A paradigm for rational prescribing.

The BJA Review that started it all;

Woodcock TE, Woodcock TM. Revised Starling equation and the glycocalyx model of transvascular fluid exchange: an improved paradigm for prescribing intravenous fluid therapy. Br J Anaesth. 2012;108:384-394.

FULL TEXT HTML or .pdf files are available from BJA
http://bja.oxfordjournals.org/content/108/3/384.abstract

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I summarise traditional teaching based on the Original Starling principle as follows;

◆ Intravascular volume consists of plasma and cellular elements.
◆ Capillaries separate plasma with high protein concentration from ISF with low protein concentration.
◆ The important Starling forces are the transendothelial pressure difference and the plasma–interstitial COP difference.
◆ Fluid is filtered from the arterial end of capillaries and absorbed from the venous end. Small proportion returns to the circulation as lymph.
◆ Raising plasma COP enhances absorption and shifts fluid from ISF to plasma.
◆ At supranormal capillary pressure, net filtration increases ISF volume
◆ At subnormal capillary pressure, net absorption increases plasma volume
◆ Infused colloid solution is distributed through the plasma volume, and

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Intravascular volume consists of a gel phase, the glycocalyx volume. a sol

phase the plasma volume, and red cell volume.

◆ Sinusoidal tissues (marrow, spleen, and liver) have discontinuous capillaries and their ISF is essentially part of the plasma volume.

◆ Open fenestrated capillaries produce the renal glomerular filtrate.

◆ Diaphragm fenestrated capillaries in specialized tissues can absorb exogenous fluid to plasma .

◆ Continuous capillaries exhibit 'no absorption'.

◆ The EGL is semi-permeable to anionic proteins and their concentration in the intercellular clefts below the glycocalyx is very low.

◆ The important Starling forces are the transendothelial pressure difference and the plasma–subglycocalyx COP difference.

◆ ISF COP is not a direct determinant of Jv.

◆ Jv is much less than predicted by Starling's principle, and the major route for return to the circulation is as lymph.

◆ Raising plasma COP reduces Jv but does not cause absorption.

◆ At subnormal capillary pressure, Jv approaches zero. Auto transfusion is acute, transient, and limited to about 500 ml.

◆ At supranormal capillary pressure, when the COP difference is maximal, Jv is proportional to transendothelial pressure difference.

◆ Infused colloid solution is initially distributed through the plasma volume, and infused ISS through the plasma volume plus glycocalyx volume.

◆ At supranormal capillary pressure, infusion of colloid solution preserves plasma COP, raises capillary pressure, and increases Jv.

◆ At supranormal capillary pressure, infusion of ISS also raises capillary pressure, but it lowers COP and so increases Jv more than the same colloid solution volume.

◆ At subnormal capillary pressure, infusion of colloid solution increases plasma volume and infusion of ISS increases intravascular volume, but Jv remains close to zero in both cases.

is returned to the circulation primarily as lymph that is regulated through sympathetically mediated responses."
Myburgh JA, Mythen MG. Resuscitation fluids. N Engl J Med. 2013;369:1243-1251.

One of the first texts to appreciate a very important consequence of the J curve;
"With low capillary pressure hypovolemic or hemorrhagic shock states, intravascular retention of crystalloids is enhanced as clearance is reduced. In this setting, crystalloids are effective intravascular volume expanders, as they are retained within the circulation for considerably longer periods with marked reduction in clearance."
Andrew Shaw, Karthik Raghunathan, Fluid Management in Cardiac Surgery. Colloid or Crystalloid? DOI: http://dx.doi.org/10.1016/j.anclin.2012.12.007

"a revision of the classical Starling principles incorporating the endothelial glycocalyx layer means a reduced absorption effect of the transcapillary oncotic pressure in favor of the hydrostatic capillary pressure. This hypothesis, however, is highly controversial and has still not been confirmed". Sorry to have the steady state Starling principle dismissed out of hand by the authors of the Lund concept, which is itself unproven and controversial! I don't find it to be incompatible with the Lund concept.
L.-O.D. Koskinen M. Olivecrona P.O. Grände. Severe traumatic brain injury management and clinical outcome using the Lund concept. Neuroscience;283:245-255
"We summarize the emerging new literature regarding the pathophysiological principles underlying the beneficial and deleterious effects of fluid administration during resuscitation, as well as current recommendations and recent clinical evidence regarding specific colloids and crystalloids. This systematic review allows us to conclude that there is no clear benefit

and the extracellular matrix. According to this revised model, when the vascular barrier is intact, transcapillary movement of fluid is unidirectional, as there is no absorption of fluid from the interstitium back to the intravascular space, and drainage of the interstitium is accomplished primarily by lymphatic clearance. Transcapillary movement is then dependent on capillary pressure. At supranormal capillary pressures, infusion of colloid solution preserves oncotic pressure and increases capillary pressure, thus increasing movement of fluid into the interstitial space. Under the same conditions, infusion of crystalloid solutions also increases capillary pressure, but by dilution decreases oncotic pressure, thus resulting in more transcapillary movement than colloids. At subnormal capillary pressures, transcapillary movement nears zero; thus, infusion of both crystalloids and colloids results in increase in capillary pressure, but no change in transcapillary movement."
Alena Lira, Michael R Pinsky. Choices in fluid type and volume during resuscitation: impact on patient outcomes. Annals of Intensive Care. 2014;4:38 DOI: 10.1186/s13613-014-0038-4

With clinicians quick to blame permeability problems but often ignorant of the science, this review of the physiology by pioneers of the Michel-Weinbaum model is a must-read. I touch on some of the issues in BJA Education's "Plasma Volume";
F.-R. E. Curry and R. H. Adamson. Tonic regulation of vascular permeability. Acta Physiologica (2013) 207: 628

It is now almost universally presumed that we can divide our patient population into two: the septic and the non-septic. I regard this as flawed division. It underpins the absurd position of the European Medicines Agency (binding on the Medicines Regulatory Health Authority of the United Kingdom) that "HES should be contraindicated in critically ill patients or patients with sepsis or burns. However, HES can be used in patients with acute blood loss,

clinical practice, plateau of cardiac volume response (to preload change) is the brightest warning light that further fluid will lead to harmful oedema, independent of the presence of sepsis {2}. This finding, which is unexpected in traditional Starling principle physiology terms, becomes expected with Michel and Weinbaum's steady state Starling principle {3}. Marik and Bellomo confirm the rational preference for volume-limited haemodynamic therapy over venous pressure-limited, but choose to explain it by claiming that the intravascular pressure determining cardiac output is the mythical mean circulatory filling pressure rather than the measurable central venous pressure. The capillary pressure is not considered; this is the main determinant of Jv whatever the resistance (1/conductance) or permeability state of the endothelial barrier.

Marik P, Bellomo R. A rational approach to fluid therapy in sepsis. Br J Anaesth. 2016;116:339-349.

The way we justify the best practical advice for volume-resistant hypotension is however much less important than the fact that patients benefit from the current fluid therapy enlightenment.

– No colloids.

– Volume limited rather than volume liberal goals.

– Early alpha one agonist (or V1 agonist?) to counteract the venodilation that reduces the effective arterial blood volume, to protect capillary pressure and to stimulate lymphatic fluid circulation.

References

1.Vassiliou AG, Mastora Z, Orfanos SE, Jahaj E, Maniatis NA, Koutsoukou A, Armaganidis A, Kotanidou A. Elevated biomarkers of endothelial dysfunction/activation at ICU admission are associated with sepsis development. Cytokine. 2014; 69(2):240-247

2.Aman J, Groeneveld AB, van Nieuw Amerongen GP. Predictors of pulmonary edema formation during fluid loading in the critically ill with presumed hypovolemia*. Crit Care Med. 2012 Mar; 40(3):793-9

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Woodcock T: F1000Prime Recommendation of Evaluation [Tatara T, J Intensive Care 2016, 4:20]. In F1000Prime, 17 May 2016; DOI: 10.3410/f.726240967.793518215. F1000Prime.com/726240967#eval793518215

RSE&GM predicts that infusion of compensatory fluid during vasodilation will avoid the rise in capillary pressure that leads to increased Jv if the fluid is 'preloaded', making the infusion a more effective preventer of reduced cardiac filling pressure. A recent meta-analysis confirms this;
"CONCLUSIONS: In case of using crystalloids for cesarean delivery, coload is more effective than preload for the prevention of maternal hypotension after spinal anesthesia."

Oh AY, Hwang JW, Song IA et al. Influence of the timing of administration of crystalloid on maternal hypotension during spinal anesthesia for cesarean delivery: preload versus coload. BMC Anesthesiol. 2014;14:36.

"enzymatic degradation (hyaluronidase) of the endothelial glycocalyx in an in vivo, whole-body model, did not induce leakage of plasma or albumin."
"experimental studies have been used as evidence for clinical recommendations in fluid therapy. Interestingly, the authors of two reviews draw different conclusions based on the same experimental literature regarding the use of colloids." Alarm bells! But "Hyaluronidase only degrades parts of the glycocalyx, and the remaining structure could be capable of preventing plasma leakage." Phew!
S. A. Landsverk, A. G. Tsai, P. Cabrales, and M. Intaglietta. Impact of Enzymatic Degradation of the Endothelial Glycocalyx on Vascular Permeability in an Awake Hamster Model. http://dx.doi.org/10.1155/2012/842545