Peritoneal Dialysis

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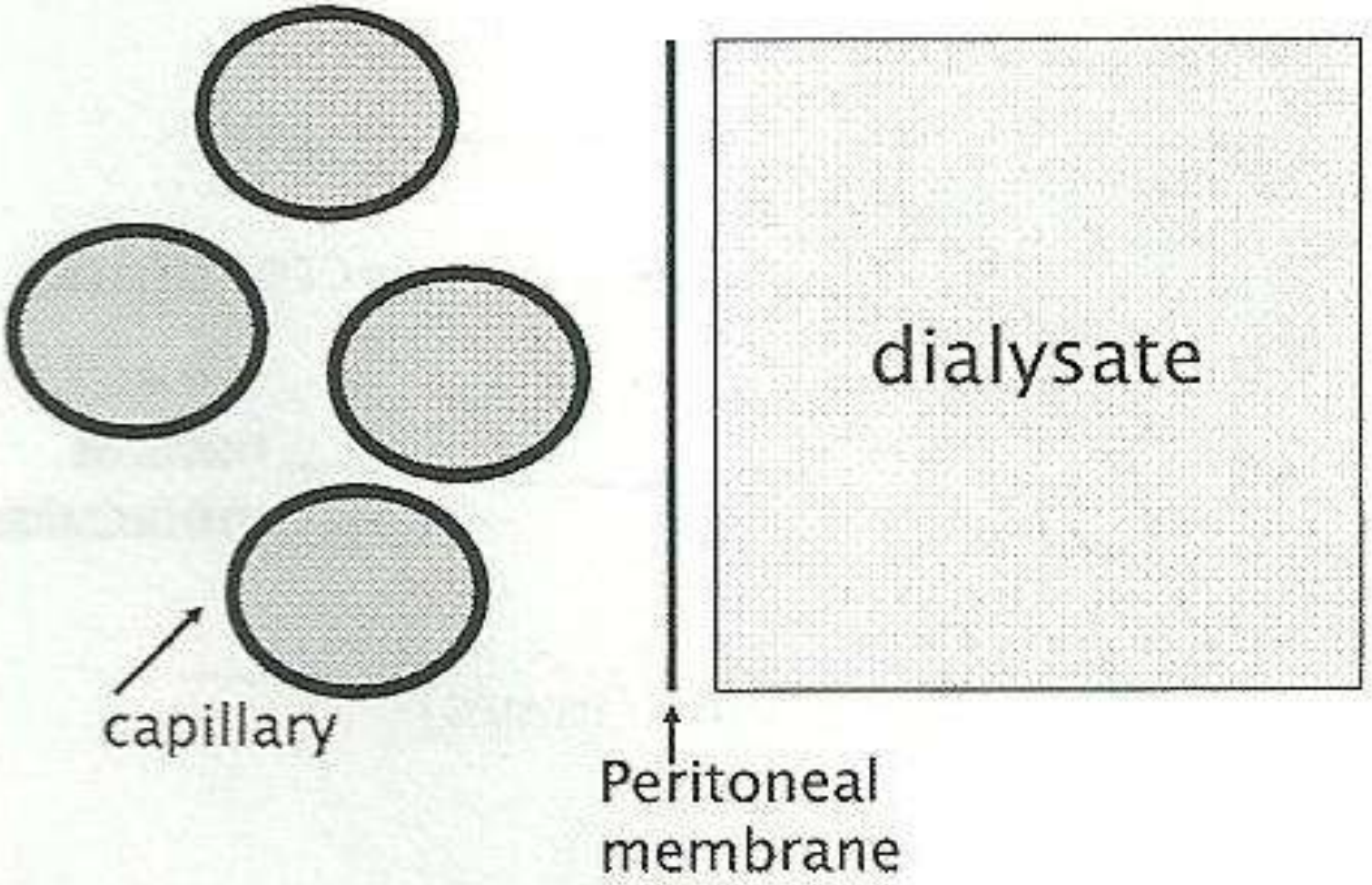
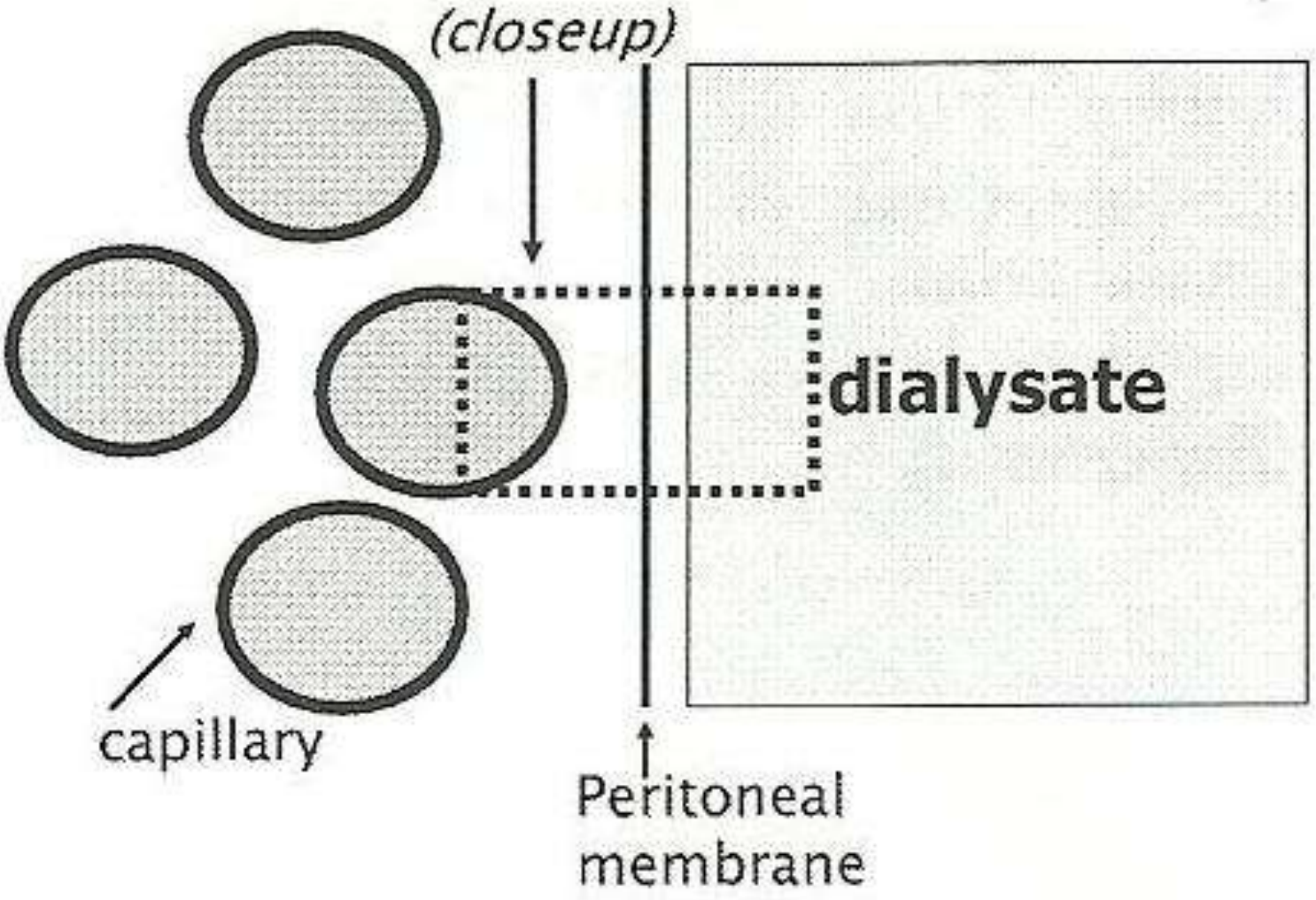
athens-NEPHROLOGY

The Peritoneal-Vascular Interface

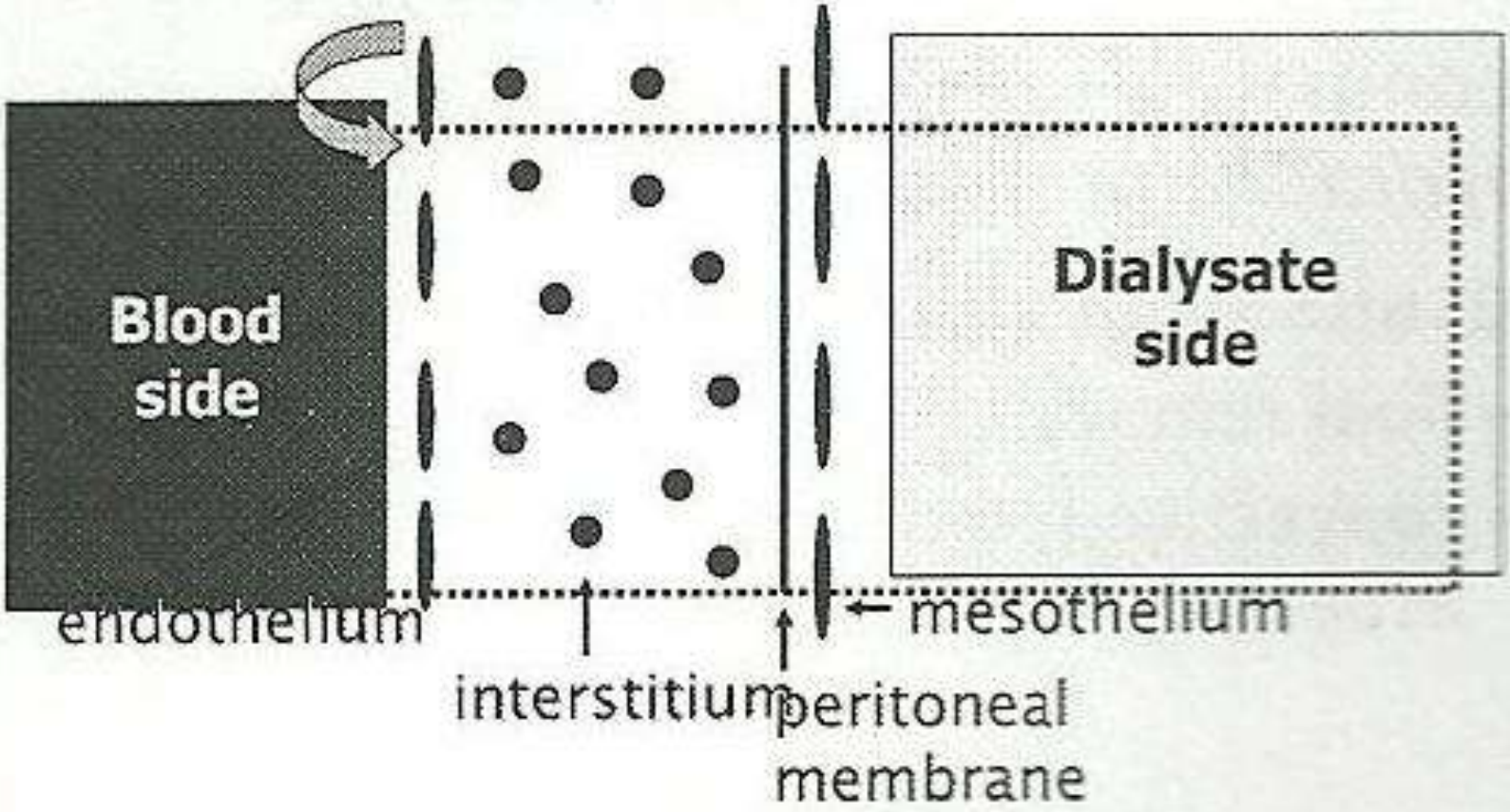


The Peritoneal-Vascular Interface



The Peritoneal–Vascular Interface

Important transport occurs here



Solute Transport in PD

How does solute enter peritoneal fluid?

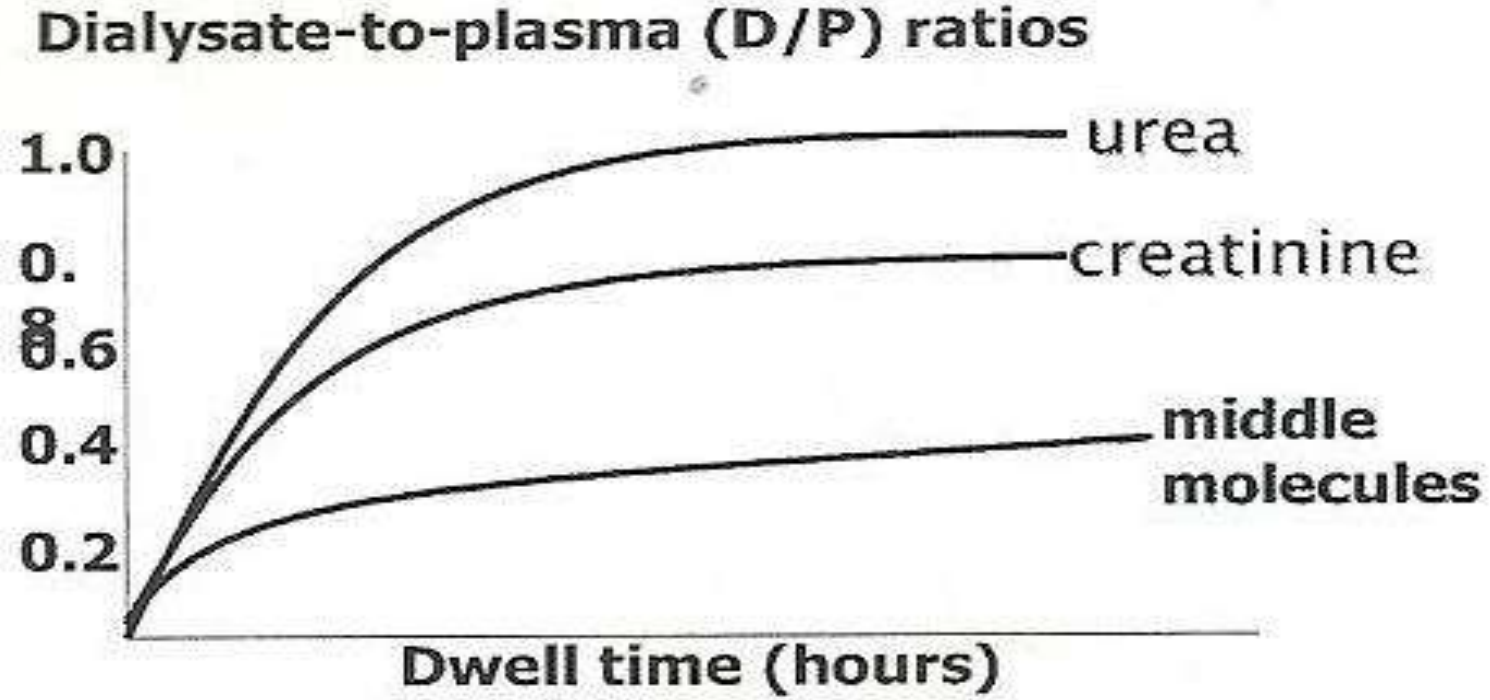
I. Diffusion

II. Convection (during ultrafiltration)

Diffusion Kinetics – *from blood to dialysate*

- diffusive flux is highest in first hour and lessens over time
- by 4 hours, urea is > 90% equilibrated, creatinine > 60% equilibrated
- further small solute removal is minimal after that
- long dwells more important for removal of *larger* MW solutes

Diffusion Curves – a Schema



Diffusion Kinetics – *from dialysate to blood*

What can you add to dialysate?

- antibiotics (not just for peritonitis)
- insulin
- KCl (up to 10 mEq/l)
- xylocaine, $NaHCO_3$ (infusion pain)
- metoclopramide, erythromycin (gastroparesis)
- erythropoietin
- calcitriol

Ultrafiltration in PD

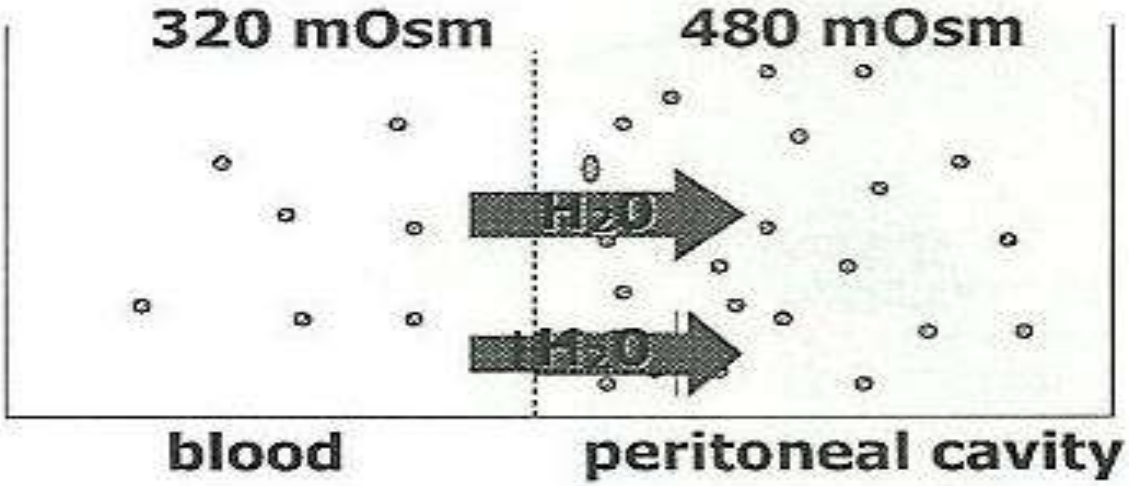
- in PD, done by *osmotic* pressure (compared to HD where done by *hydraulic* pressure)
- results of ultrafiltration:
  - fluid removal
  - convective removal of solutes, especially middle molecules

Composition of Peritoneal Dialysate: Osmolality

- 1.5% dextrose – 347 mOsm/l (*isotonic*)
- 2.5% dextrose – 397 mOsm/l (*hypertonic*)
- 4.25% dextrose – 485 mOsm/l (*hypertonic*)

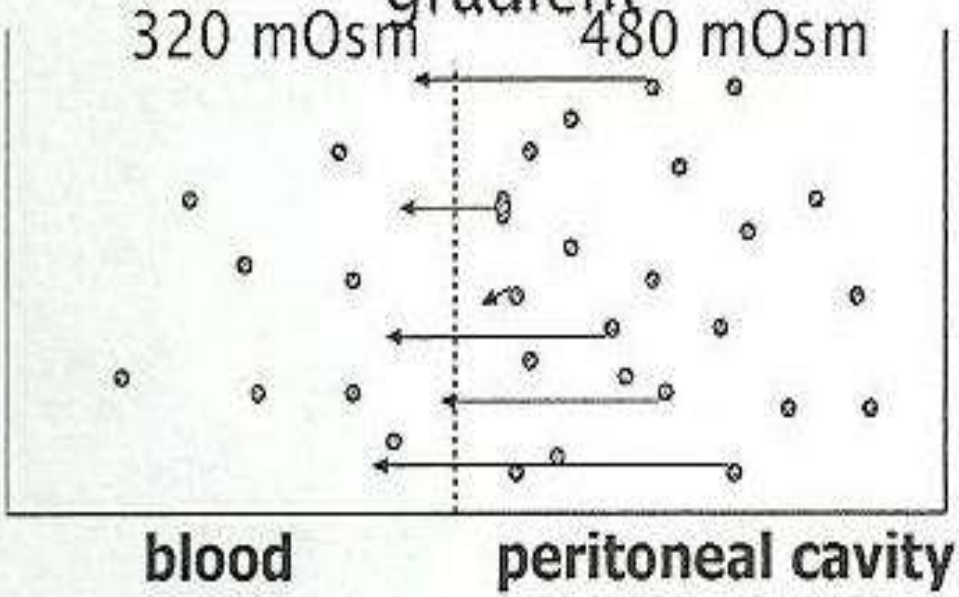
Ultrafiltration – Example of 4.25% Dialysate

Water will move from lower to higher osmolality



Ultrafiltration

Glucose itself will diffuse out of peritoneal cavity along its own concentration gradient



Ultrafiltration in Peritoneal Dialysis

Some examples of UF from studies in humans:

1.5 % Dialysate

maximum UF 330 +/- 187 ml

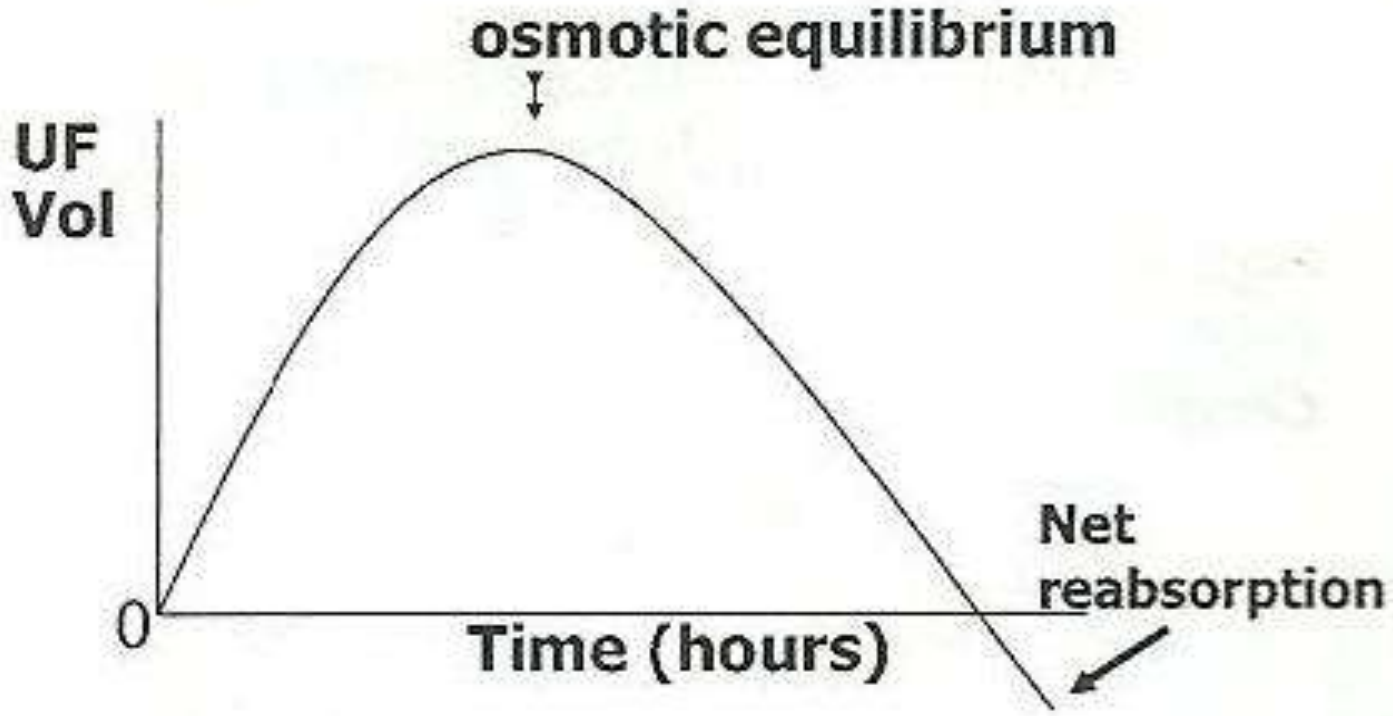
time to maximum UF 140 +/- 48 minutes

4.25 % Dialysate

maximum UF 1028 +/- 258 ml

time to maximum UF 247 +/- 61 minutes

Ultrafiltration

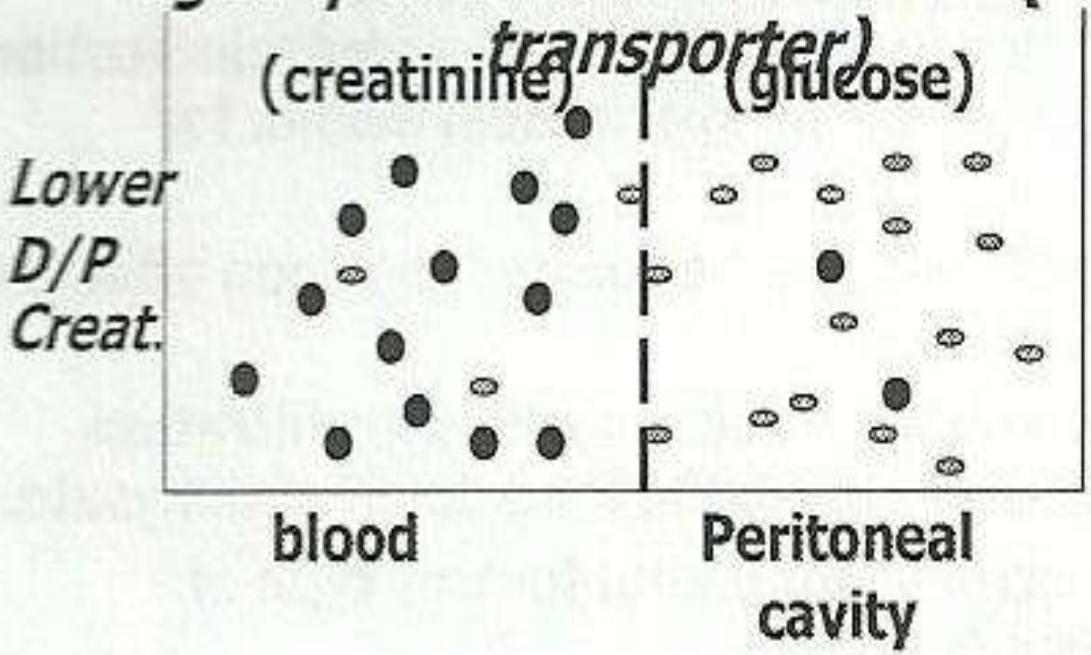


The Peritoneal Equilibration Test (PET):

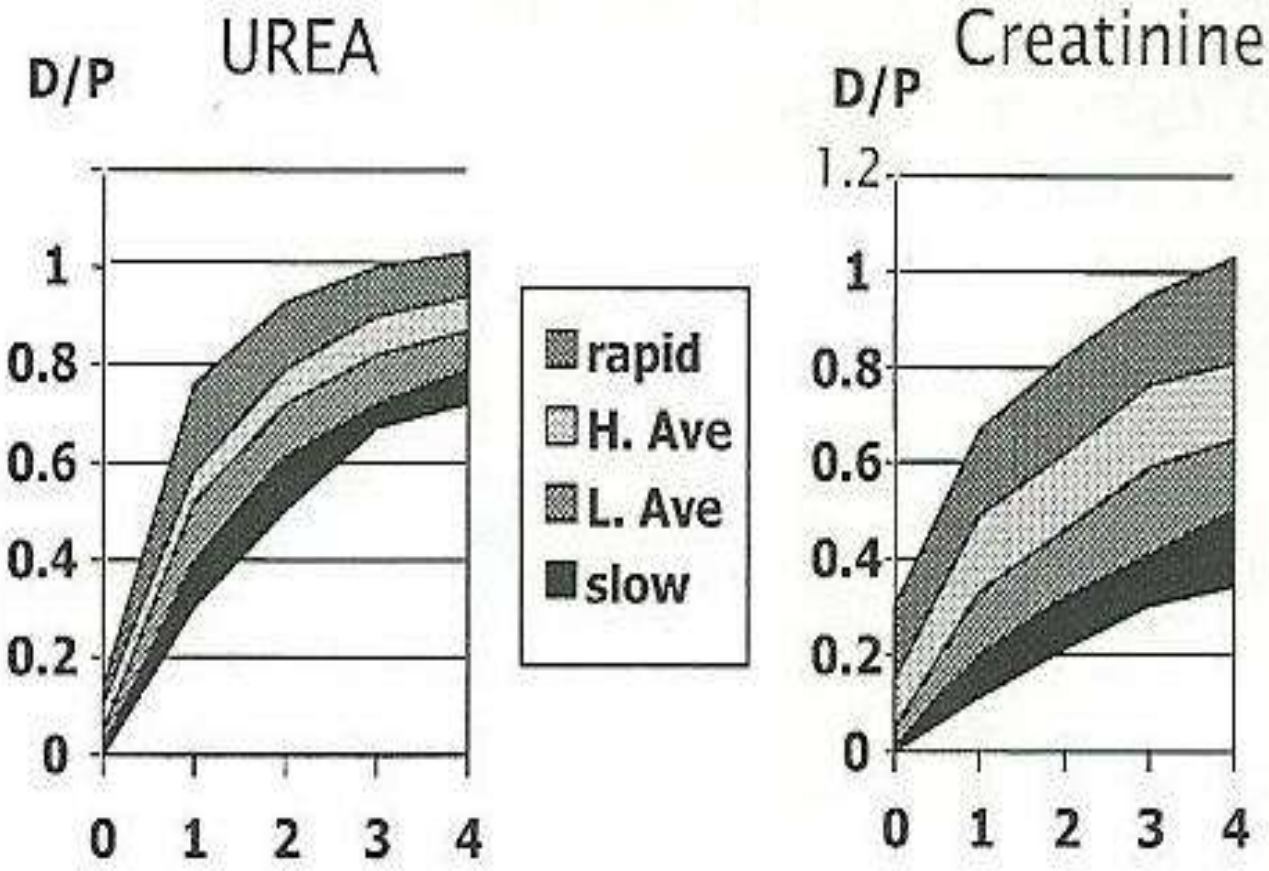
A Way to Characterize the Peritoneal Membrane

At time t = 4 hours

"tight" peritoneal membrane (slow transporter)



Peritoneal Equilibration Test



Twardowski et al.
PDB

Membrane Permeability and Ultrafiltration – "*rapid transporters*"

the "***leakier***" the peritoneal membrane (more vascular beds are open)

⇩

the faster glucose will diffuse out of the peritoneal cavity

⇩

the faster the osmotic gradient will dissipate

Why is Someone a Rapid Transporter from the Start?

- association with higher CRP, lower serum albumin, less residual renal function
- in some studies, more common in diabetics
- lower serum albumin seen *before* the start of PD

This suggests that rapid transporter status may be a marker of inflammation!

Membrane Permeability and Ultrafiltration – "*slow transporters*"

the "***tighter***" the peritoneal membrane

⇩

the slower glucose will diffuse out of the peritoneal cavity

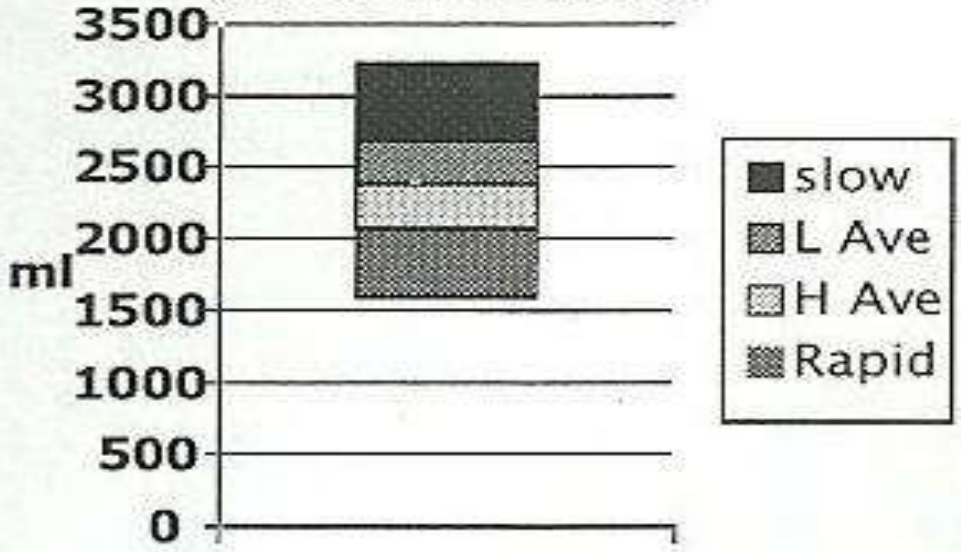
⇩

the osmotic gradient will be maintained longer

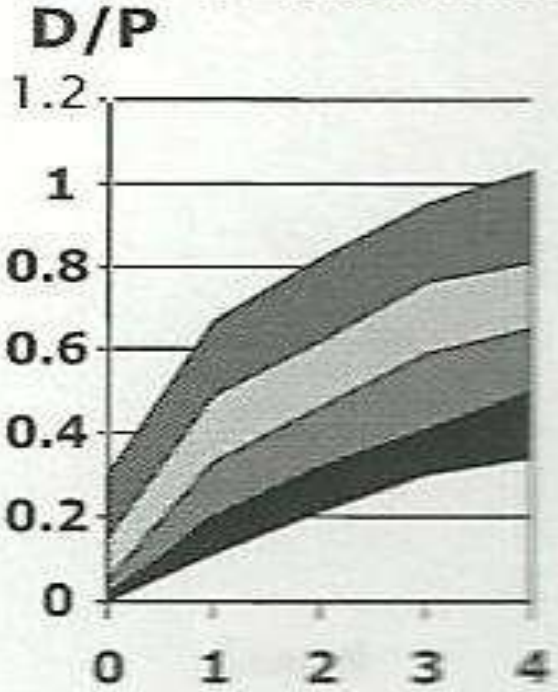
Transport Status – Implications for Ultrafiltration

Drain Volume

(2000 ml infused)



Creatinine

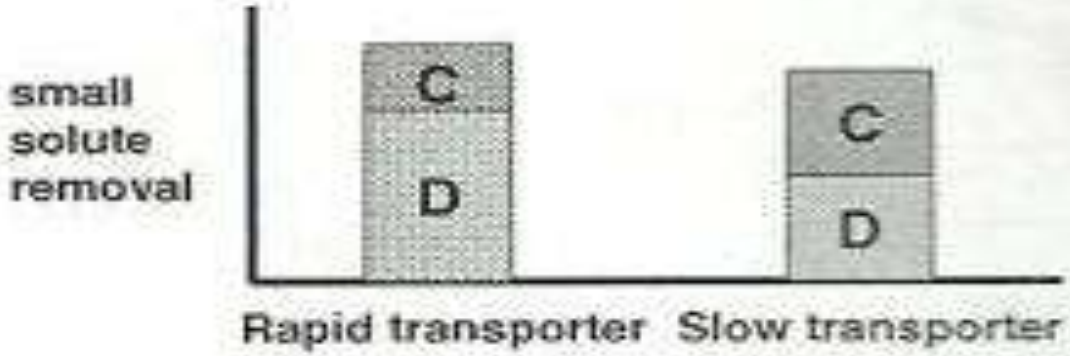


Rapid vs Slow Transporters: Why Solute Removal Isn't that Different

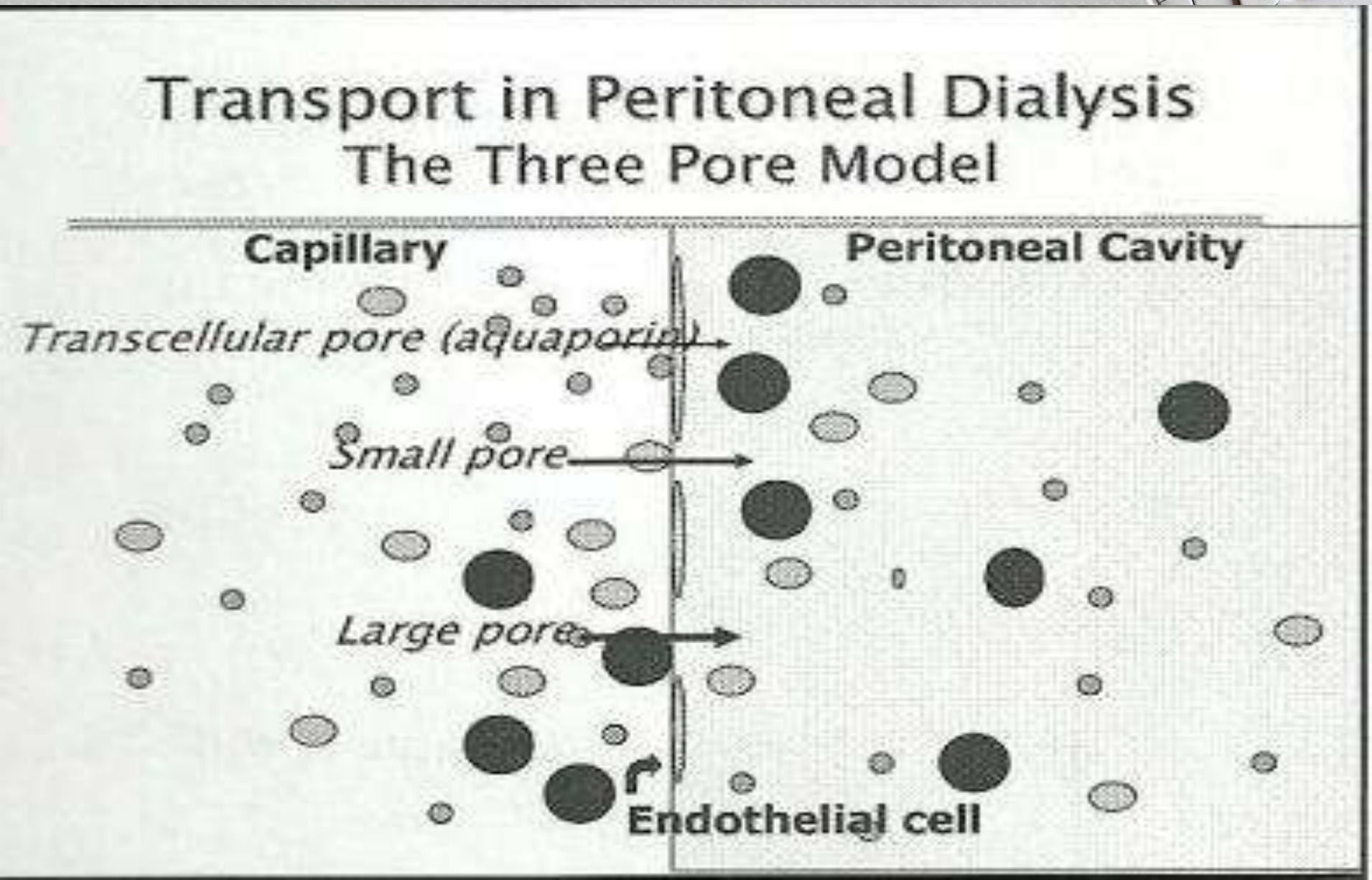
- **the better UF in the slow transporters will increase solute removal through convective transport**

C=convective flux

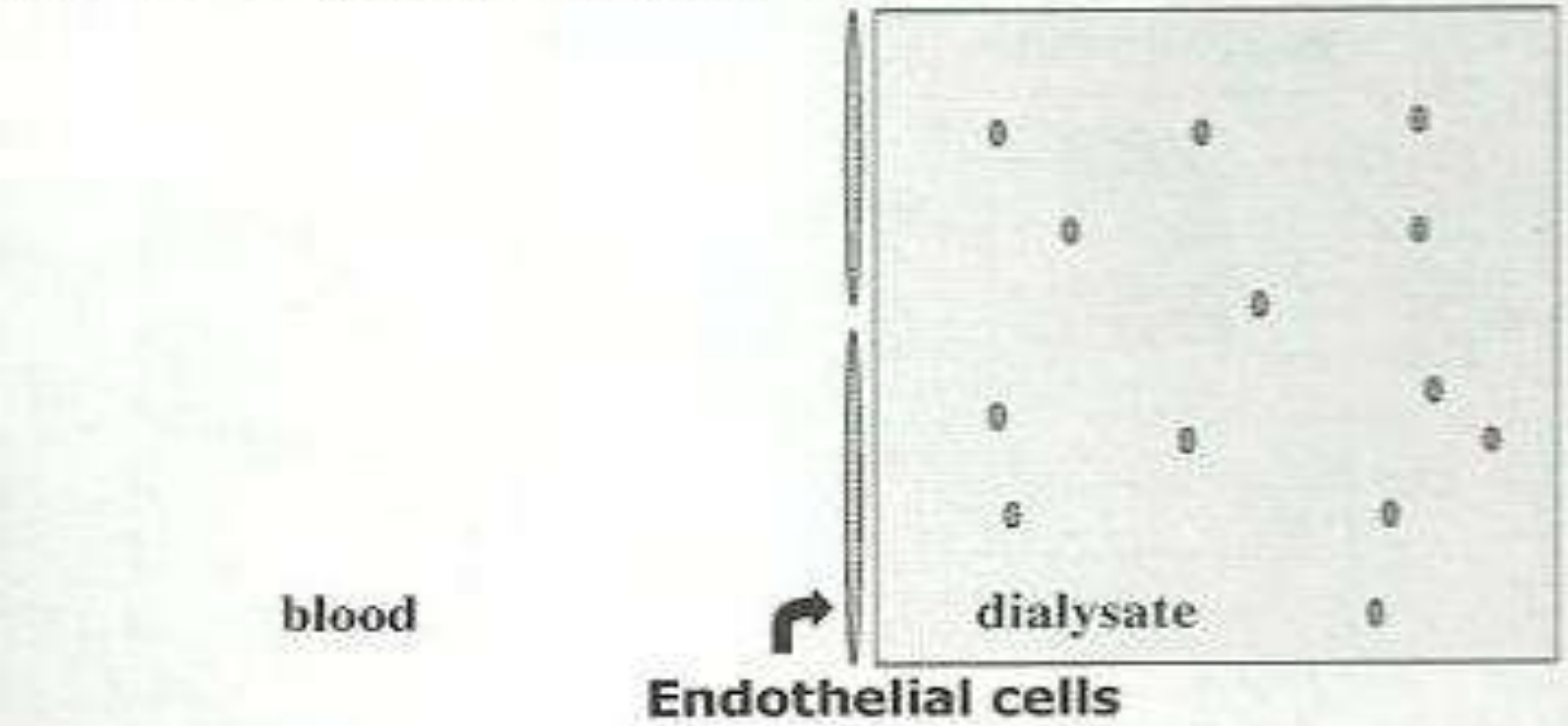
D=diffusive flux



Transport in Peritoneal Dialysis
The Three Pore Model



The Concept of Sodium Sieving



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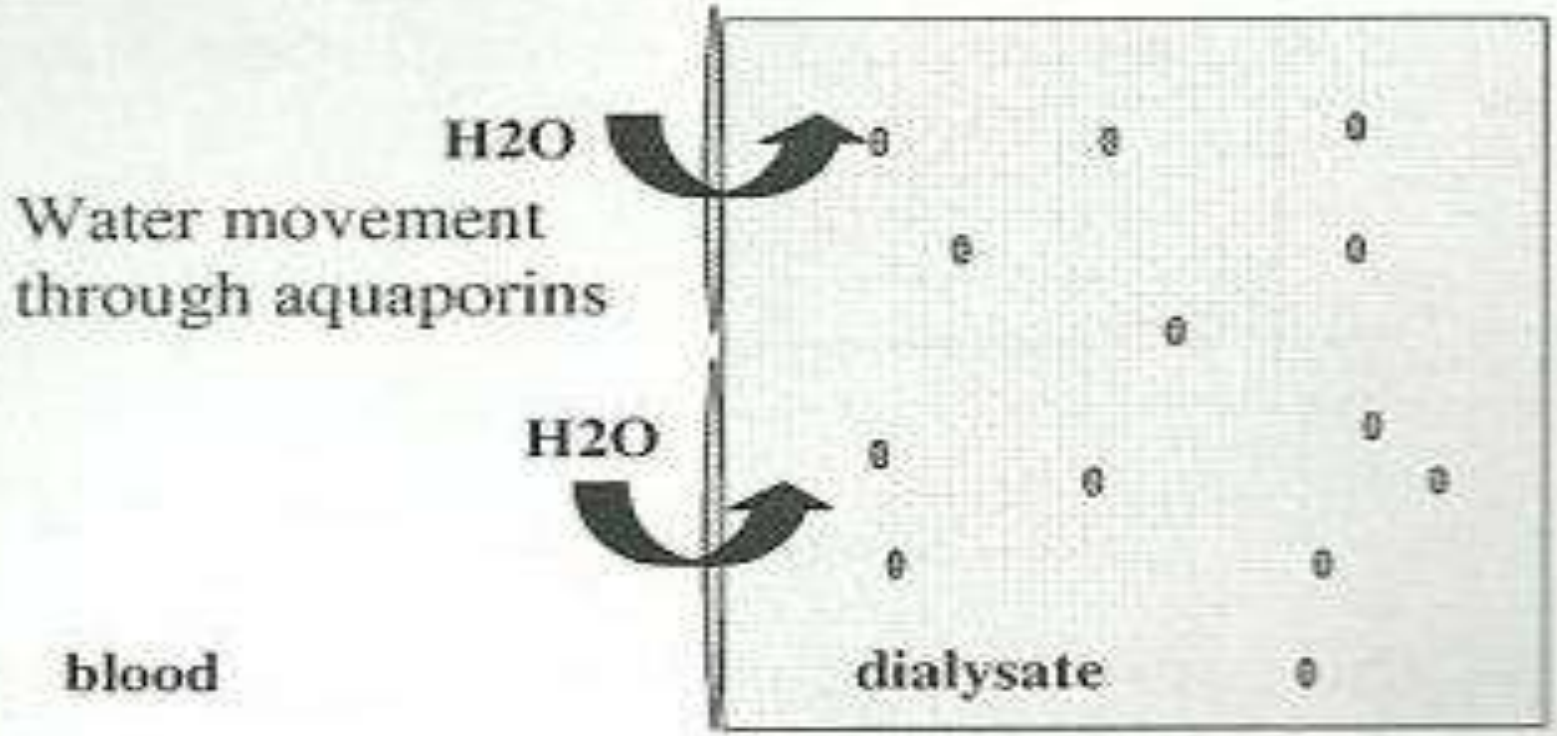


Icodextrin

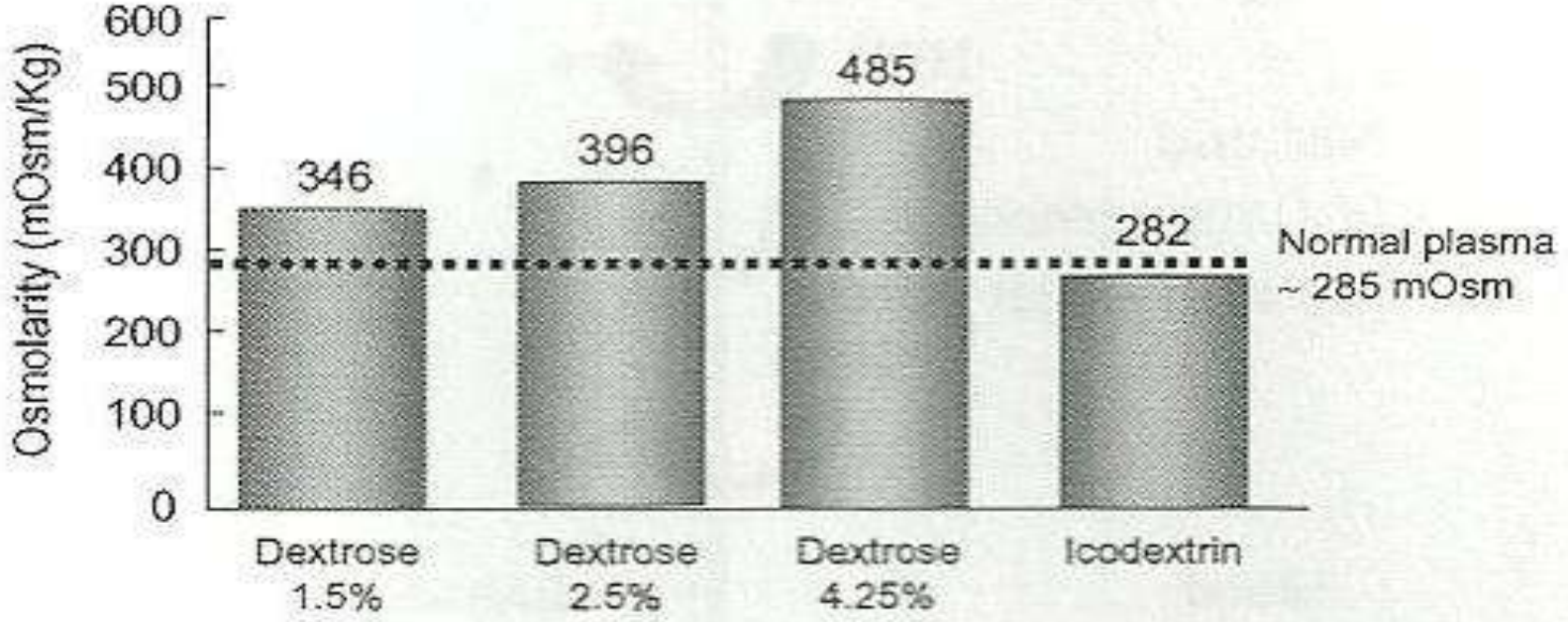
Mechanism of Action:

colloid osmosis – analogous to the Starling force of albumin( ) causing fluid flux from the interstitial to vascular compartment

Plasma osm

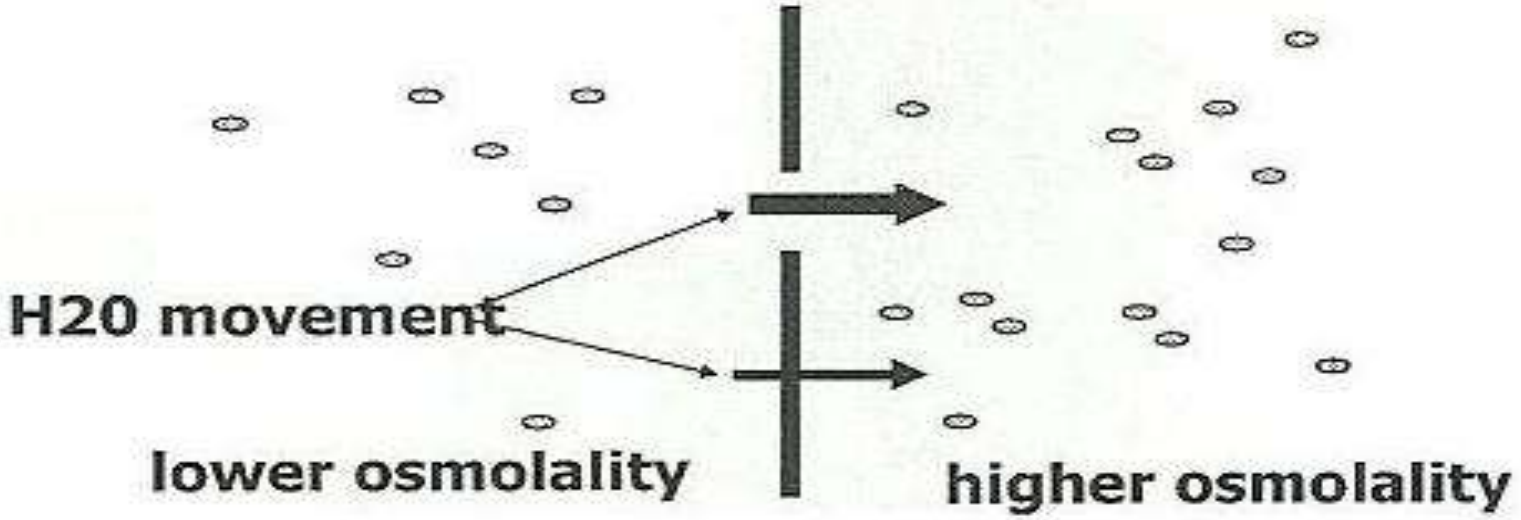
=

Interstitial osm


Osmolarity (mOsm/Kg)
600
500
400
300
200
100
0
346
396
485
282
Normal plasma
~ 285 mOsm
Dextrose
1.5%
Dextrose
2.5%
Dextrose
4.25%
Icodextrin

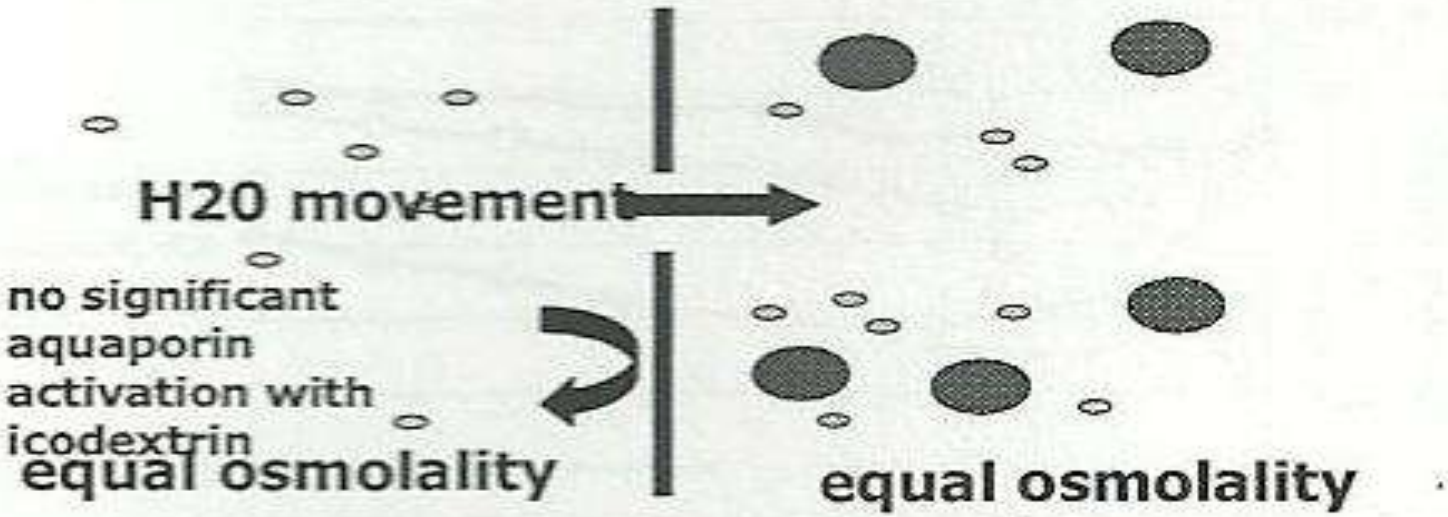
Dextrose vs Icodextrin

Crystalloid osmosis with dextrose

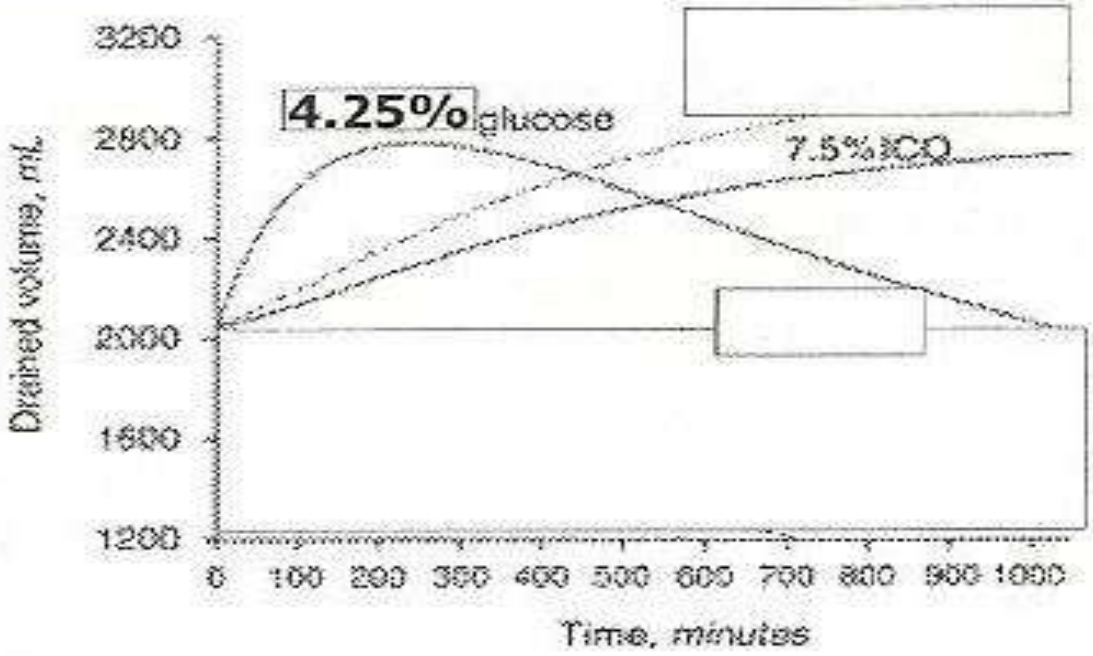


Dextrose vs Icodextrin

Colloid osmosis with Icodextrin



Peritoneal Ultrafiltration: Glucose vs Icodextrin (Computer Simulation)



Rippe and Levin Kidney Int 2000

Variability of UF with Icodextrin in the Long Dwell of APD

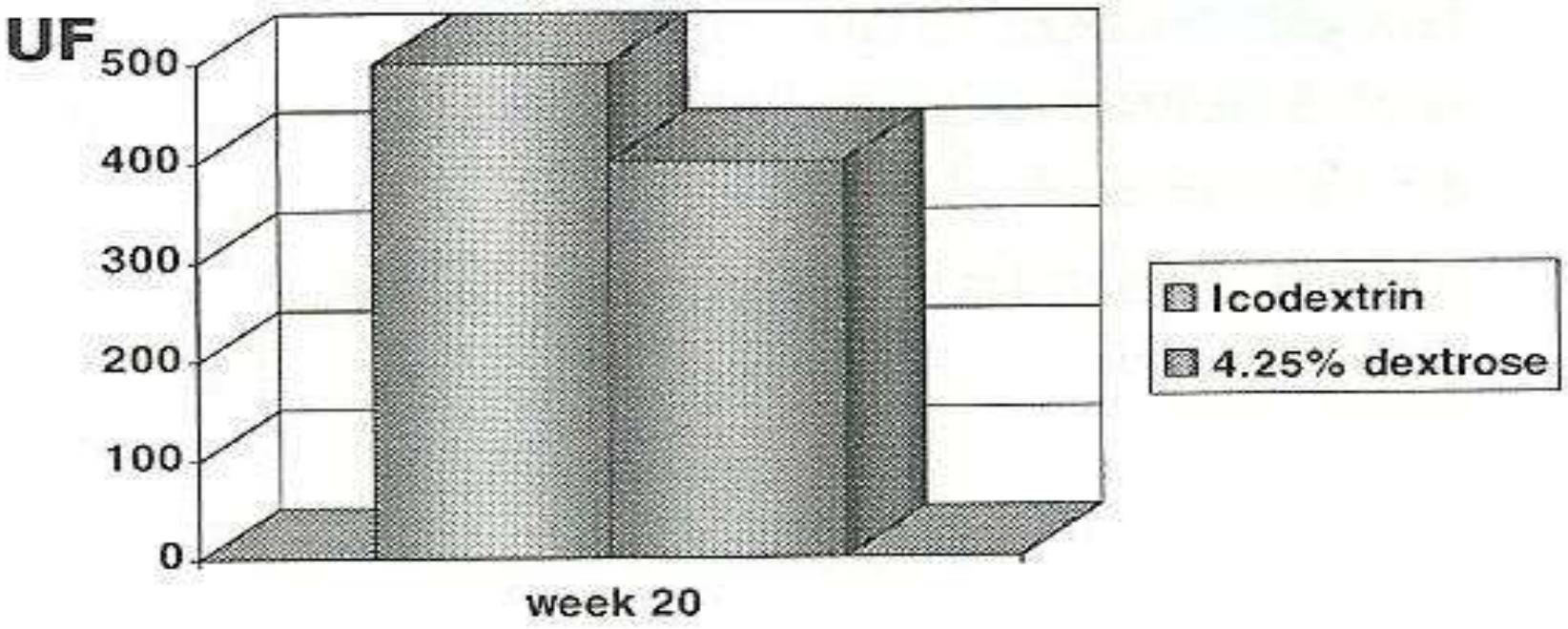
TABLE 2
Mean Ultrafiltration (in milliliters) with Icodextrin for Each Week of Increasing Dwell Time

Dwell	N	Mean[a]	SD	SE	Minimum	Median	Maximum
Week 1: 10 hours	31	351.73	250.59	45.00	−330.86	312	1126.29
Week 2: 11 hours	35	348.71	234.72	39.67	−302.29	362	1153.43
Week 3: 12 hours	36	386.83	240.86	40.14	−338.00	390	1233.43
Week 4: 13 hours	35	390.34	257.68	43.55	−388.00	375.28	1240.57
Week 5: 14 hours	35	371.75	258.25	43.65	−309.43	382.42	1012.00

Jeloka et al 2006

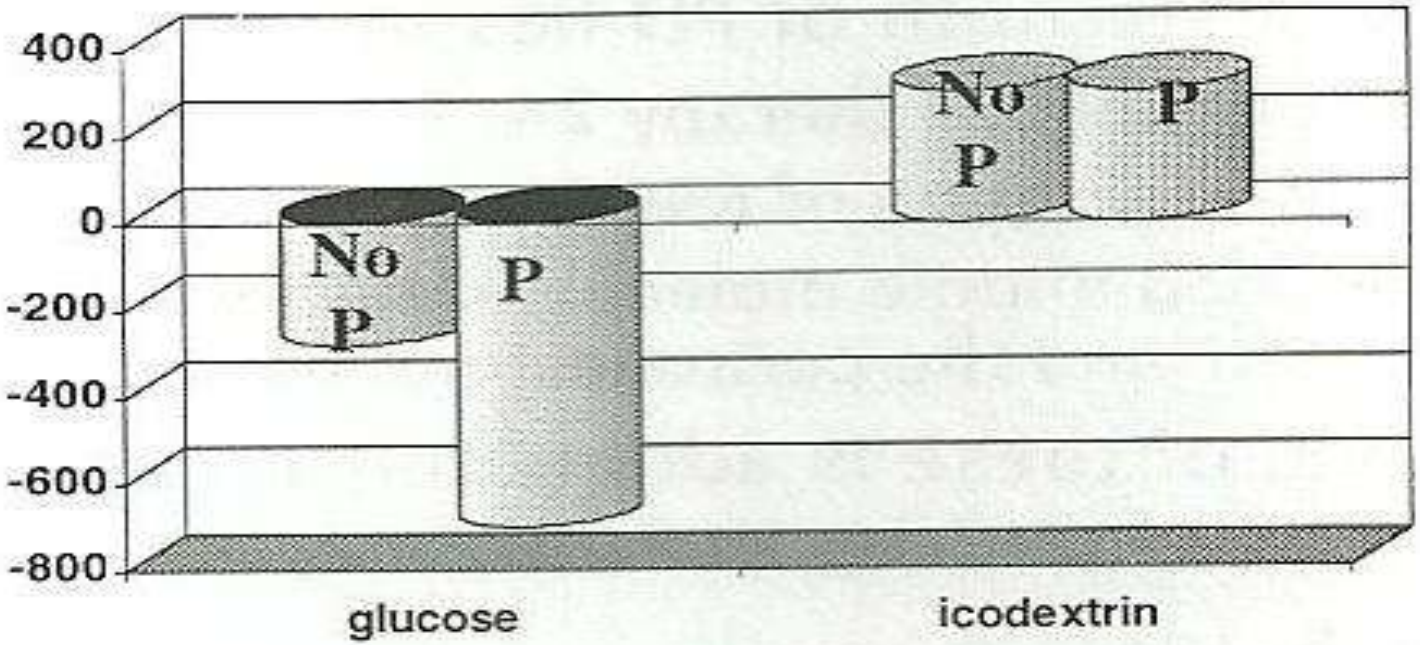
Mean net overnight UF at **12 hours**

Mistry et al 1994



Maintenance of UF during Peritonitis

(*Posthuma, 1997*)



Adequacy of Dialysis in PD

- The strength of PD lies in
  - continuous therapy 24/7
  - preservation of RRF
  - good middle molecule clearance (by RRF and the peritoneal membrane)

None of these is adequately measured by Kt/V urea

Adequacy of Dialysis in PD

- randomized, controlled trials have not shown a survival benefit for any Kt/V urea > 1.7
- lower limit for Kt/V urea also unknown

Adequacy of Dialysis in PD

The KDOQI Guidelines 2006

- minimum total (renal + peritoneal) Kt/V urea of 1.7
- monitor and protect RRF
- careful attention to volume status
- trial of increased dialysis is indicated if patient not doing well without another explanation

Fluid Balance

Intake		Output
Na+ and water	=	Urine and UF

Failure of Fluid Volume Management – Volume Overload

- Intake
  - excessive salt and water consumption
- Output
  - loss of residual renal function
  - inadequate provision of UF conditions
  - failure of peritoneal membrane to respond (true ultrafiltration failure)
  - mechanical problems like leaks

Failure of Fluid Volume Management – Volume Overload

- Intake – excessive salt and water consumption
  - PD has often been "advertised" as allowing a more liberal dietary intake
  - patients with high salt intake are protected from volume overload while they have residual renal function (RRF)
    - *once urine volume diminishes, patient may develop fluid overload*

Failure of Fluid Volume Management – Volume Overload

- Output: Loss of Residual Renal Function
  - probably the commonest cause of progressive fluid overload
  - rate of loss of RRF is variable and unpredictable from patient to patient

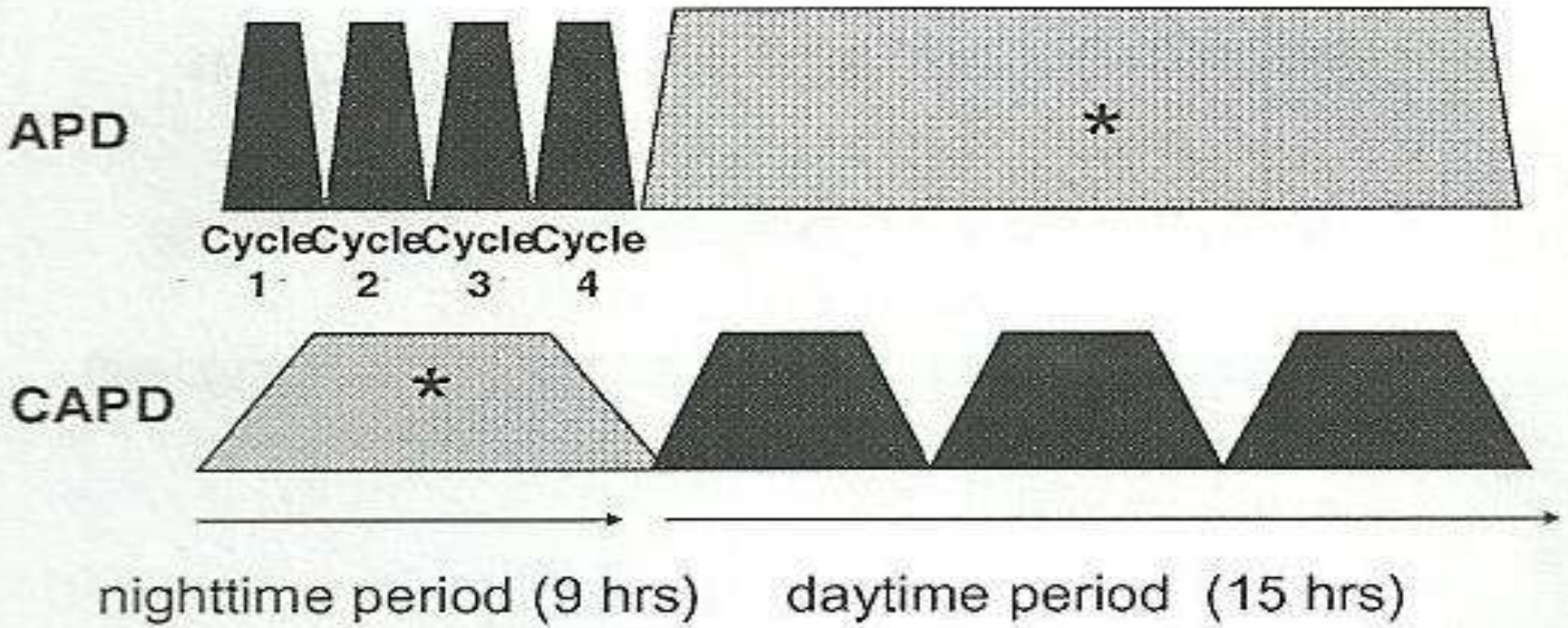
Failure of Fluid Volume Management – Volume Overload

- Output: Loss of Residual Renal Function
  - protect RRF
    - avoid NSAID's, COX 2-inhibitors, dye studies, aminoglycosides, volume depletion
  - use diuretics to augment urine Na^+ & water output
    - eg furosemide, metolazone
  - continue immunosuppression for failed transplant kidneys that still have function

Failure of Fluid Volume Management – Volume Overload

- Inadequate provision of ultrafiltration conditions
  - usually this means failure to account for the long dwell

Temporal Profiles of APD and CAPD



Ultrafiltration Failure

- Definition: Inability to maintain volume homeostasis despite the use of hypertonic dialysate solutions (3 or more daily)

or

- Failure to ultrafilter > 400 ml using a 4.25% bag for 4 hours

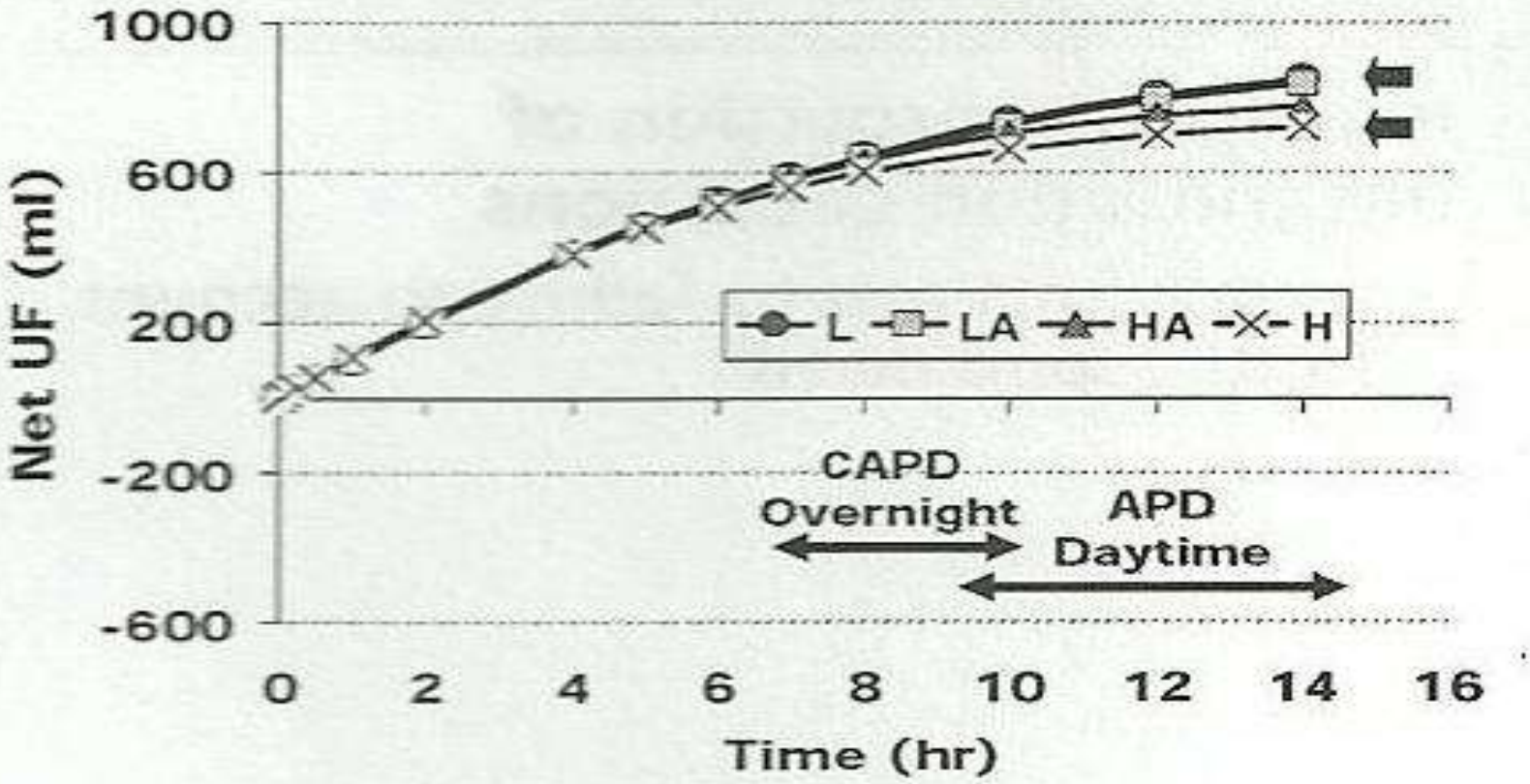
Ultrafiltration Failure

- on PET test, D/P creatinine is high
- these high transporters have rapid absorption of glucose across peritoneal membrane
- rapid dissipation of osmotic gradient
- poor ultrafiltration

Ultrafiltration Failure

- Management of rapid transporters (I):
  - reinforce salt and water restriction
  - use more hypertonic dialysate
  - icodextrin can be quite helpful here (*almost as effective in high transporters as other transport types*)

Temporal Profile: Icodextrin



Summary of Important Points

- The transport characteristics can be determined by a Peritoneal Equilibration Test
  - **"rapid transporter" has increased peritoneal vascularity and transports small solutes quickly; but loses glucose osmotic gradient quickly and so has problems with ultrafiltration**
  - **"low transporter" has slower removal of small solutes but excellent ultrafiltration**
  - **PD peritonitis can lead to transient "rapid transporter" state because of inflammation**

Summary of Important Points

- in all PD patients (except rapid transporters) short PD dwells leads to removal of more water than sodium;
  - **avoid short dwells except in rapid transporters**
- residual renal function is a more important predictor of outcome than dose of PD measured by small solute kinetics
  - **try to protect residual function**
  - **don't obsess about Kt/V – get at least to minimum target and obsess about RRF and volume status**