

Mini Review

Twenty-one Reasons Affirming Starling's Law on the Capillary-interstitial Fluid Transfer Wrong and the Correct Replacement is the Hydrodynamic of the Porous Orifice (G) Tube

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ABSTRACT

Many reasons why Starling's law wrong and the correct replacement is the hydrodynamic of porous orifice (G) tube exist. Starling's hypothesis is based on Poiseuille's work in which the hydrostatic pressure causes filtration. The oncotic pressure force of plasma proteins causes re-absorption. Starling's law is wrong on both forces.

The capillary has a pre-capillary sphincter and pores that allow the passage of plasma proteins. This makes the capillary a porous orifice (G) tube with different hydrodynamic; side pressure causes suction not filtration. The pores nullify the oncotic force in vivo. There is evidence to show that the osmotic chemical composition of various body fluids is identical to plasma proteins. The interstitial fluid (ISF) space has a negative pressure of -7 cm water. Evidence on Albumin versus Saline for fluid resuscitation shows no significant difference. This affirms that the oncotic force does not exist in vivo that partly prove Starling's law wrong. Inadequacy in explaining the capillary-ISF transfer, has previously called for reconsideration of Starling's hypothesis.

Physics and physiological research demonstrate that pressure does not cause filtration across the wall of G tube, it causes suction. In G tube negative side pressure gradient causing suction maximum near the inlet and turns positive maximum near the exit causing filtration. Physiological study completed the evidence that Starling's law is wrong as the capillary works as G tube not Poiseuille's tube. Both absorption and filtration are autonomous functions of G tube thus fit to replace Starling's law. The clinical significance is discussed.

Keywords: Capillary-interstitial fluid; Hydrodynamic; Osmotic chemical composition; Plasma; Starling's law.

MINI REVIEW

The complete evidence that Starling's law is wrong and the correct replacement is the hydrodynamic of the porous orifice tube has been reported as summarized here¹: Dr. Starling² proposed his hypothesis >80 years prior to the discovery of the capillary ultrastructure and correct capillary physiology as shown here. He based his hypothesis on Poiseuille's² work on strait uniform brass tube in which the hydrostatic pressure is a positive force of the arterial pressure causing filtration.³ The oncotic pressure force of plasma albumin causes re-absorption. Starling's law is wrong on both forces because of the following reasons.³

1. In the pulmonary circulation arterial pressure is less than the plasma oncotic π_c pressure. In the liver, muscles and lung intersti-

tial fluid (ISF) has high protein content. Thus fluid filtration in the lungs and reabsorption in the liver and muscles lacks explanation.³

2. The capillary has a pre-capillary sphincter as reported by Rhodin in 1967^{4,5} which makes it different from Poiseuille's tube of uniform diameter as modern research mentioned below demonstrates.

3. The capillary has porous wall of intercellular slits that allow the passage of molecules larger than plasma proteins as shown by Karnovsky in 1967.⁶ Hence plasma proteins cannot exert an oncotic pressure in vivo.

4. The osmotic chemical composition of various body fluids is iden-

tical to plasma proteins as demonstrated by Hendry in 1962,⁷ Hence the oncotic pressure if it exists is too weak and too slow force to cause absorption.

5. The oncotic pressure of plasma proteins does not work as absorption force neither in physiology as proved by Hendry in 1962⁷ nor in clinical practice demonstrated by Cochrane Injuries Group and other authors in 1998^{8,9} and 2006.¹⁰ Also most recent study using hydroxyethyl Starch (HES) as plasma substitutes for fluid resuscitation in 2020 demonstrated, like albumin, that there is no significant difference from using Saline.¹¹

6. Guyton and Coleman (1968)¹² demonstrated that the interstitial fluid (ISF) space has a negative pressure of -7 cm water and Calnan et al (1972)¹³ showed that the lymph has the same negative pressure. The pressure under the skin is negative. That cannot be explained by Starling's law.

7. Inadequacy in explaining the capillary-ISF transfer in many parts of the body as reported by Keele et al in 1982,⁴ particularly vital organs, has previously called for reconsideration of Starling's hypothesis by Renkin in 1986.¹⁴

8. Recently reported evidence on plasma protein⁸⁻¹⁰ and HES¹¹ versus Saline for volume replacement therapy during major surgery shows no significant difference. This affirms that the oncotic force does not exist in vivo that partly prove Starling's law wrong.

9. Both physics^{15,16} and physiological¹⁷ research has demonstrated that the hydrostatic or rather dynamic flow pressure induced by the proximal akin to arterial pressure does not cause filtration, as proposed by Starling, across the wall of porous orifice (G) tube. It causes suction.^{15,16}

10. The proximal or arterial pressure induces negative side pressure gradient along the G tube wall causing suction maximum near the inlet and turns positive maximum near the exit causing filtration as based on physics experiments^{15,16} (Figure 1) and physiological research¹⁷. Venous pressure enhances filtration and causes oedema but arterial pressure does not- it causes absorption by suction. Both absorption and filtration are autonomous functions of G tube making it the correct replacement for the faulty law.¹

11. The physiological study on the hind limb of sheep¹⁷ has completed the evidence that Starling's law is wrong as the capillary works as G tube not Poiseuille's tube.¹

12. The physiological study showed that plasma proteins versus Saline as circulation fluid has no significant difference. First set of experiments the fluid is run through the artery. This produced no oedema formation but irrigated the limb well. Second set of experiments the fluid is run through the vein; both plasma and saline induced oedema and accumulation of fluid under the cling membrane that replaced the skin.

13. Received thinking that elevating central venous pressure (CVP)

is synonymous with elevating arterial pressure is prevailing in current clinical practice during fluid therapy for shock, the resuscitation of the acutely ill patients and prolonged major surgery. This may be correct during restoration therapy for hypovolemic and haemorrhagic shock, but vascular expansion or volumetric overload (VO) is a different issue as it induces volumetric overload shocks (VOS)¹⁸⁻²³ and causes the acute respiratory distress syndrome (ARDS)^{23,24} that was originally reported by Ashbaugh et al,²⁴ in 1967.

14. Persistent attempts to elevate CVP up to levels of 18 to 22 cm water are common received practice, but wrong.²³ The normal CVP is around 0 and most textbooks report a range of -7 to +7 cm water.^{3,4,25} The question of: Does raising CVP up to level of 18-22 cm water cause VOS?. Has been positively answered.²⁶

15. Clinical observations demonstrate that, in addition to the well-known effect of high venous pressure causing oedema, arterial hypertension has no such effect, if not exact opposite. In clinical practice, although arterial hypertension is common, ISF oedema is unknown among its complications.²³

16. In the G-C model of the physics experiments,^{15,16} a minor increase in distal pressure (DP), akin to venous pressure, increases fluid volume in chamber C around the G tube (Figure 1) reverting chamber pressure (CP) from negative to positive while slowing the G-C circulation. Increasing DP has similar effect to decreasing proximal pressure (PP) akin to arterial pressure on the G-C circulation and CP and volume.

17. Vascular expansion of volumetric overload with hypervolaemia causes VO shocks.¹⁸⁻²² There is no doubt that the erroneous Starling's law is responsible for the many errors and misconceptions prevailing on fluid therapy²² for shock, the acutely ill patients and during major surgery which mislead physicians into giving too much fluid that induce VOS and cause the multiple vital organ dysfunction syndrome (MODS) or ARDS.^{23,24}

18. This wrong law dictates faulty rules on fluid therapy that underlies the treating physician's thought when embarking on the overzealous fluid infusion during the resuscitation of shock, acutely ill and prolonged major surgery.

19. A concept based on the new hydrodynamic phenomenon of G tube is proposed to replace Starling's law for the capillary-ISF circulation. It explains this vital circulation in every organ and tissue.

20. A rapid autonomous dynamic magnetic field-like G-C circulation occurs between fluid in the G tube's lumen and a surrounding fluid compartment C akin to ISF around the capillaries (Figure 1).

21. The presented evidence does not only prove that Starling's law is wrong but also provides the correct replacement that is the hydrodynamic of the G tube explaining the capillary-ISF circulation in every tissue and organ of the body. This is the only way to resolve the puzzles of the transurethral resection of the prostate (TURP) syndrome, acute dilution hyponatraemia (HN) and ARDS.^{23,26,27}

Figure 1

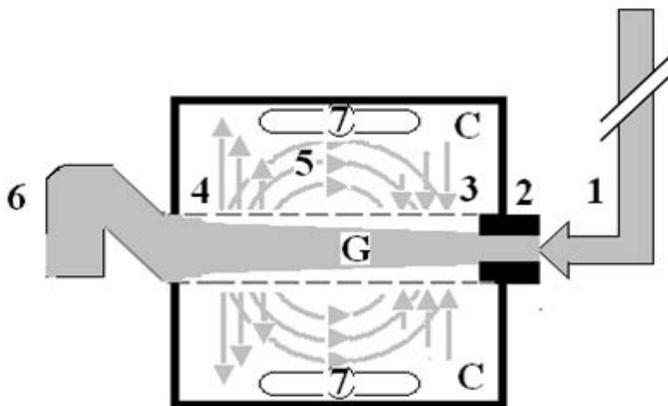


Figure 1 shows a diagrammatic representation of the hydrodynamic of G tube based on G tubes and chamber C seen in 5.

This 38-years old diagrammatic representation of the hydrodynamic of G tube in chamber C. The G tube is the plastic tube with narrow inlet and pores in its wall built on a scale to capillary ultra-structure of precapillary sphincter and wide inter cellular slit pores, and the chamber C around it is another bigger plastic tube to form the G-C apparatus. The chamber C represents the interstitial fluid space. The diagram represents a capillary-ISF unit, and the numbers should read as follows:

1. The inflow pressure pushes fluid through the orifice
2. Creating fluid jet in the lumen of the G tube**.
3. The fluid jet creates negative side pressure gradient causing suction maximal over the proximal part of the G tube near the inlet that sucks fluid into lumen.
4. The side pressure gradient turns positive pushing fluid out of lumen over the distal part maximally near the outlet.
5. Thus, the fluid around G tube inside C moves in magnetic field-like circulation (5) taking an opposite direction to lumen flow of G tube.
6. The inflow pressure 1 and orifice 2 induce the negative side pressure energy creating the dynamic G-C circulation phenomenon that is rapid, autonomous and efficient in moving fluid and particles out from the G tube lumen at 4, irrigating C at 5, then sucking it back again at 3,
7. Maintaining net negative energy pressure inside chamber C.

**Note the shape of the fluid jet inside the G tube (Cone shaped), having a diameter of the inlet on right hand side and the diameter of the exit at left hand side (G tube diameter). I lost the photo on which the fluid jet was drawn, using tea leaves of fine and coarse sizes that runs in the centre of G tube leaving the outer zone near the wall of G tube clear. This may explain the finding in real capillary of the

protein-free (and erythrocyte-free) sub-endothelial zone in the Glycocalyx paradigm (Woodcock and Woodcock 2012).

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REFERENCES

1. Ghanem AN. The Correct Replacement for the Wrong Starling's law is the Hydrodynamic of the Porous Orifice (G) Tube: The Complete Physics and physiological Evidence with Clinical Relevance and Significance. *Cardio Open*. 2020; 5(1): 7
2. Starling EH. Factors involved in the causation of dropsy. *Lancet*. 1886; ii: 1266–1270, 1330–1334 and 1406–1410.
3. Folkow B, Neil E. Circulation. Oxford University Press: London 1971; 1–125.
4. Keele CA, Neil E, Joels N. Sampson Wright Applied Physiology. 13th ed. Oxford University Press; Oxford, 1982.
5. Rhodin JA. The ultra-structure of mammalian arterioles and pre-capillary sphincters. *J Ultrastructure Res*. 1967; 18(1-2): 181–223.
6. Karnovsky MJ. The ultra-structural basis of capillary permeability studied with peroxidase as a tracer. *J Cell Biol*. 1967; 35(1): 213–236. doi: [10.1083/jcb.35.1.213](https://doi.org/10.1083/jcb.35.1.213)
7. Hendry EB. The osmotic pressure and chemical composition of human body fluids. *Clin Chem*. 1962; 8(3): 246–265.
8. Cochrane Injuries Group. Human albumin administration in the critically ill patients: Systemic review of randomized controlled trials: Why albumin may not work. *BMJ*. 1998; 317: 235-40. doi: [10.1136/bmj.317.7153.235](https://doi.org/10.1136/bmj.317.7153.235)
9. SAFE Study Investigators, Finfer S, Bellomo R, et al. Effect of baseline serum albumin concentration on outcome of resuscitation with albumin or saline in patients in intensive care units: Analysis of data from the saline versus albumin fluid evaluation (SAFE) study. *BMJ*; 333(7577): 1044. doi: [10.1136/bmj.38985.398704.7C](https://doi.org/10.1136/bmj.38985.398704.7C)
10. Vincent JL. Resuscitation using albumin in critically ill patients: Research in patients at high risk of complications is now needed. *BMJ*; 333(7577): 1029-1030. doi: [10.1136/bmj.39029.490081.80](https://doi.org/10.1136/bmj.39029.490081.80)
11. Futier E, Garot M, Godet T, et al. 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. *JAMA*. 2020; 323(3): 225–236. doi:[10.1001/jama.2019.20833](https://doi.org/10.1001/jama.2019.20833)
12. Guyton AC, Coleman TG. Regulation of interstitial fluid volume and pressure. *Ann N Y Acad Sci*. 1968; 150(3): 537–547. doi: [10.1111/](https://doi.org/10.1111/)

[j.1749-6632.1968.tb14705.x](https://doi.org/10.1749-6632.1968.tb14705.x)

13. Calnan JS, Pflug JJ, Chisholm GD, Taylor LM. Lymphatic surgery. *Proceedings Royal Soc Med.* 1972; 65: 715–719.

14. Renkin EM. Some consequences of capillary permeability to macromolecules: Starling's hypothesis reconsidered. *Am J Physiol.* 1986; 250(5 Pt 2): H706–H710. doi: [10.1152/ajpheart.1986.250.5.H706](https://doi.org/10.1152/ajpheart.1986.250.5.H706)

15. Ghanem AN. Magnetic field-like fluid circulation of a porous orifice tube and relevance to the capillary-interstitial fluid circulation: Preliminary report. *Med Hypotheses.* 2001; 56 (3): 325-334. doi: [10.1054/mehy.2000.1149](https://doi.org/10.1054/mehy.2000.1149)

16. Ghanem KA, Ghanem AN. The proof and reasons that Starling's law for the capillary- interstitial fluid transfer is wrong, advancing the hydrodynamics of a porous orifice (G) tube as the real mechanism. *Blood Heart Circ.* 2017; 1(1): 1-7 doi:[10.15761/BHC.1000102](https://doi.org/10.15761/BHC.1000102)

17. Ghanem KA, Ghanem AN. The Physiological Proof that Starling's Law for the Capillary-Interstitial Fluid Transfer is wrong: Advancing the Porous Orifice (G) Tube Phenomenon as Replacement. *Open Acc Res Anatomy.* 1(2).

18. Ghanem AN, Ward JP. Osmotic and metabolic sequelae of volumetric overload in relation to the TURP syndrome. *Br J Urol.* 1990; 66(1): 71–78. doi: [10.1111/j.1464-410x.1990.tb14868.x](https://doi.org/10.1111/j.1464-410x.1990.tb14868.x)

19. Ghanem AN, Ghanem SA. Volumetric Overload Shocks: Why Is Starling's Law for Capillary Interstitial Fluid Transfer Wrong? The Hydrodynamics of a Porous Orifice Tube as Alternative. *Surgical Science.* 2016; 7(): 245-249. doi: [10.4236/ss.2016.76035](https://doi.org/10.4236/ss.2016.76035)

20. Pindoria N, Ghanem SA, Ghanem KA and Ghanem AN. Volumetric overload shocks in the patho-etiology of the transurethral resection prostatectomy syndrome and acute dilution hyponatraemia. *Integr Mol*

Med, 2017; 4. doi: [10.15761/IMM.1000279](https://doi.org/10.15761/IMM.1000279)

21. Ghanem KA, Ghanem AN. Volumetric overload shocks in the patho-etiology of the transurethral resection prostatectomy syndrome and acute dilution hyponatraemia: The clinical evidence based on 23 case series. 2018; 7(5): 555724. doi: [10.19080/OAJS.2018.07.555724](https://doi.org/10.19080/OAJS.2018.07.555724)

22. Ghanem SA, Ghanem KA, Ghanem AN. Volumetric Overload Shocks in the Patho-Etiology of the Transurethral Resection of the Prostate (TURP) Syndrome and Acute Dilution Hyponatraemia: The Clinical Evidence Based on Prospective Clinical Study of 100 Consecutive TURP Patients. *Surg Med Open Access J.* 2017: 1(1);1-7. Doi: [10.15761/IMM.1000279](https://doi.org/10.15761/IMM.1000279)

23. Ghanem AN. The Adult Respiratory Distress Syndrome: Volumetric Overload Shocks in Patho-Etiology Correcting Errors and Misconceptions on Fluid Therapy, Vascular and Capillary Physiology. *Surg Med Open Acc J.* 2018; 2(2): 534. doi: [10.31031/SMOAJ.2018.02.000534](https://doi.org/10.31031/SMOAJ.2018.02.000534)

24. Ashbaugh DG, Bigelow DB, Petty TL, Levine BE. Acute respiratory distress in adults. *Lancet.* 1967; 2(7511): 319-323. doi: [10.1016/s0140-6736\(67\)90168-7](https://doi.org/10.1016/s0140-6736(67)90168-7)

25. Guyton A C. (1986) Textbook of Medical Physiology. An HBJ International Seventh Edn. WB Saunders Company. Philadelphia London; 19: 221.

26. Ghanem AN. Does Raising the Central Venous Pressure (CVP) in Treating Shock with Fluids Induce Volumetric Overload Shocks (VOS)?. *Adv Card Res.* 2019; 1(5). doi: [10.32474/ACR.2019.01.000121](https://doi.org/10.32474/ACR.2019.01.000121)

27. Ghanem AN. Volumetric Overload Shocks: Resolving the puzzles of the transurethral resection of the prostate (TURP) syndrome, acute dilution hyponatraemia (HN) and the acute respiratory distress syndrome (ARDS). Scholars Press USA, 2018.