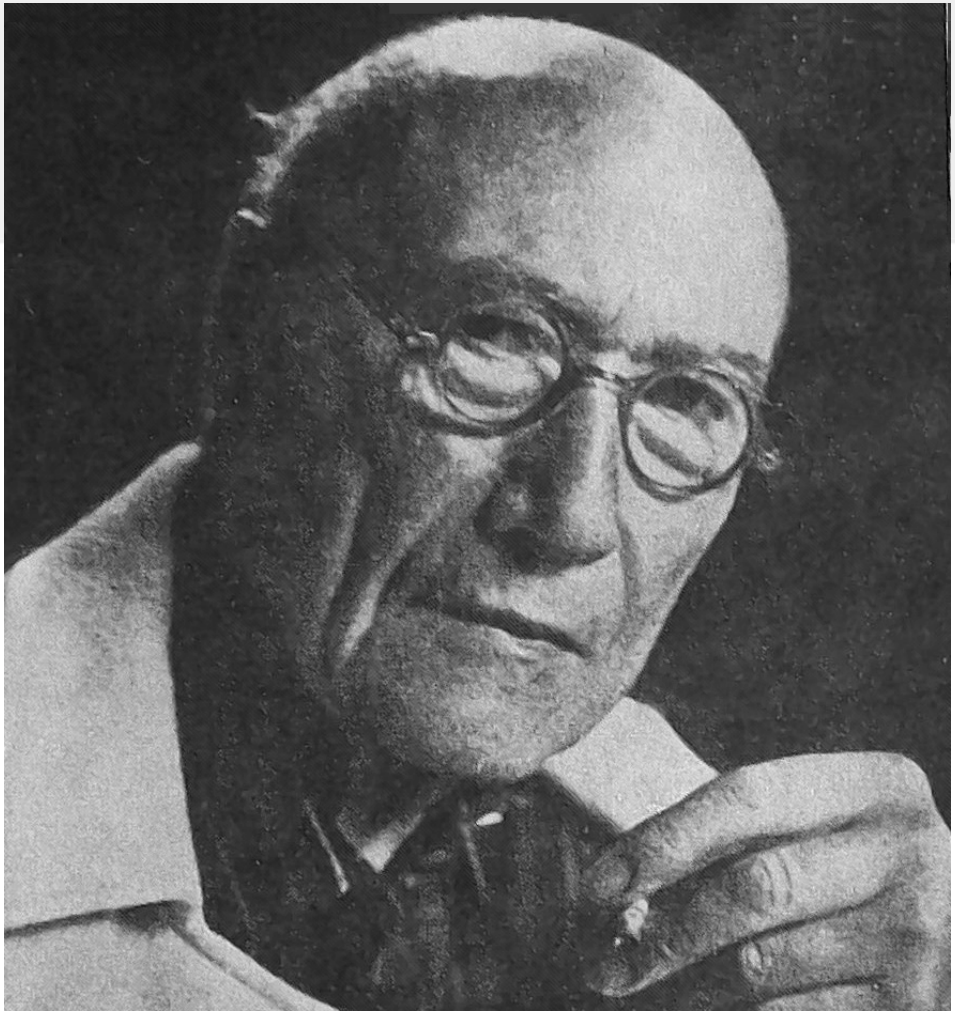
In Which Patients can we expect a Benefit from Using Colloids Instead of Crystalloids?

In Those with an Indication for Volume Replacement Therapy

Where can we do Harm When Using Colloids Instead of Crystalloids?

Where can we do Harm When Using Colloids Instead of Crystalloids?

In Those Without!



André Paul Guillaume Gidé

(1869 – 1951)

Nobel Prize Winner

„trust in those looking for the truth,
but be careful with those who found it“

Matthias Jacob

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University Hospital Munich

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