Ultrafiltration in PD: Physiologic Principles

Ali K. Abu-Alfa, MD, FASN
Professor of Medicine
Head, Division of Nephrology and Hypertension
American University of Beirut
Beirut, Lebanon

Adjunct Faculty
Section of Nephrology
Yale School of Medicine
New Haven, CT

Version Date: February 2012

DISCLOSURES

Dr Abu-Alfa has served as a Consultant for Baxter Healthcare, and has received research grants and honoraria for speaking engagements and/or organization of PD educational conferences from Baxter Healthcare.

Dr Abu-Alfa is the immediate past co-President for the North American Chapter of the International Society for Peritoneal Dialysis.

Educational Objectives

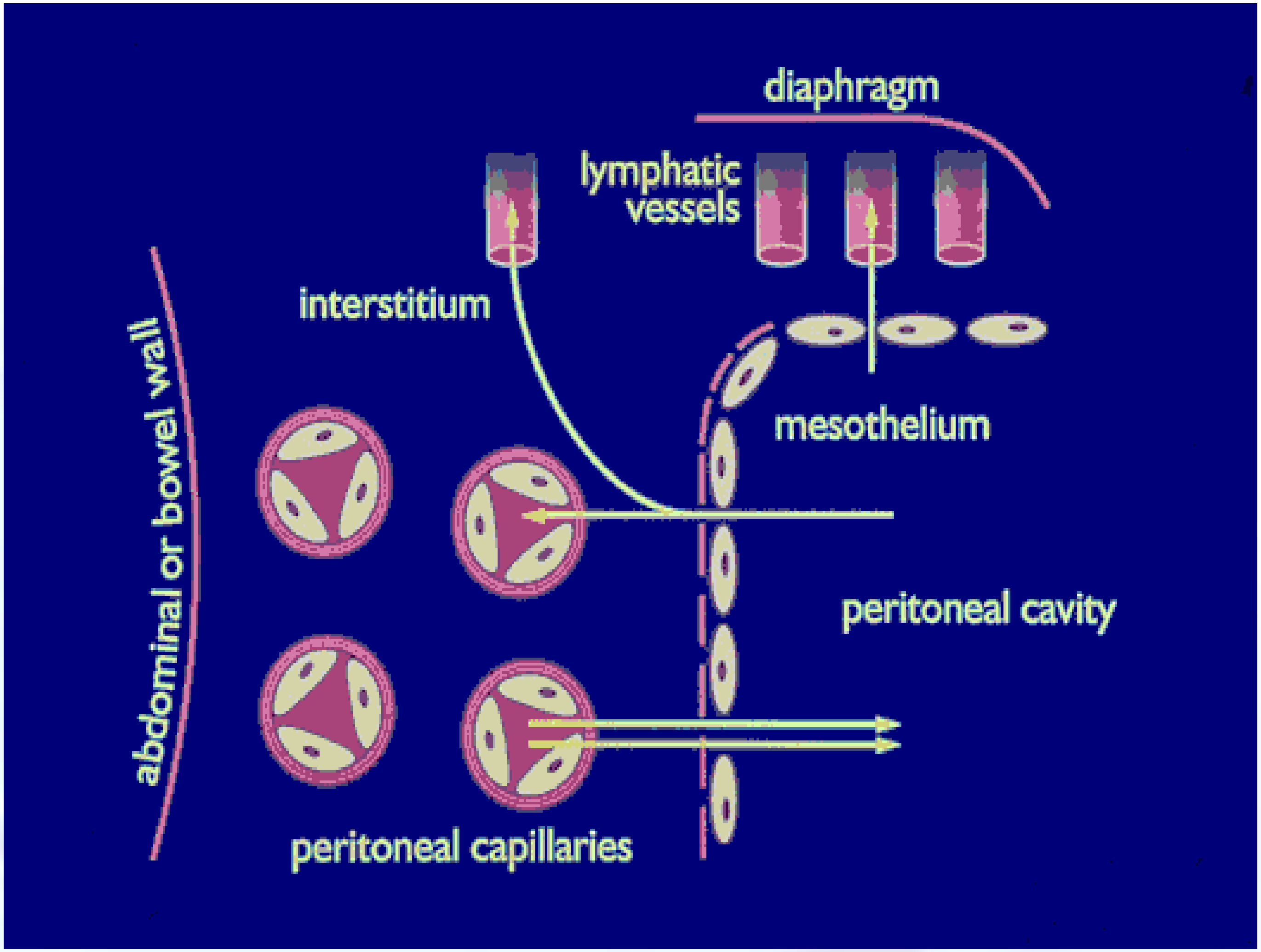
- Review physiologic basis of ultrafiltration
- Review the impact of membrane transport characteristics in UF volume.
- Compare osmotic and oncotic forces and effect on UF.
- Discuss Na sieveing and Na removal.
- Review membrane changes over time.

Physiology of Ultrafiltration: Mechanisms at Play

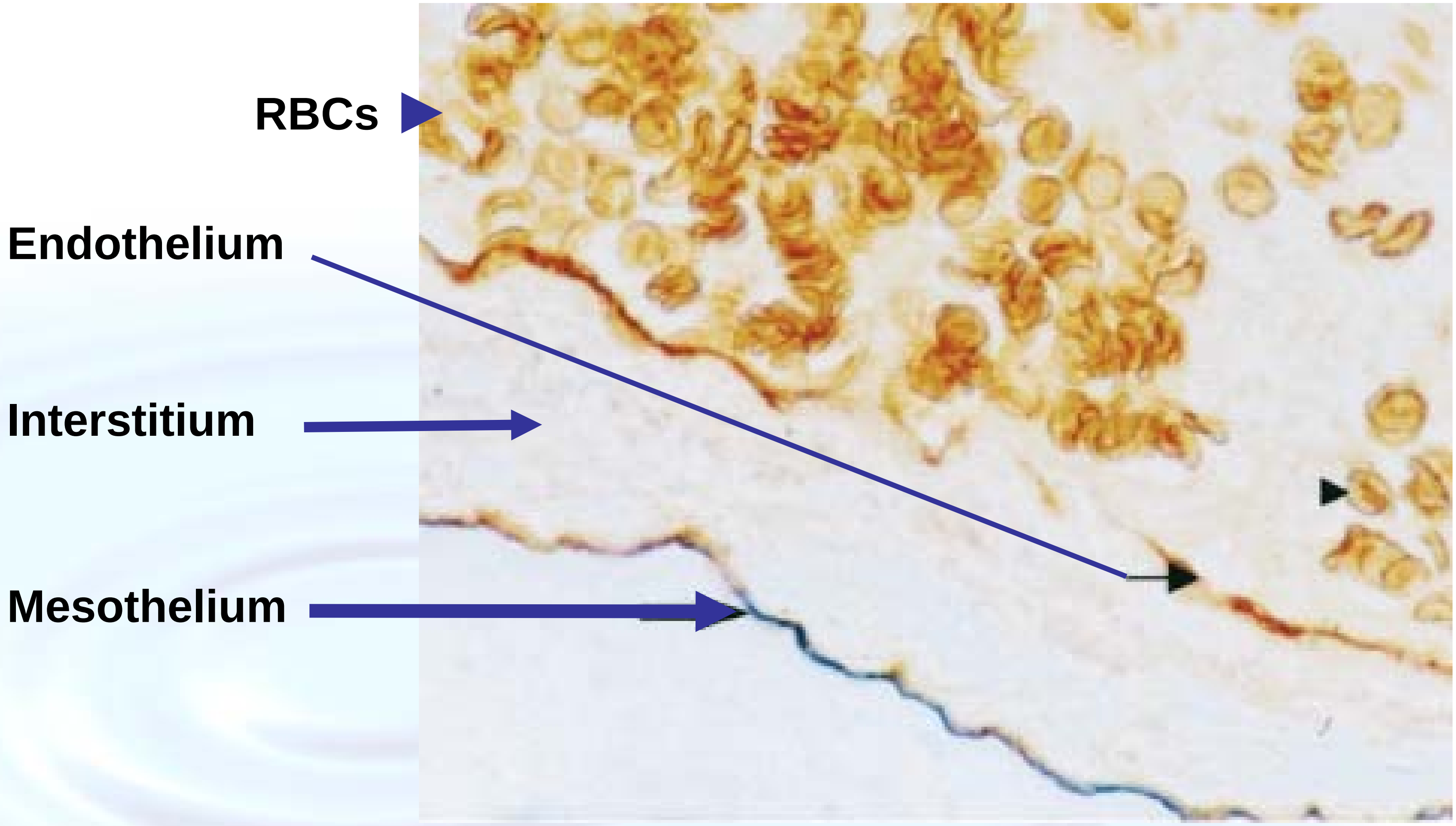
- Trans-capillary fluid movement:
  - Osmotic / Oncotic gradient (first and foremost).
  - Hydrostatic pressure (much less so).
  - Membrane function / surface area.

- Lymphatic re-absorption.

Physiology of Ultrafiltration: Structure of Peritoneal Membrane

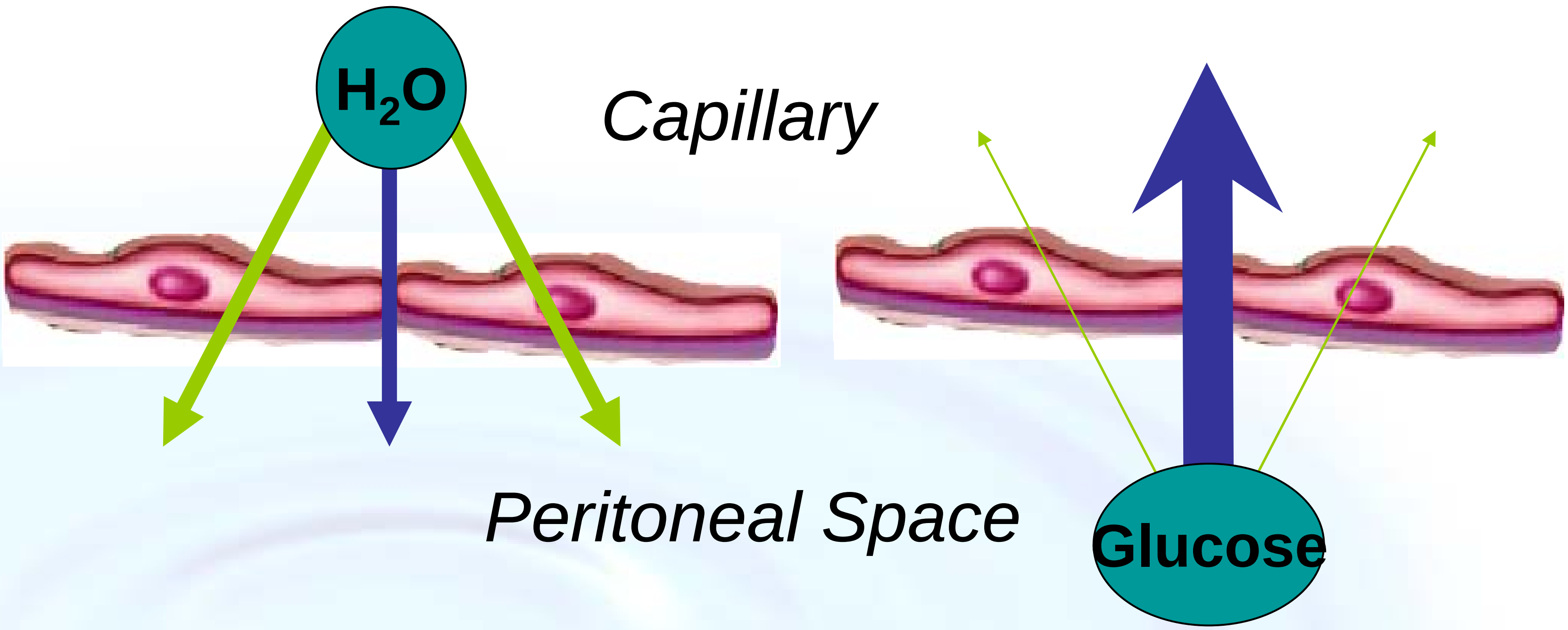


Physiology of Ultrafiltration: Normal Human Peritoneum



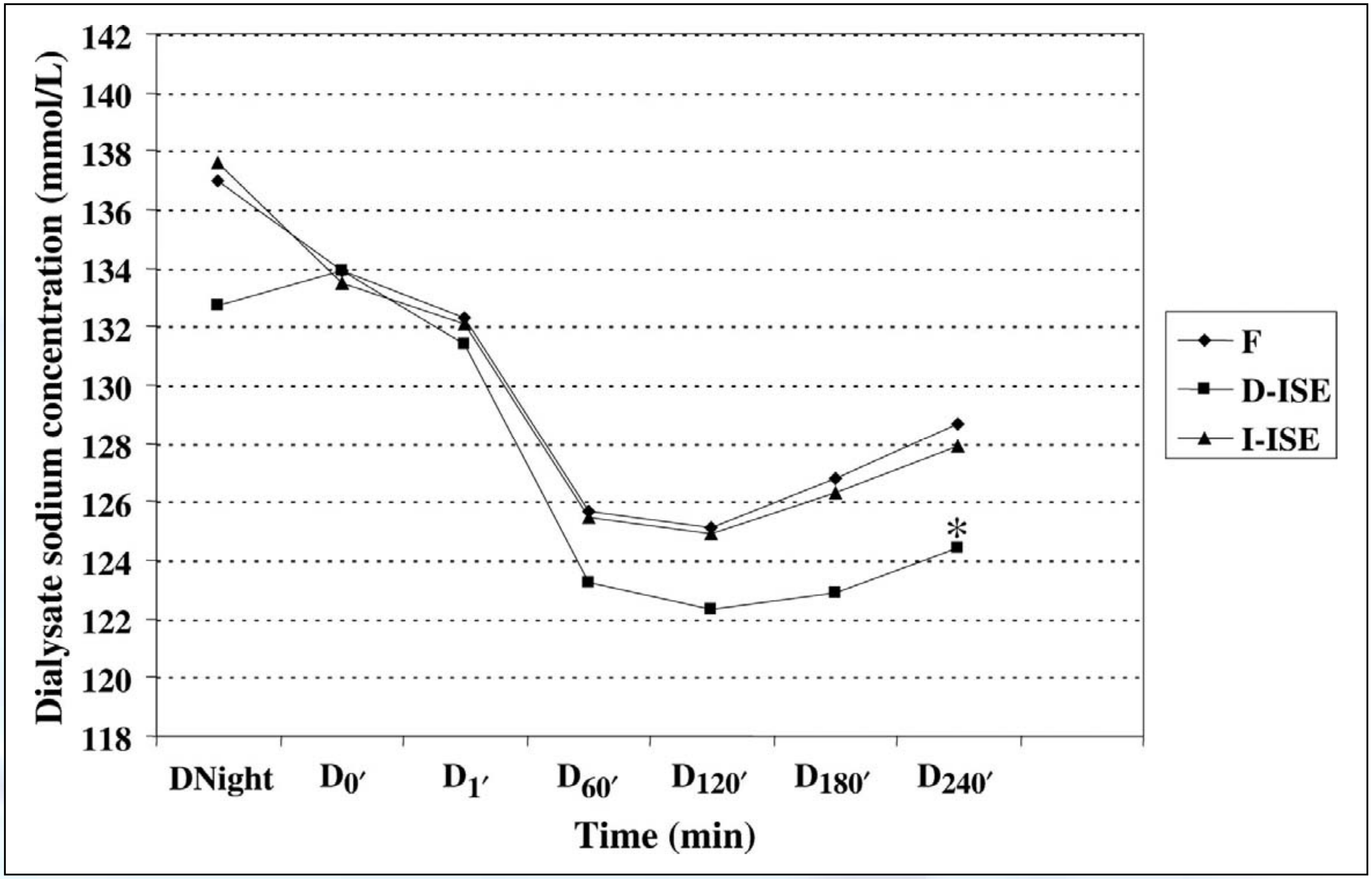
Adapted from Lai et al: *J Am Soc Nephrol* 12: 1036–1045, 2001

Physiology of Ultrafiltration: Structure of Peritoneal Membrane



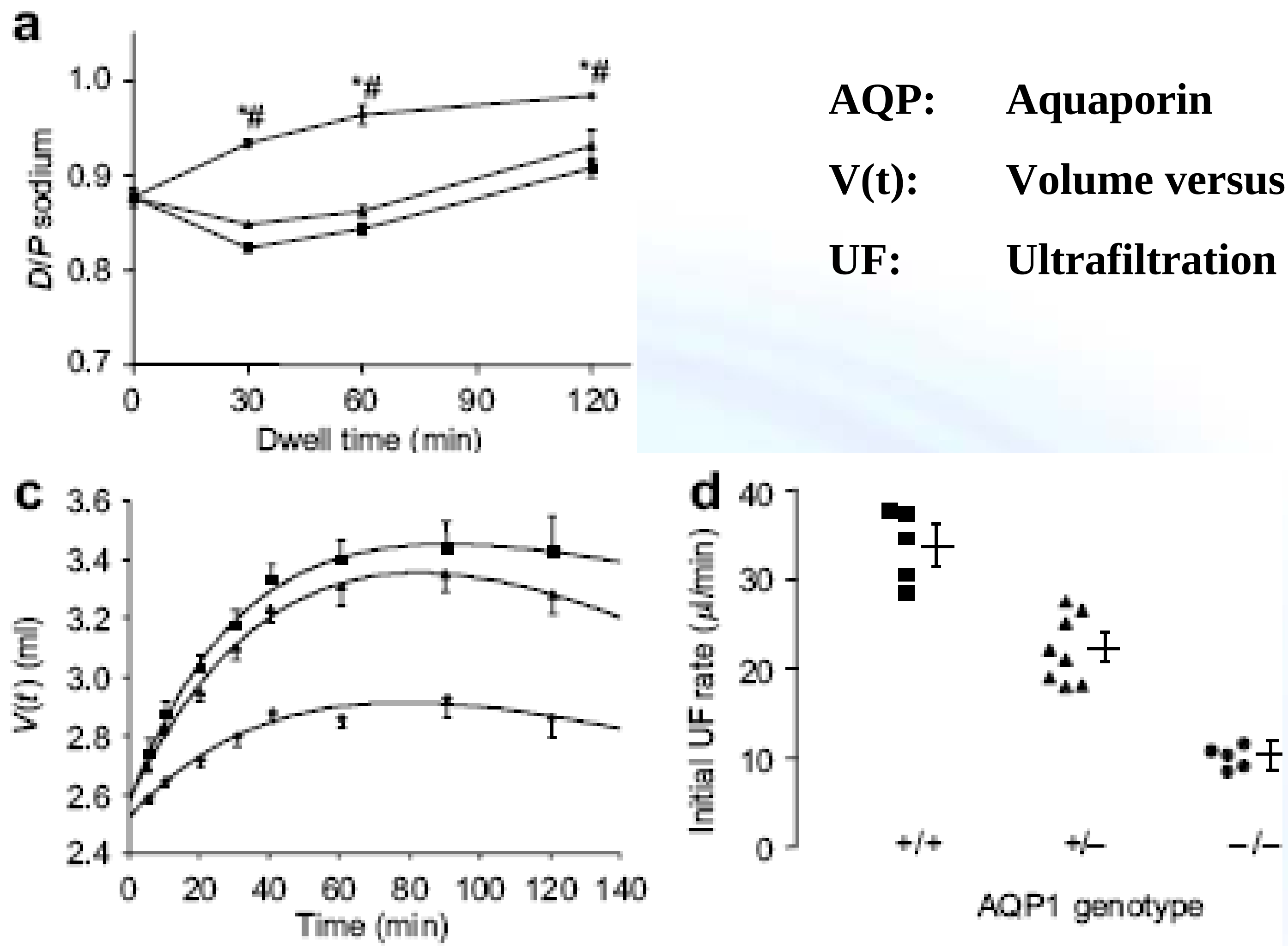
- Aquaporin mediated: 50%
- Intercellular: 50%
- Glucose transporter mediated: minimal
- Intercellular: >90%

Physiology of Ultrafiltration: Sodium Sieving with 4.25% Glucose



LaMilia et al, Nephrol Dial Transplant (2004) 19: 1849-1855

Physiology of Ultrafiltration: Role of Aquaporins: Aqp1$^{-/-}$ mouse



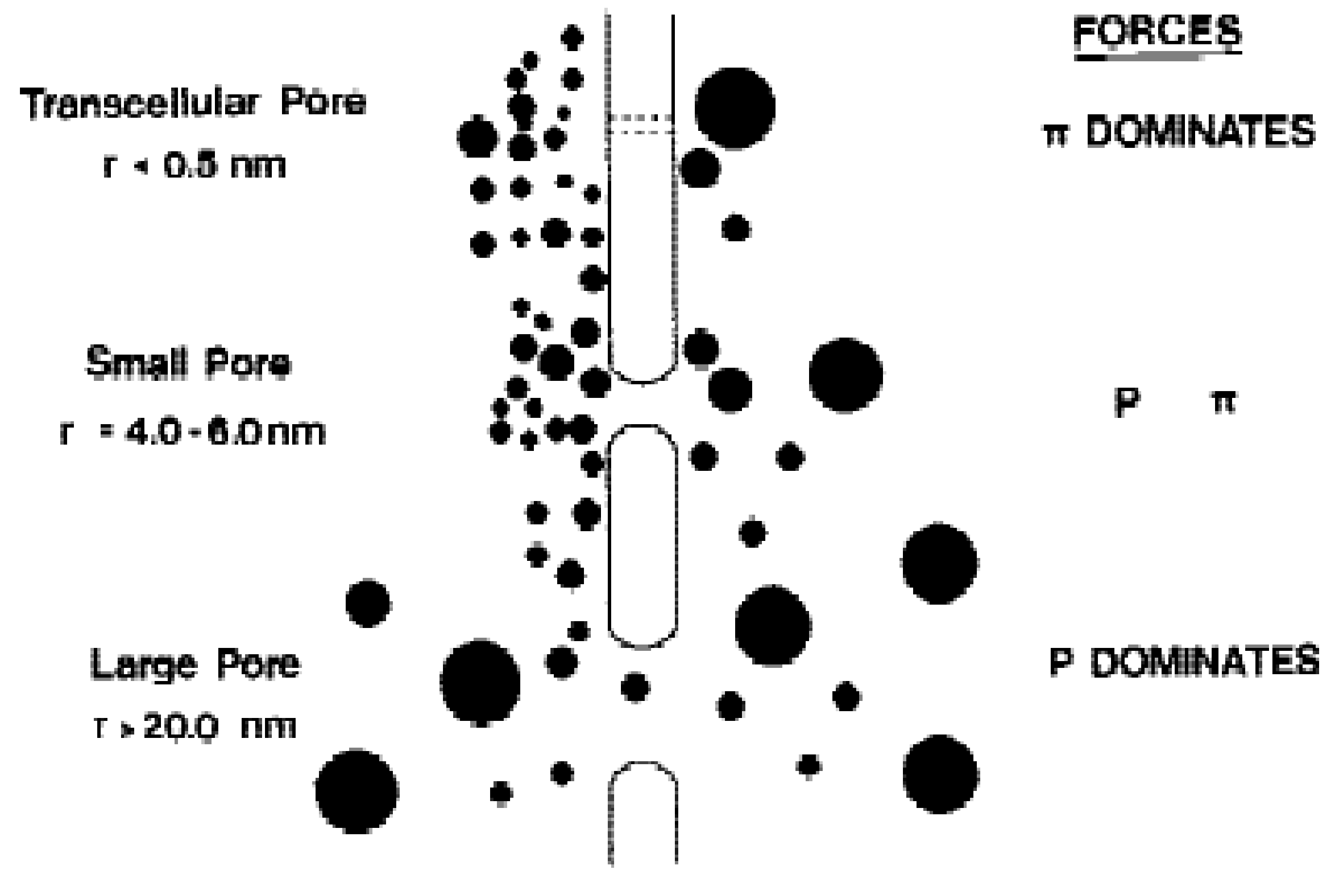
AQP: **Aquaporin**

V(t): **Volume versus time**

UF: **Ultrafiltration**

Ni J et al: Kidney International (2006) 69, 1518–1525

Physiology of Ultrafiltration: Three-pore model



π = Osmotic

P = Hydraulic

r = Radius

Rippe et al: Microcirculation 8, 303–320, 2001

Physiology of Ultrafiltration: Small Pores and Aquaporins

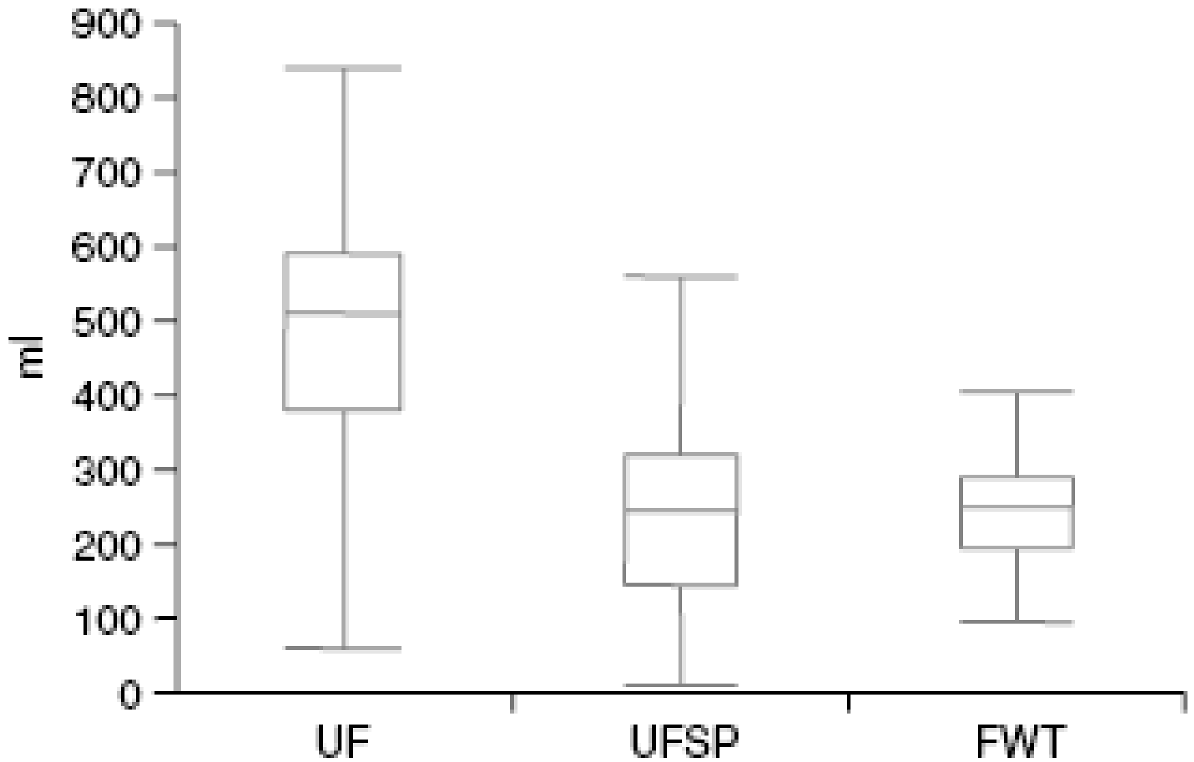


Figure 2 | UF, UFSP and FWT during the 4.25% test of Double Mini-PET. UF, ultrafiltration; UFSP, ultrafiltration through small pores; FWT, free water transport.

PET: Peritoneal Equilibration test

LaMilia et al, Kidney Int 72:643-50, 2007

Physiology of Ultrafiltration: Crystalloid Osmosis

- Normal serum osmolality = 270 mOsm/L
- Uremic serum osmolality = 305 mOsm/L

Dialysate Glucose	mOsm/L
1.5 %	345
2.5 %	395
4.25 %	484

Physiology of Ultrafiltration: UF with 4.25% Glucose: Small Pores

	Capillary Pressure	Dialysate Pressure	Pressure Gradient
Hydrostatic (mmHg)	**17**	**12-18**	**0 - 6**
Colloid (mmHg)	**26**	**0.1**	**-26**
Osmolality (mosm/kg H_2O)	***305***	***(Glu) 486***	
Crystalloid (mmHg)	**-**	**-**	**105**

Van't Hoff Law: Osmolar gradient * 19.3 * reflection coefficient (0.03)

Krediet R et al: *Peritoneal Dialysis International* 1997: 17, 35-41

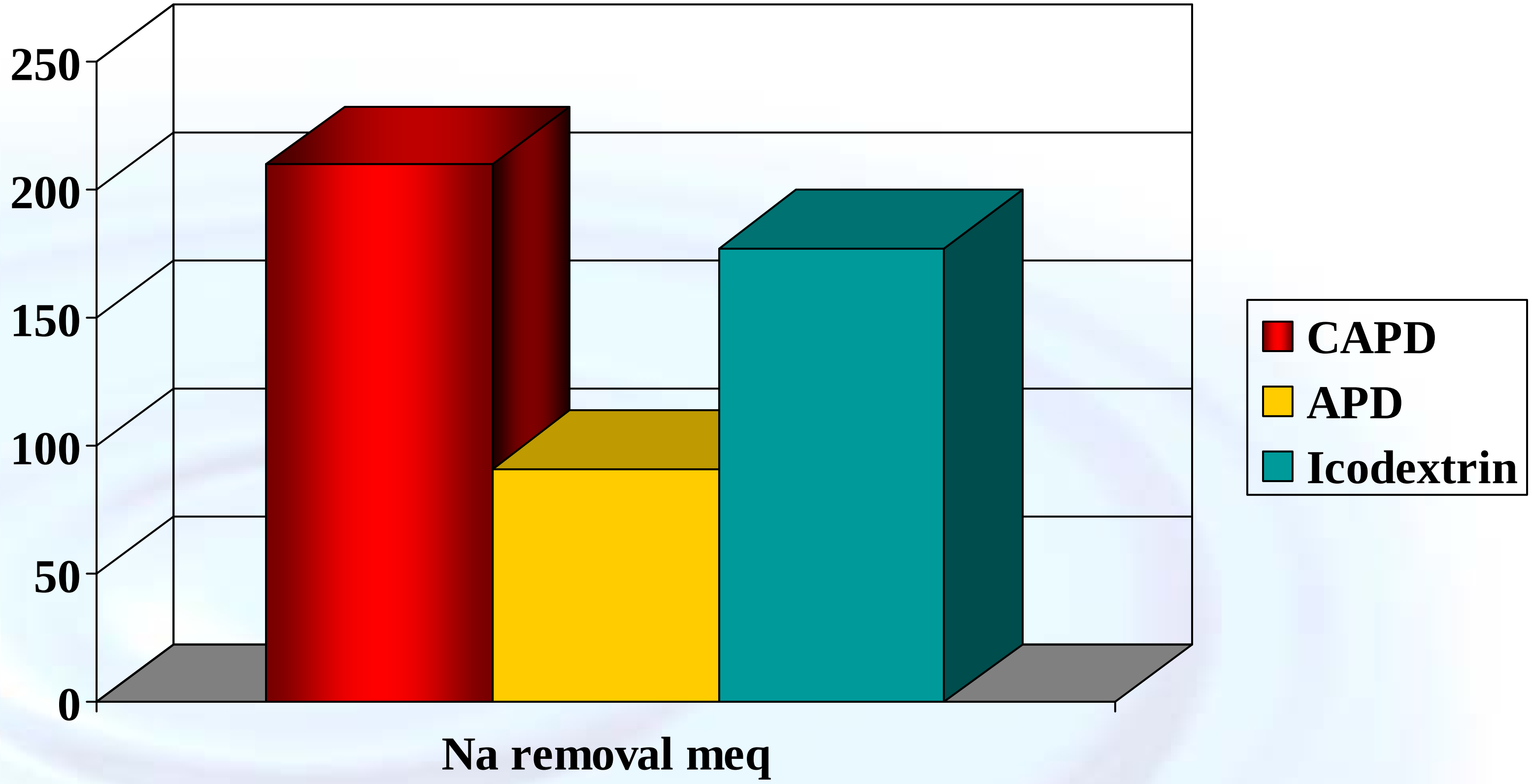
Physiology of Ultrafiltration: UF with 4.25% Glucose: Aquaporins

	Capillary Pressure	Dialysate Pressure	Pressure Gradient
Hydrostatic (mmHg)	17	12-18	0 - 6
Colloid (mmHg)	26	0.1	-26
Osmolality (mosm/kg H_2O)	*305*	*486*	
Crystalloid (mmHg)	Across Small pores Across Aquaporins		105 3559

Van't Hoff Law: Osmolar gradient * 19.3 * reflection coefficient (0.03)

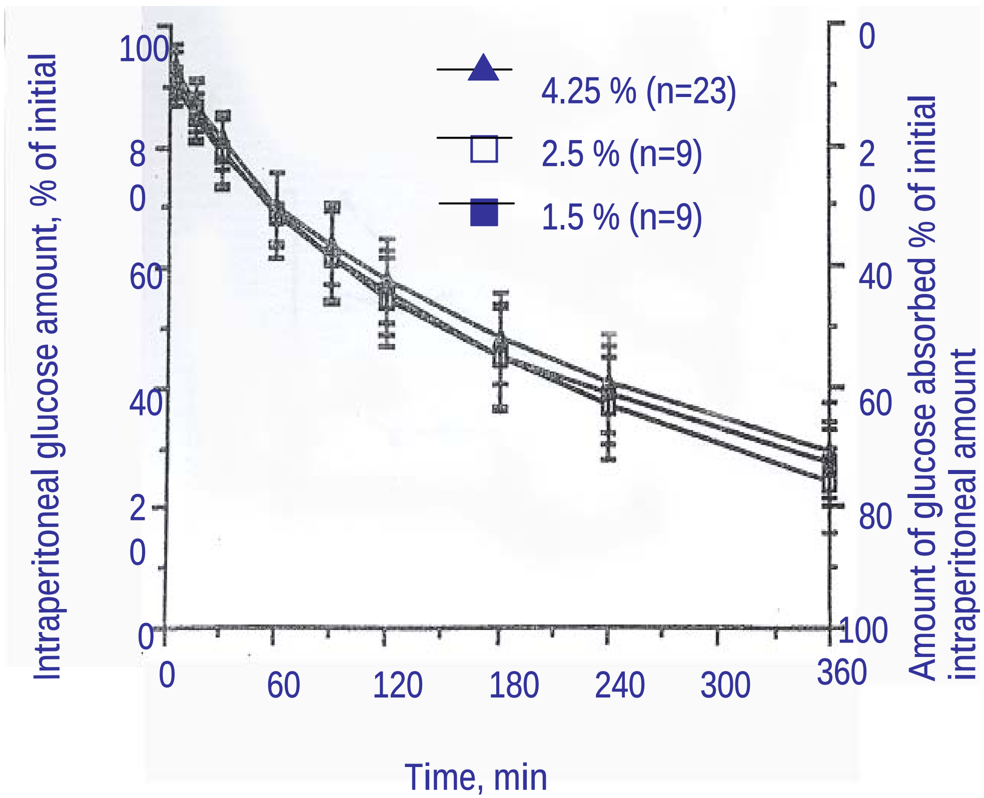
Krediet R et al: *Peritoneal Dialysis International* 1997: 17, 35-41

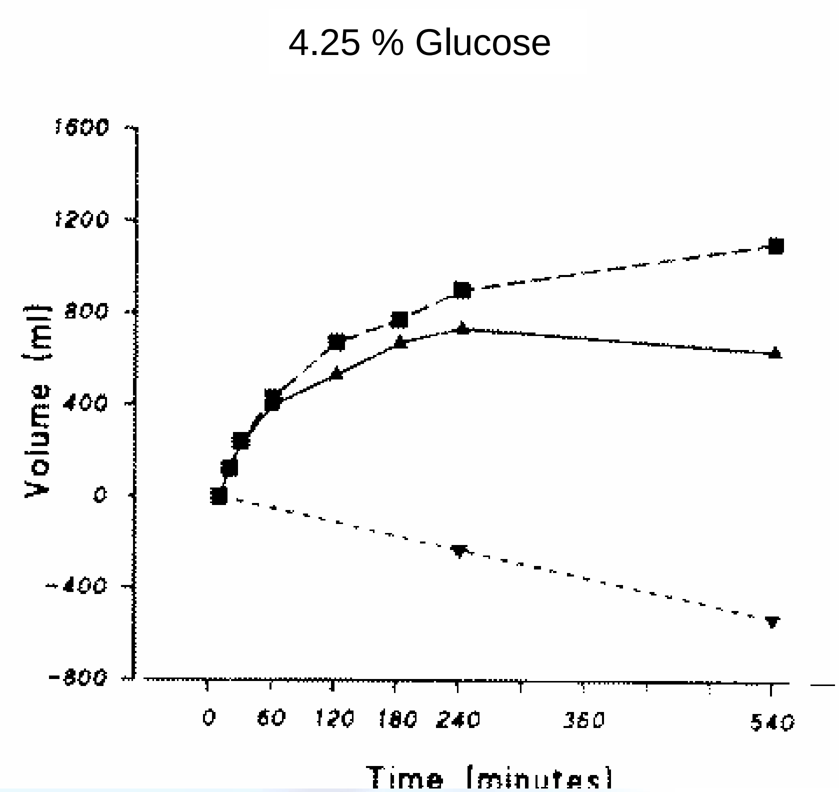
Physiology of Ultrafiltration: Sodium Sieving and Na Removal



Rodriguez-Carmona, PDI 2003 (22): 705-713.

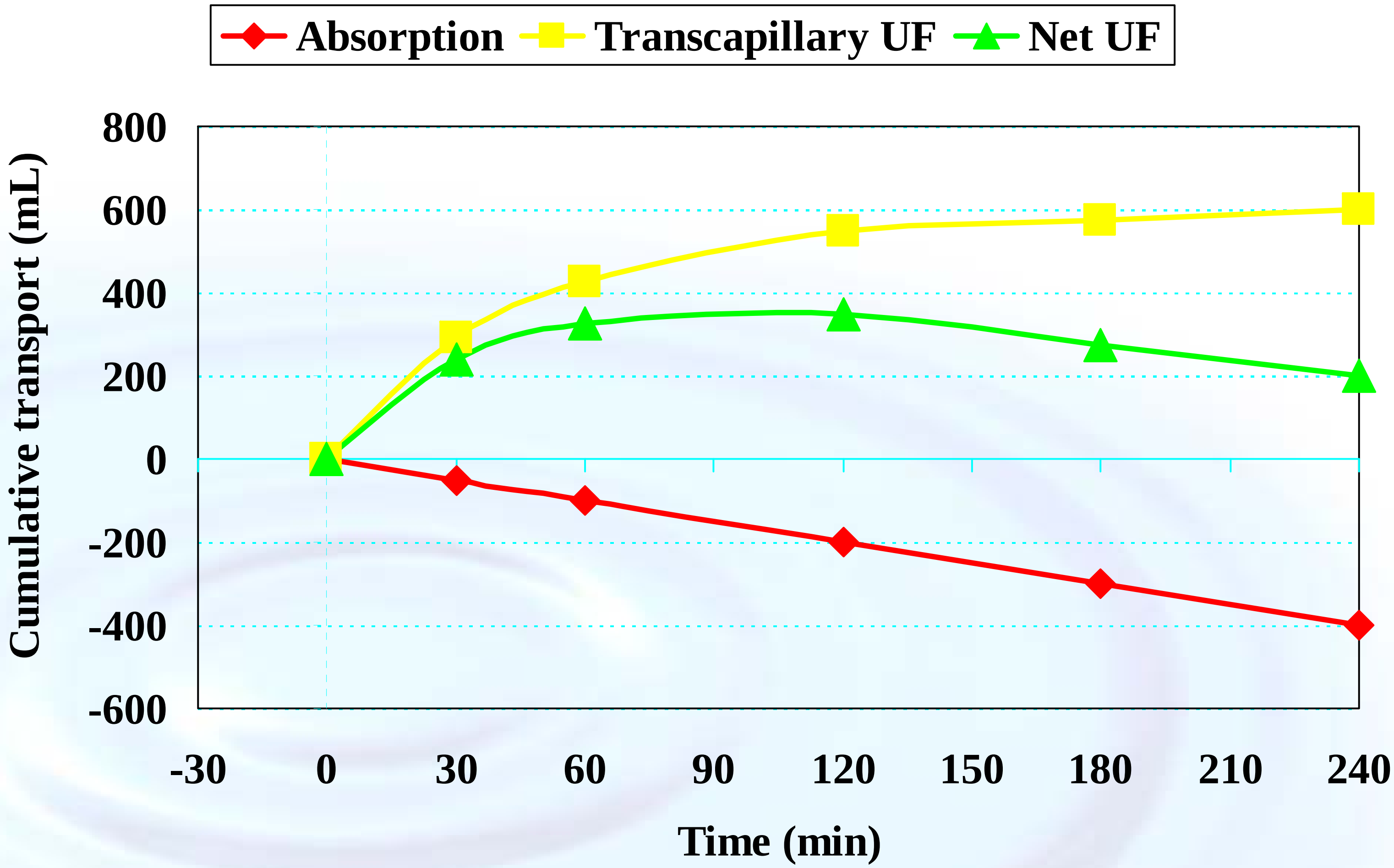
Physiology of Ultrafiltration: Glucose Absorption and UF Profile





Heimbürger et al. Kidney Int 1992: 41: 1320-32
Krediet R et al: *Peritoneal Dialysis International 1997:* 17, 35-41

Physiology of Ultrafiltration: Net Ultrafiltration Profile



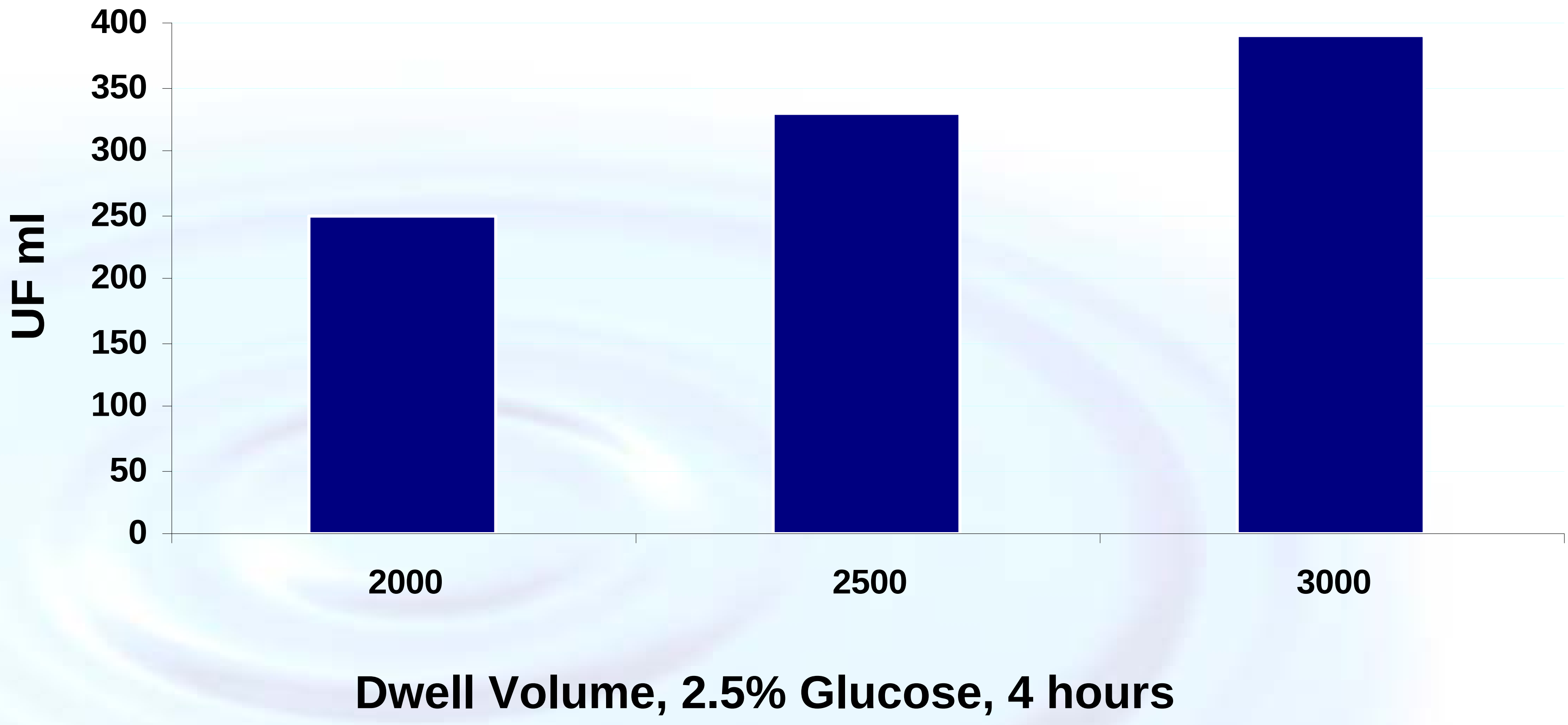
Adapted from Mactier RA, et al. *J Clin Invest.* 1987;80:1311-1316.

UF: Ultrafiltration

Physiology of Ultrafiltration: Variables to Consider

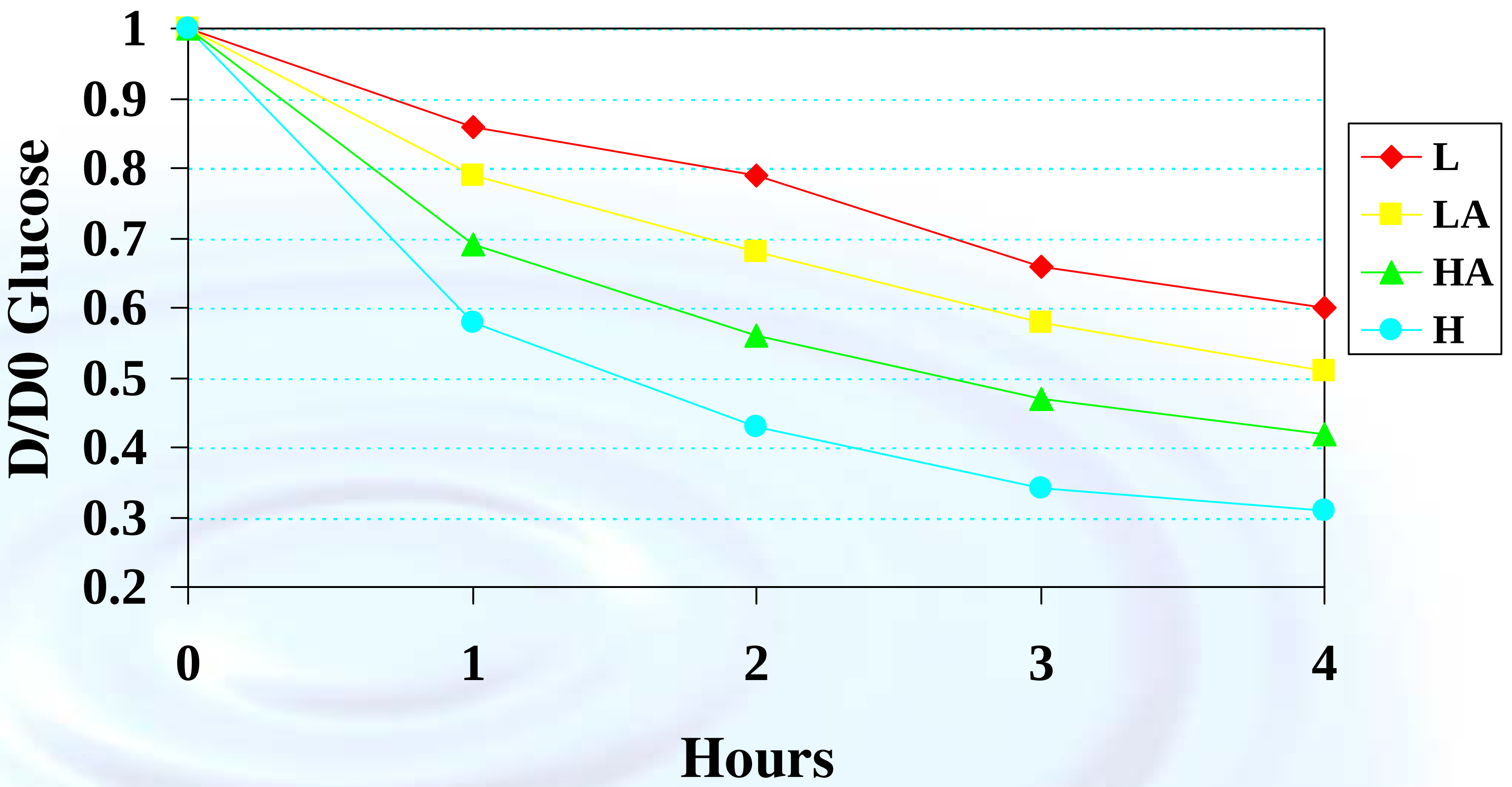
- Effect of dwell time
- Effect of fill volume
- Effect of membrane transport profile
- Effect of larger molecules

Physiology of Ultrafiltration:
Effect of Fill Volume: Net UF Volume



Abu-Alfa, American Society of Nephrology, Abstract 2001

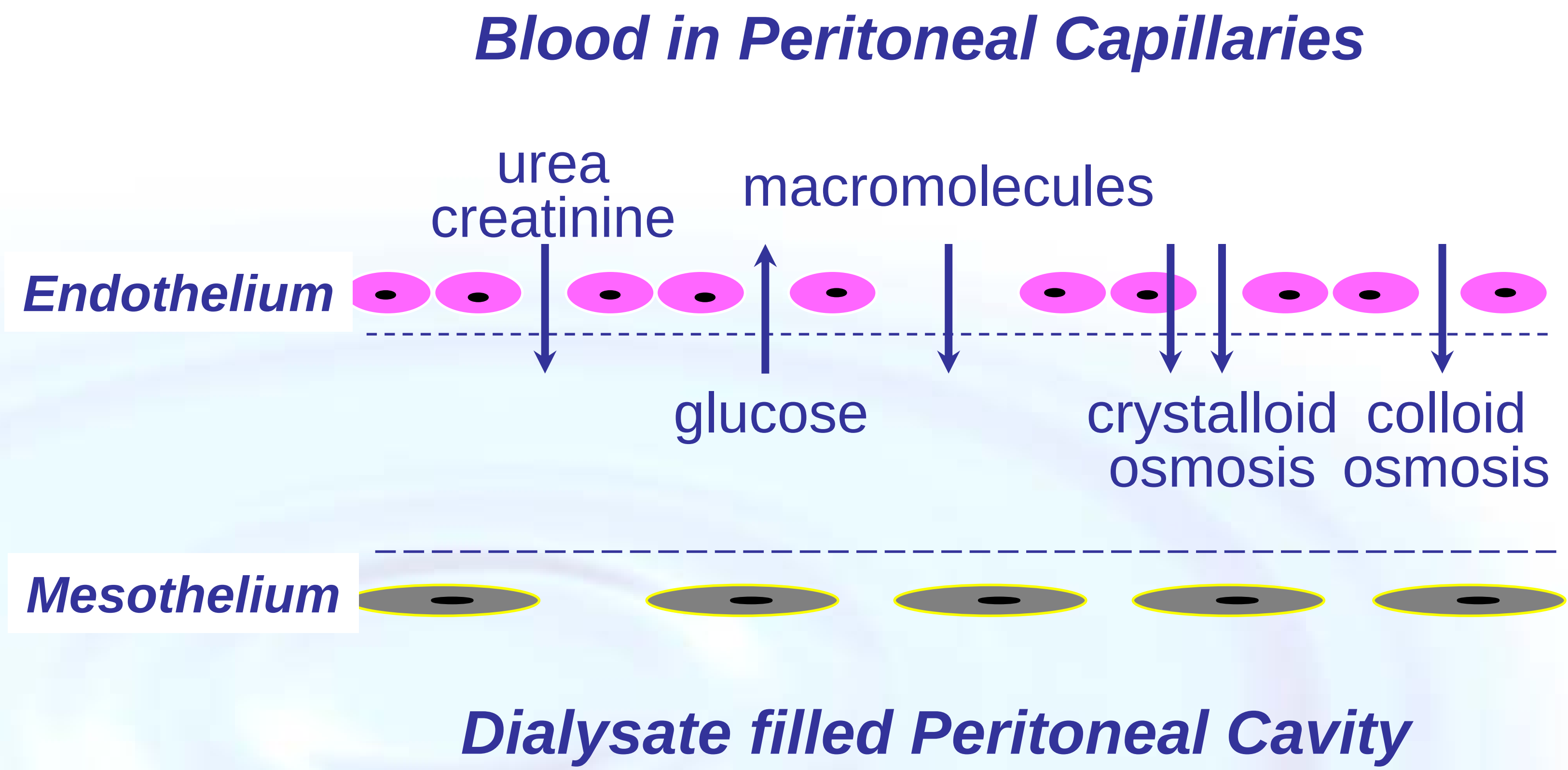
Physiology of Ultrafiltration: Glucose Kinetics by Transport Status



L: Low Transporter
LA: Low Average Transporter
HA: High Average Transporter
H: High Transporter

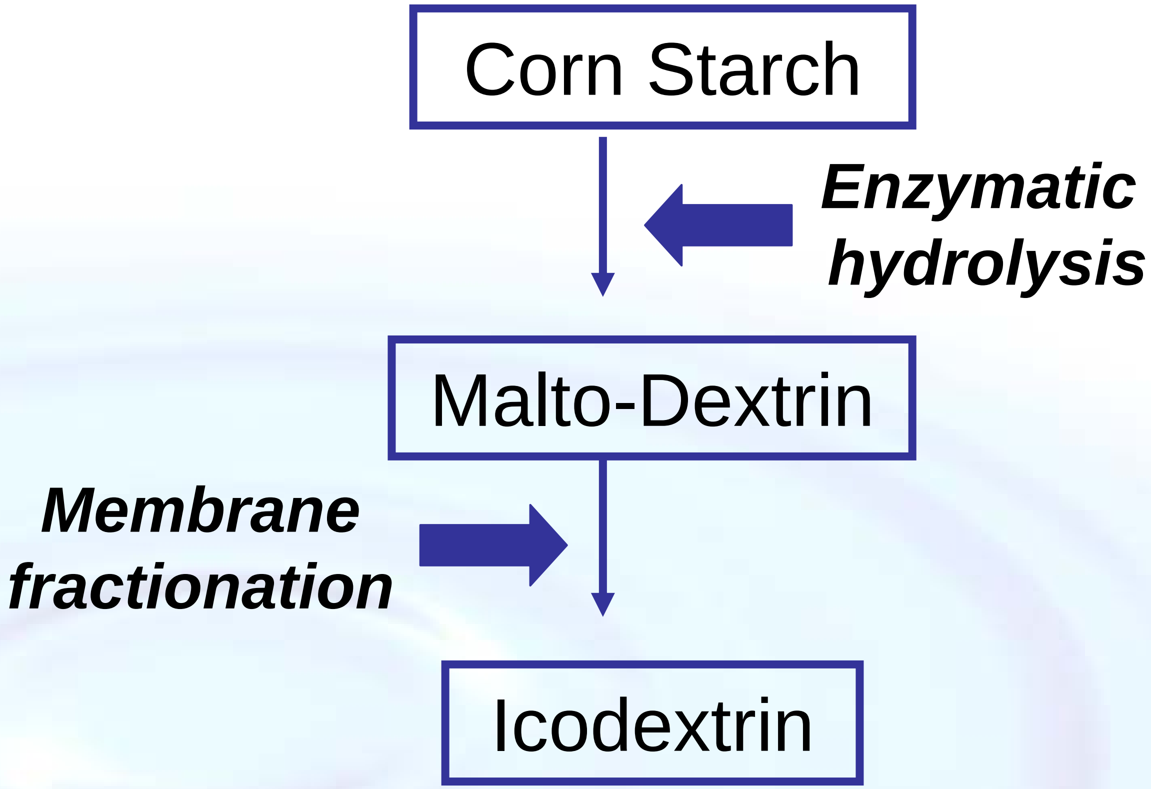
D/P: Dialysate / Plasma

Physiology of Ultrafiltration: Crystalloid versus colloid osmosis



Adapted from Krediet R et al: Peritoneal Dialysis International 17, 35-41; 1997

Colloid Osmosis:
Source and Structure of Icodextrin



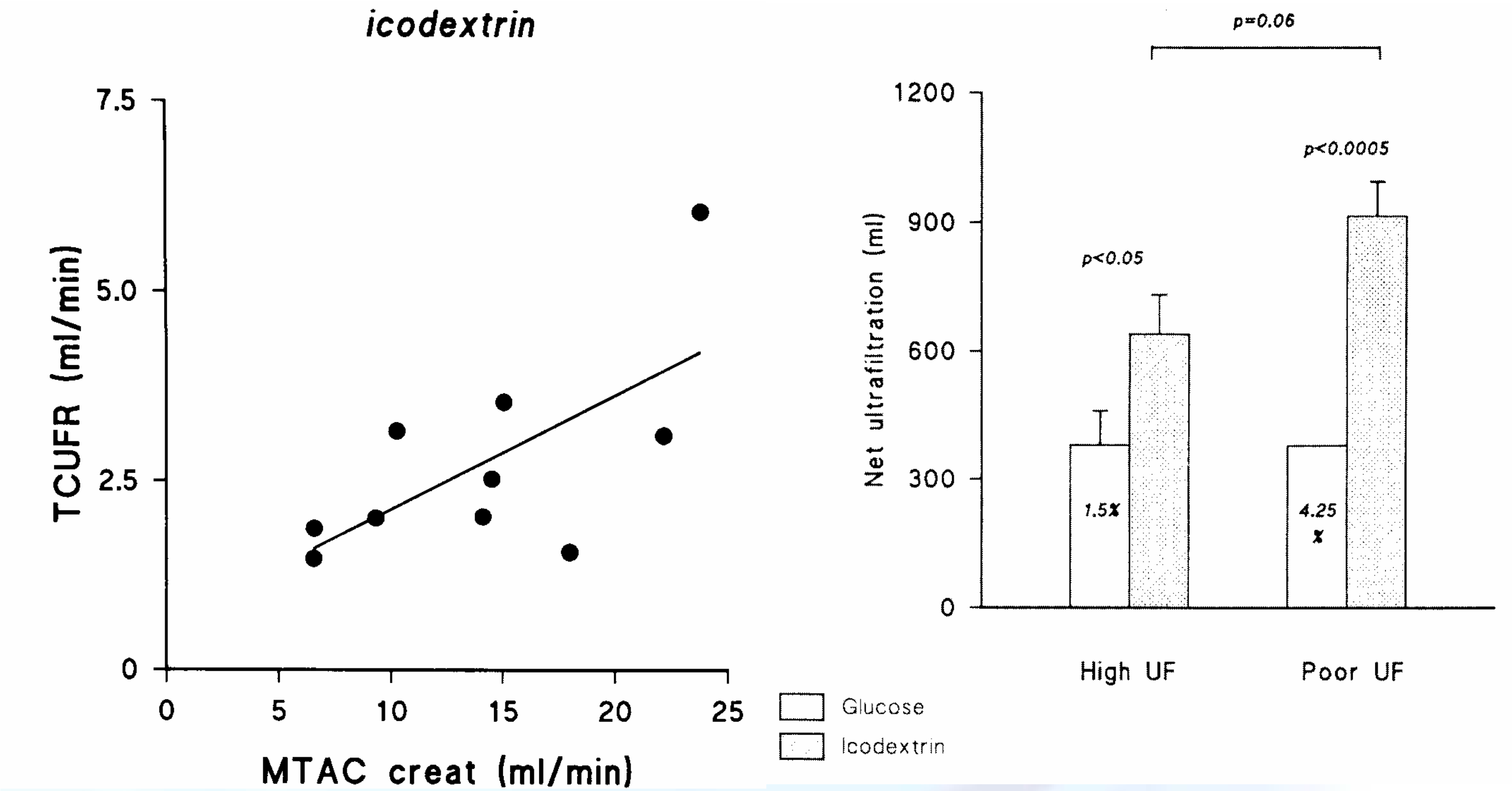
Physiology of Ultrafiltration: UF with 7.5% Icodextrin

	Capillary Pressure	Dialysate Pressure	Pressure Gradient
Hydrostatic (mmHg)	**17**	**12-18**	**0 - 6**
Colloid (mmHg)	**26**	**66**	**40**
Osmolality (mosm/kg H_2O)	***305***	***285***	
Crystalloid (mmHg)	**-**	**-**	**–12**

Van't Hoff Law: Osmolar gradient * 19.3 * reflection coefficient (0.03)

Krediet R et al: *Peritoneal Dialysis International* 1997: 17, 35-41

Physiology of Ultrafiltration: Transport Status and Icodextrin

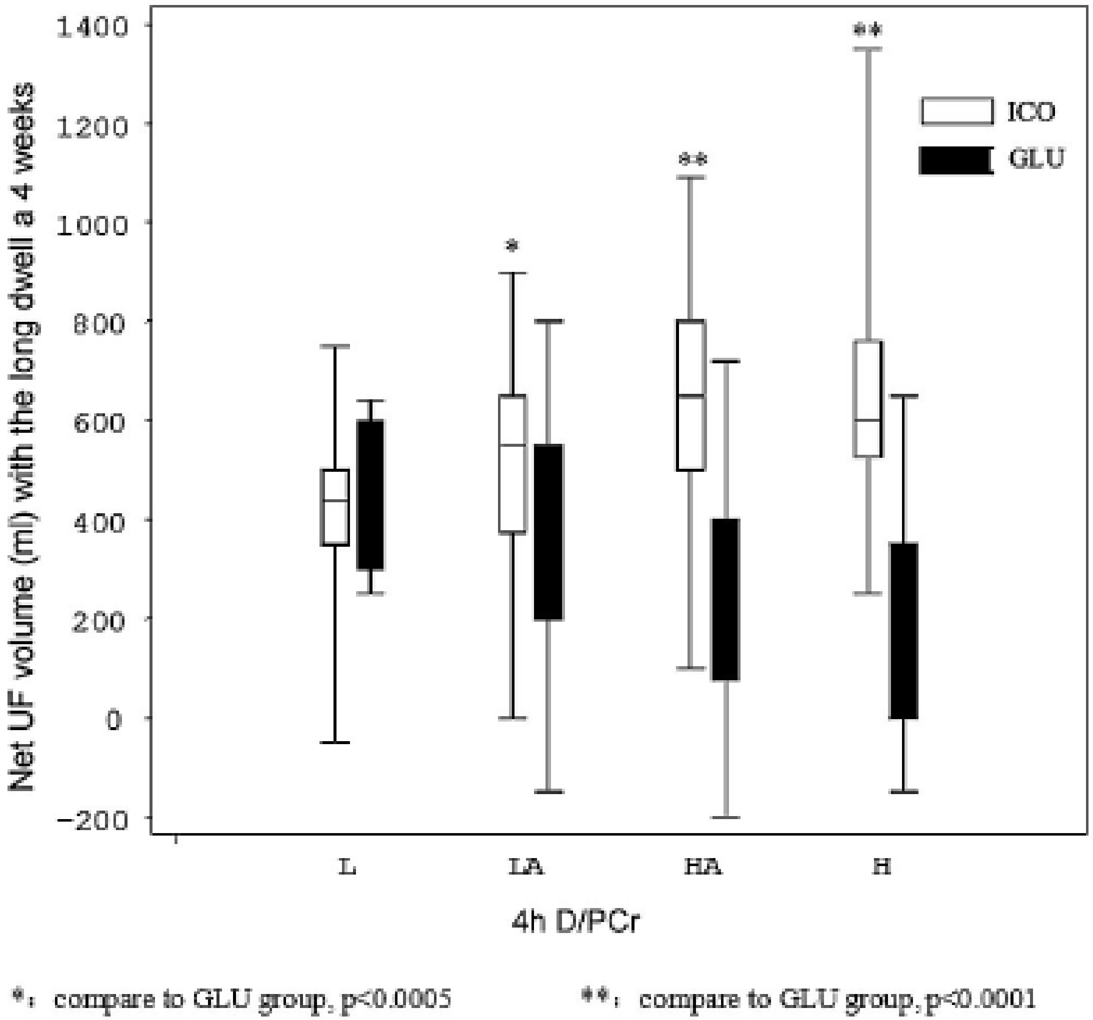


TCUFR: Transcapillary UF rate

MTAC: Mean Transport Area Coefficient

Krediet R et al: *Peritoneal Dialysis International 1997:* 17, 35-41

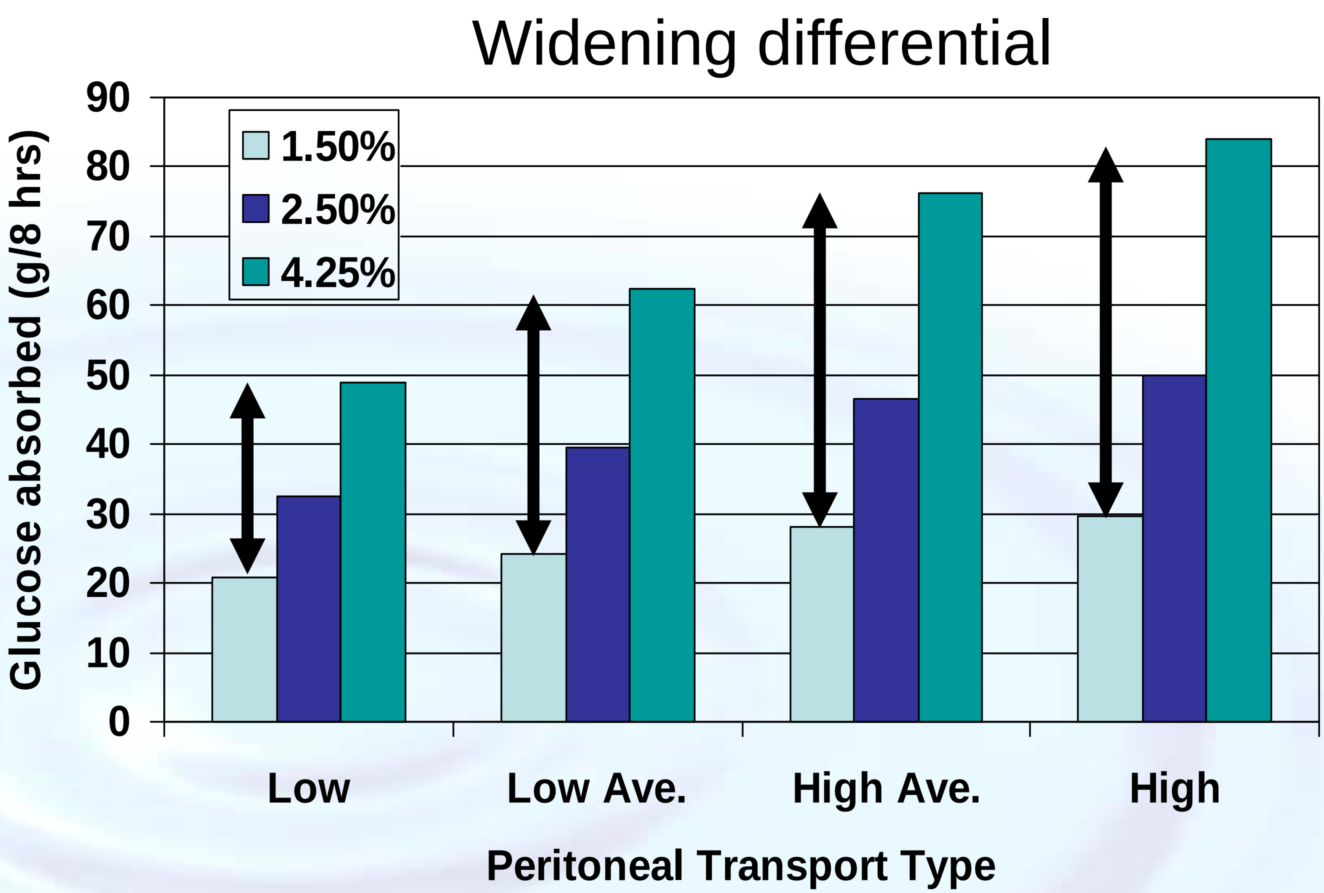
Physiology of Ultrafiltration: Transport Status: Icodextrin vs 2.5%



D/P:	**Dialysate/Plasma**
ICO:	**Icodextrin**
GLU:	**Glucose**
Cr:	**Creatinine**

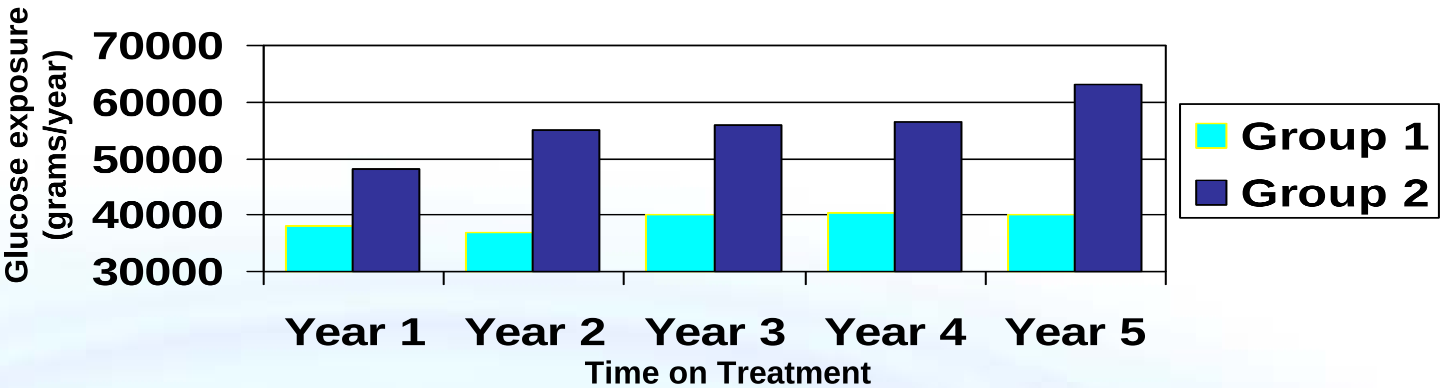
Lin A et al: *Clin J Am Soc Nephrol* 2009: 4: 1799–1804

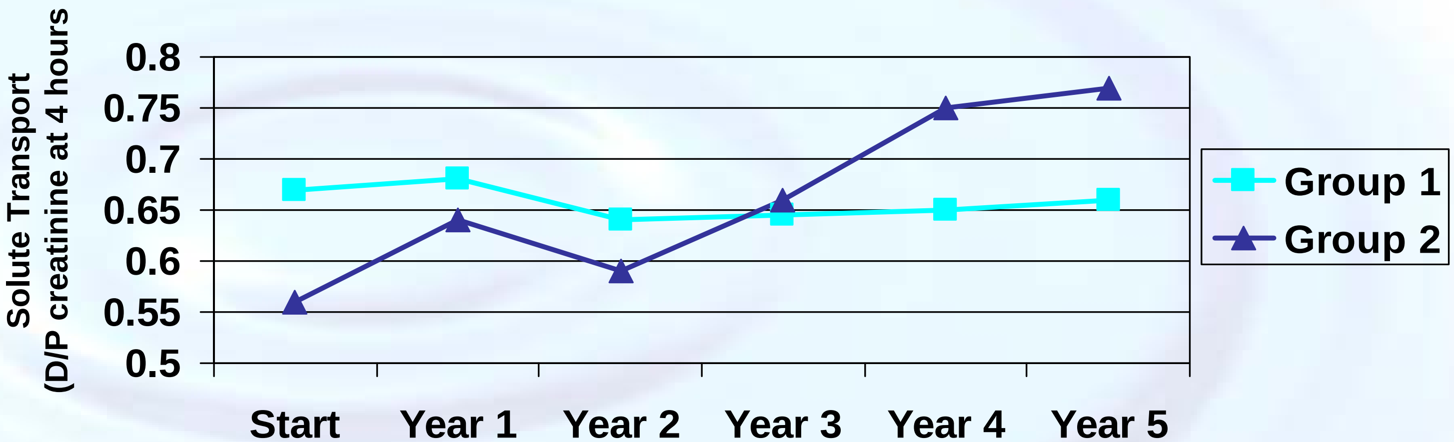
Physiology of Ultrafiltration: Glucose absorption: Caloric Cost



Courtesy of Dr Salim Mujais, Baxter Healthcare 2002

Physiology of Ultrafiltration: Changes in Transport Profile





Davies et al. *J Am Soc Nephrol*. 2001;12:1046-51

Physiologic Principles for UF in PD Summary

- UF in PD is primarily driven by osmotic (Glucose) or oncotic (icodextrin) forces across the membrane.
- Sodium sieving is maximal at about 60 – 90 minutes of a dwell, and will result in and decreased Na concentration in the dialysate if dwell is drained, as with cyclic PD.
- Na sieving negatively impacts total Na removed.
- Many factors modulate UF volume such as glucose concentration, dwell time, dwell volume and intrinsic membrane transport type of each patient.
- Higher transport rates result in less UF with glucose solutions but not with icodextrin solution.

Question 1

The removal of sodium with PD is dependent on convection and diffusion. Calculate the approximate amount of Na removed during a dwell for each of the following conditions:

1) No net ultrafiltration after a 4 hours dwell using 2 liters of 2.5% dextrose solution with [Na]=132 meq/L and plasma [Na]=140 meq/L.

2) 500 cc of net ultrafiltration after a 10 hours dwell using 2 liters of 7.5% icodextrin solution with [Na]=132 meq/L and plasma [Na]=140 meq/L.

3) 250 cc of net UF after a 1 hour dwell using 2 liters of 2.5% dextrose solution with [Na]=132 meq/L and 60 mins dialysate [Na]=128 meq/L, with a short APD cycle.

Answer 1

The removal of sodium with PD is dependent on convection and diffusion. Calculate the approximate amount of Na removed during a dwell for each of the following conditions:

1) No net ultrafiltration after a 4 hours dwell using 2 liters of 2.5% dextrose solution with [Na]=132 meq/L and plasma [Na]=140 meq/L. Answer: 16 meq

2) 500 cc of net ultrafiltration after a 10 hours dwell using 2 liters of 7.5% icodextrin solution with [Na]=132 meq/L and plasma [Na]=140 meq/L. Answer: 16+70=86 meq

3) 250 cc of net UF after a 1 hour dwell using 2 liters of 2.5% dextrose solution with [Na]=132 meq/L and 60 mins dialysate [Na]=128 meq/L, with a short APD cycle.. Answer: 24 meq