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What goes in...

(heroes and villains: plasma proteins, hydroxyethyl starch, normal saline)

Dr Tom Woodcock,
Southampton

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Perioperative Fluid Management

Editors: **Farag**, Ehab, **Kurz**, Andrea (Eds.)

2nd Edition 2020

Authored by influential physicians in perioperative fluid management

The Revised Starling Principle and Its Relevance to Perioperative Fluid Management — Pages 31-74
Michel, C. Charles, DPhil, BM.BCh, FRCP (et al.)
Preview | Buy Chapter 30,19 €

The Functions of Endothelial Glycocalyx and Their Effects on Patient Outcomes During the Perioperative Period. A Review of Current Methods to Evaluate Structure-Function Relations in the Glycocalyx in Both Basic Research and Clinical Settings — Pages 75-116
Curry, FitzRoy E., PhD (et al.)
Preview | Buy Chapter 30,19 €

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JAMA | Original Investigation

Effect of Hydroxyethyl Starch vs Saline for Volume Replacement Therapy on Death or Postoperative Complications Among High-Risk Patients Undergoing Major Abdominal Surgery
The FLASH Randomized Clinical Trial

Emmanuel Futier, MD, PhD; Matthias Garot, MD; Thomas Godet, MD, PhD; Matthieu Biais, MD, PhD; Daniel Verzilli, MD; Alexandre Ouattara, MD, PhD; Olivier Huet, MD, PhD; Thomas Lescot, MD, PhD; Gilles Lebuffe, MD, PhD; Antoine Dewitte, MD, PhD; Anna Cadic, MD; Aymeric Restoux, MD, PhD; Karim Asehnoune, MD, PhD; Catherine Paugam-Burtz, MD, PhD; Philippe Cuvillon, MD, PhD; Marion Faucher, MD, PhD; Camille Vaisse, MD; Younes El Amine, MD; Hélène Beloeil, MD, PhD; Marc Leone, MD, PhD; Eric Noll, MD, PhD; Vincent Piriou, MD, PhD; Sigismond Lasocki, MD, PhD; Jean-Etienne Bazin, MD, PhD; Bruno Pereira, PhD; Samir Jaber, MD, PhD; for the FLASH Trial Group

n=826. All received "maintenance" infusion of RL 300 ml/h.

Fluid bolus volumes used (litres): NS 1.5, HES 1.25.
i.e. 6x 250ml NS, 5x 250ml HES
No other differences between NS or HES.

"These findings do not support the use of HES for volume replacement therapy in such patients."

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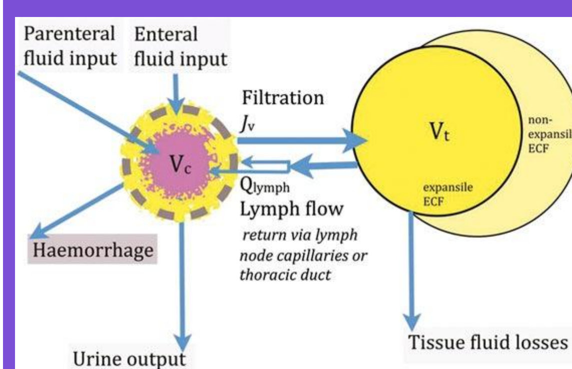

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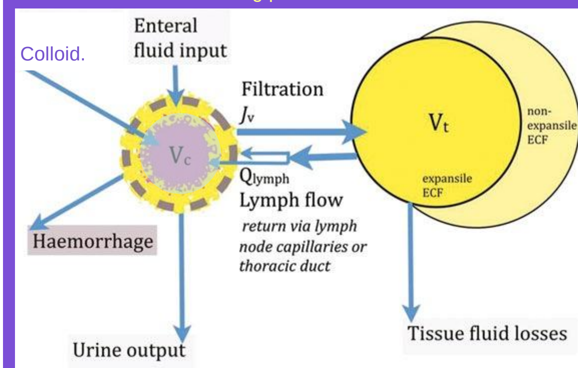
Colloid Vc is the free flowing plasma volume



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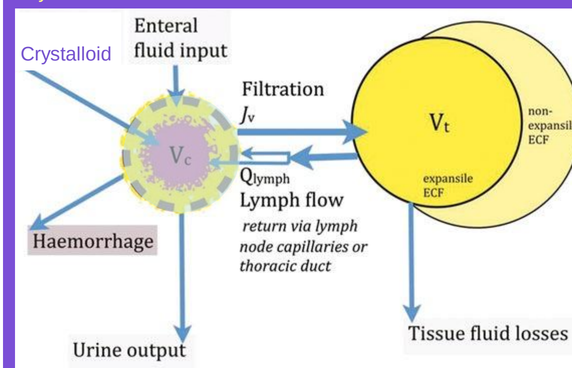
Crystalloid Vc is the intravascular volume



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REVIEW ARTICLE: PDF ONLY

Resuscitation Fluids in Septic Shock

A Network Meta-Analysis of Randomized Controlled Trials

Li, Binghu; Zhao, Hongliang; Zhang, Jie; Yan, Qingguang; Li, Tao; Liu, Liangming

Author Information

SHOCK: November 5, 2019 - Volume Publish Ahead of Print - Issue -

doi: 10.1097/SHK.0000000000001468

13 RCTs.

28-day and 90-day mortality: no significant differences among various resuscitation fluids.
Need for RRT: H-HES was associated cf BS and NS, L-HES was associated cf BS.
Starches should be avoided for septic shock.

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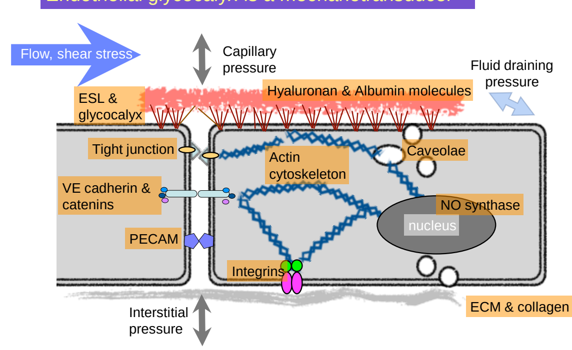
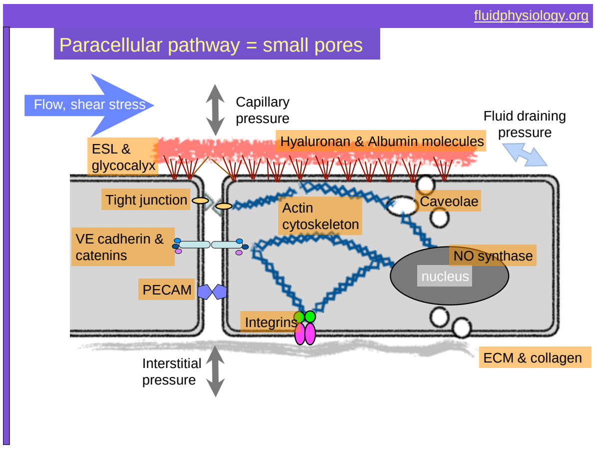
Endothelial glycocalyx is a mechanotransducer

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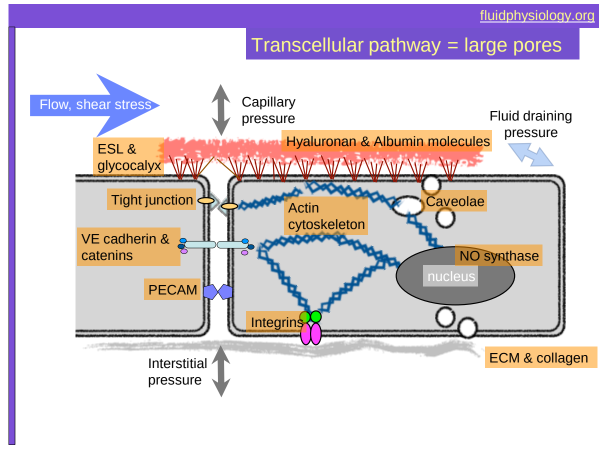
Paracellular pathway = small pores
Flow, shear stress
Capillary pressure
Fluid draining pressure
Hyaluronan & Albumin molecules
ESL & glycocalyx
Tight junction
Actin cytoskeleton
Caveolae
VE cadherin & catenins
NO synthase
nucleus
PECAM
Integrins
ECM & collagen
Interstitial pressure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Transcellular pathway = large pores
Flow, shear stress
Capillary pressure
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Hyaluronan & Albumin molecules
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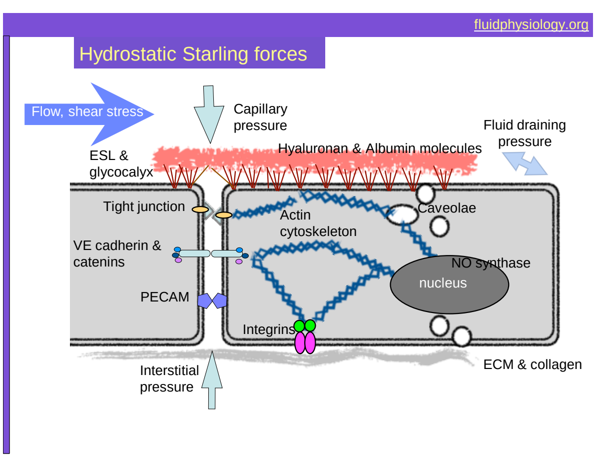
Interstitial pressure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Hydrostatic Starling forces
Flow, shear stress
Capillary pressure
Fluid draining pressure
Hyaluronan & Albumin molecules
ESL & glycocalyx
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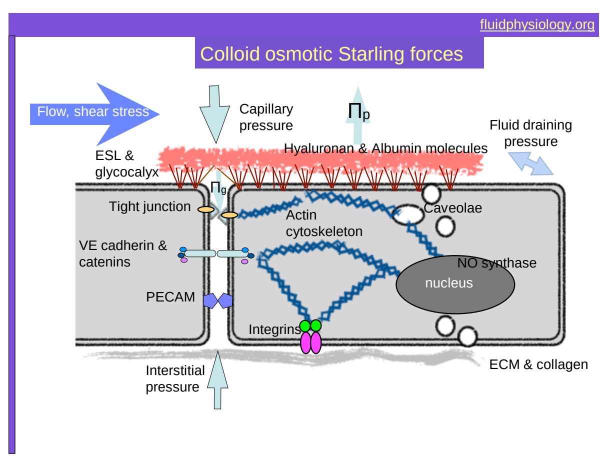
Actin cytoskeleton
Caveolae
VE cadherin & catenins
NO synthase
nucleus
PECAM
Integrins
ECM & collagen
Interstitial pressure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Colloid osmotic Starling forces
Flow, shear stress
Capillary pressure
Π_p
Fluid draining pressure
Hyaluronan & Albumin molecules
ESL & glycocalyx
Π_g
Tight junction
Actin cytoskeleton
Caveolae
VE cadherin & catenins
NO synthase
nucleus
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ECM & collagen
Interstitial pressure

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The COP difference (Π_p - Π_g) influencing transendothelial filtration rate (J_v) is exerted across the endothelial glycocalyx

The subglycocalyx COP (Π_g) varies with J_v.

As J_v falls, Π_g rises and preserves filtration.

Staverman's reflection coefficient σ is an indicator of Glycocalyx filter function.

$\sigma\Delta\Pi$ is the effective colloid osmotic pressure difference.

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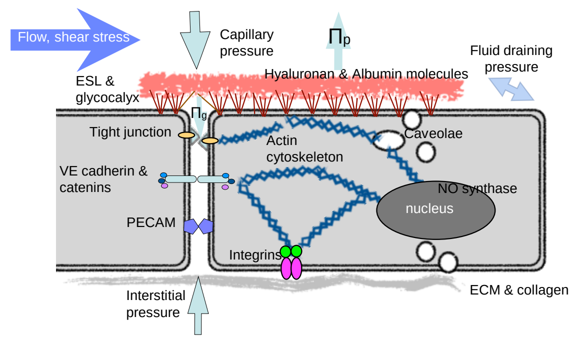
Permeability unit regulation and S-1-P



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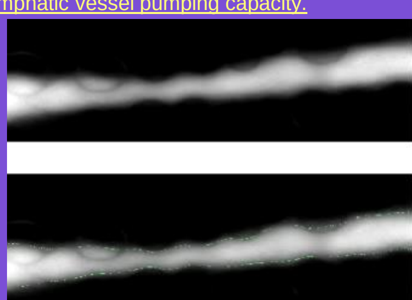
At steady state, transendothelial flow is unidirectional from plasma to the interstitium.

Tissue fluid balance therefore depends on lymphatic vessel pumping capacity.



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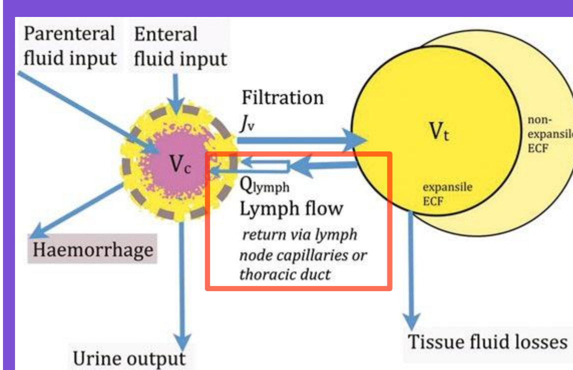

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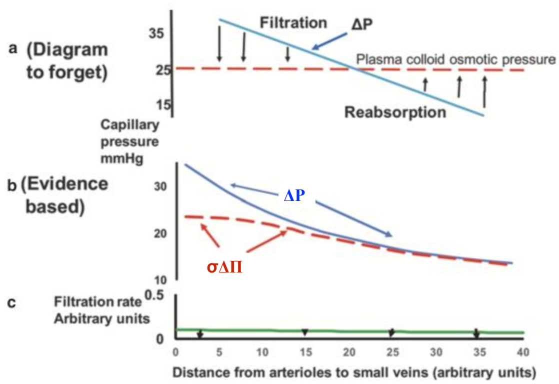
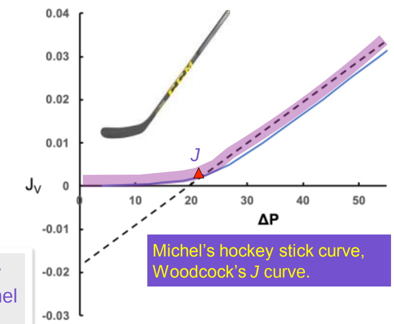
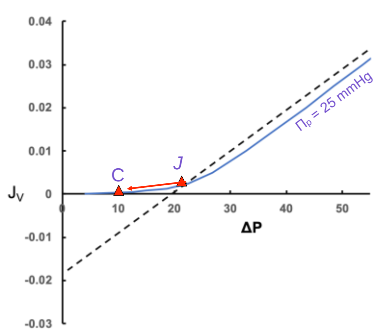


The relationship between J_v and the transendothelial pressure difference according to the steady state Starling equation.

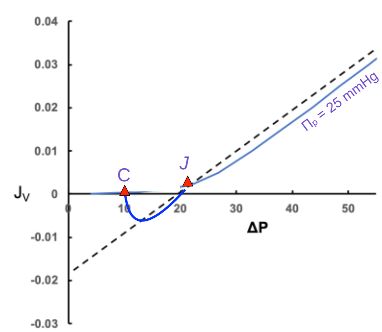


Calculations by C Charles Michel & Fitzroy Curry

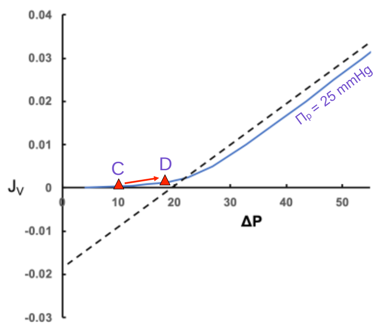
J-C: steady state decline in capillary pressure.



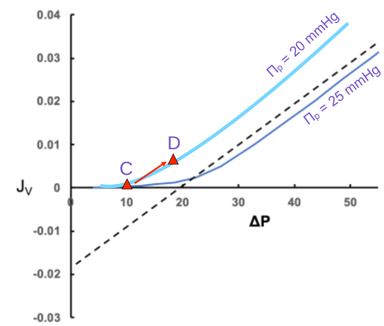
J-C: disequilibrium; transient autotransfusion.



C-D: Isosmotic colloid infusion from low capillary pressure.



C-D: Crystalloid infusion from low capillary pressure.



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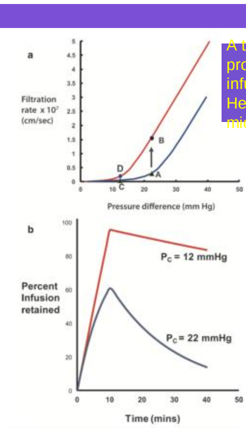

A to B filtration rate when the plasma proteins have been diluted by crystalloid infusion.
Healthy subject at rest with average mean microvascular pressure of 22 mmHg.

C to D filtration rate when the plasma proteins have been diluted by crystalloid infusion.
Hypovolaemia with average mean microvascular pressure of 12 mmHg.

Crystalloids more effectively resuscitate intravascular volume when microvascular pressure is low.

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20% Human Albumin Solution Fluid Bolus Administration Therapy in Patients After Cardiac Surgery (the HAS FLAIR Study)

Geoffrey J. Wigmore, MD, James R. Anstey, MD, Ashley St. John, MD, Joel Greaney, MD, Marc Morales-Codina, MD, Jeffrey J. Presneill, MD, PhD, Adam M. Deane, MD, PhD, Christopher M. MacIsaac, MD, PhD, Michael Bailey, PhD, James Tatoulis, MD, Rinaldo Bellomo, MD, PhD

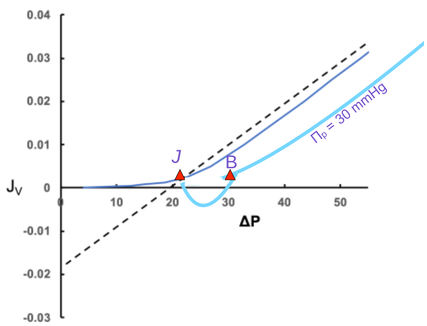
PlumX Metrics

DOI: https://doi.org/10.1053/j.jvca.2019.03.049 | Check for updates

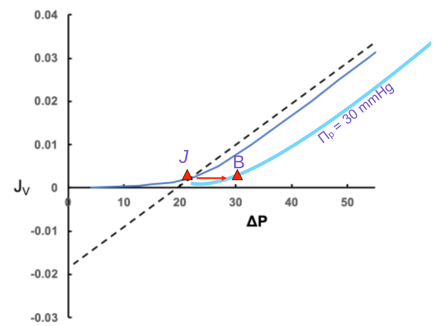
n=100 (sequential, non-blinded)

The intervention: 100 or 200mL of 20% HAS
Effect: less positive median fluid balance in the first 24 hours (albumin: 1.1 v no albumin: 1.9)

J-B: Hyperosmotic bolus, a disequilibrium event.



J-B: Hyperosmotic infusion.



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Maitland et al. BMC Medicine 2013, 11:68
http://www.biomedcentral.com/1741-7015/11/68

BMC Medicine

RESEARCH Open Access

Exploring mechanisms of excess mortality with early fluid resuscitation: insights from the FEAST trial

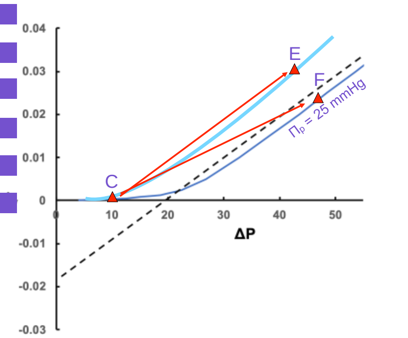
Kathryn Maitland[1,2*], Elizabeth C George[3], Jennifer A Evans[4], Sarah Kiguli[5], Peter Olupot-Olupot[6], Samuel O Akech[2],

n=2396 shocked children in Africa.
Intervention: Fluid bolus (HAS or NS) v NS infusion .

Shock resolution at 1h bolus v NS infusion 43% v 32%.
Excess mortality with boluses in responders and 'non-responders', RR 1.7.

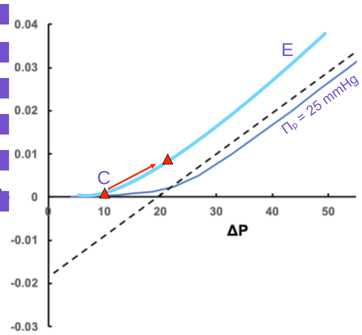
Over resuscitation to capillary hypertension,
0.9% NaCl (C-E) or 5% HAS (C-F).

- Boluses
- Arterial pressure target
- Not stopping when SVV < 10%
- Urine output target
- Lactate target
- CVP target



C-E: Norepinephrine 3-4 mcg/ min as adjunctive therapy to crystalloid infusion.

- Reduces capillary pressure
- Supports stressed blood volume
- Supports arterial pressure
- Enhances lymphatic pumping
- Supports urine output
- *Increases lactate*



FLUID RESUSCITATION STRATEGY

- Crystalloid First to pay back the auto-transfusion and provide solvent for the Na^+ released from the interstitium, restoring intracellular fluid.
- Plasma and Red Cells Early in massive haemorrhage.
- Small frequent doses of resuscitation fluid until arterial pressure starts to rise; no rush to normalise arterial pressure.

FLUID RESUSCITATION STRATEGY

In “Sepsis” patients give immediate vasopressor such as norepinephrine to lower J_V and enhance Q_{lymph}

CENSER STUDY used 4mg of norepinephrine added to 250ml of 5% Dextrose at 0.05 ug/kg/min (for a 70kg person this equals 13ml/hr, or 3.5 mcg/min) for 24 hours without titration.

Permpikul et al.

Early Use of Norepinephrine in Septic Shock Resuscitation (CENSER): A Randomized Trial. AJRCCM 2019

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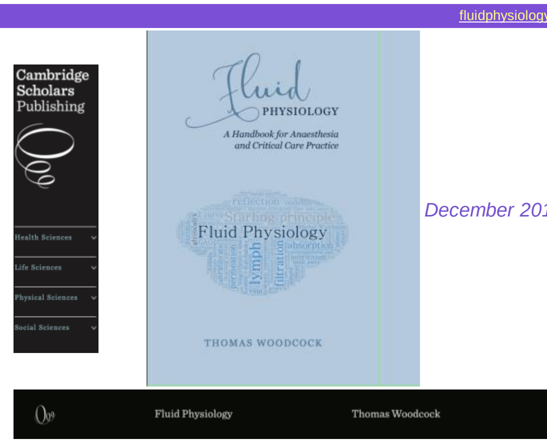

December 2019

Disequilibrium events
- rapid blood loss,
- blood pressure dipping,
- flash pulmonary edema,
- burns,
- sepsis,

are problems of short term Na^+ storage and interstitial volume homeostasis.

Bhave G, Neilson EG. **Body Fluid Dynamics: Back to the Future**. *J Am Soc Nephrol* 2011. 22:2166-2181

Future investigations will hopefully unify the molecular and structural biology of interstitial cell-matrix interactions with Starling physiology to identify new therapeutic targets for hemodynamic derangements.

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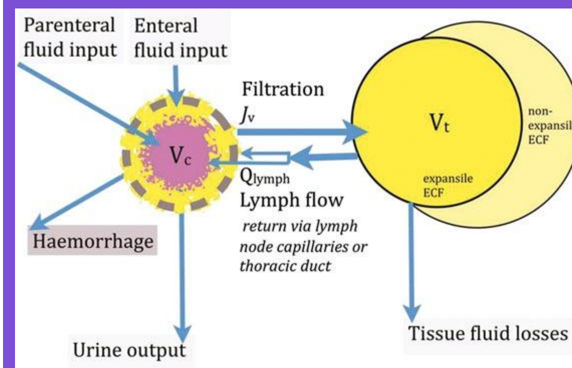

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FLUID PHYSIOLOGY

Learning objectives

1. to understand the steady-state Starling Principle
2. to apply state of the art fluid physiology to a rational prescribing paradigm
3. to appreciate an emerging hypothesis that traditional fluid resuscitation may in fact be harmful
4. learn the best ways to 'keep fluid intravascular'

Thomas Woodcock

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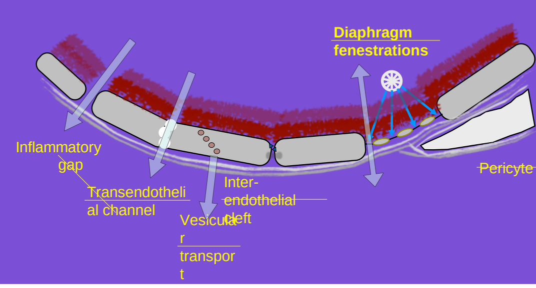
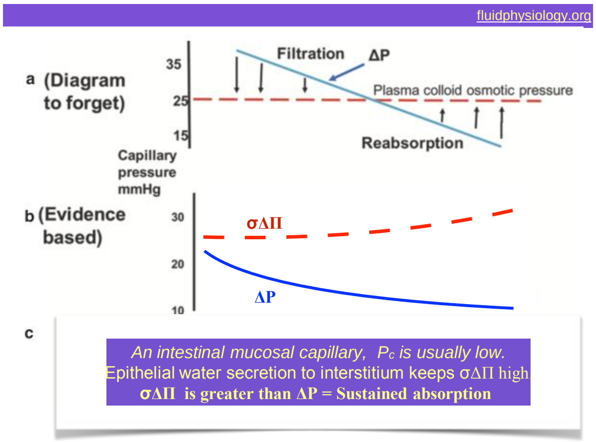
There are Capillaries with a continuous endothelial surface layer and basement membrane that feature transendothelial fenestrations to permit solvent to pass easily.





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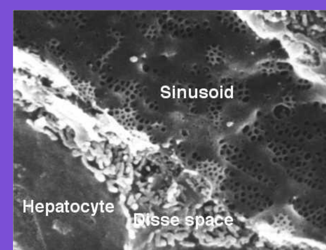
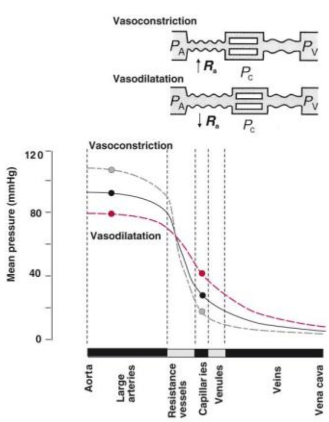
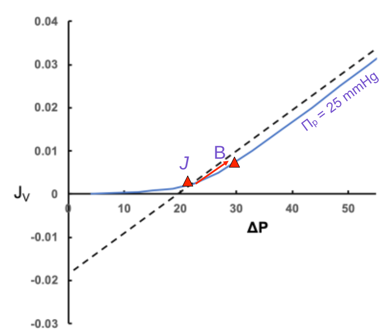
Sinusoidal tissue (liver, spleen and bone marrow) capillaries have a discontinuous endothelial surface layer and basement membrane.

Interstitial fluid here has the same COP as plasma.





J-B: Isosmotic colloid infusion from normal capillary pressure.



J-B: Crystalloid infusion from normal capillary pressure.