Brigham and Women's Hospital
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Introduction to Peritoneal Dialysis

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Disclosures

DaVita Healthcare: Speaker and Consultant
Baxter Canada: Speaker and Consultant
Baxter Global: Speaker
Opterion: Consultant

Objectives

We will use patient cases to illustrate the following:

Peritoneal transport

- solute flux
- ultrafiltration

Peritoneal dialysis solutions

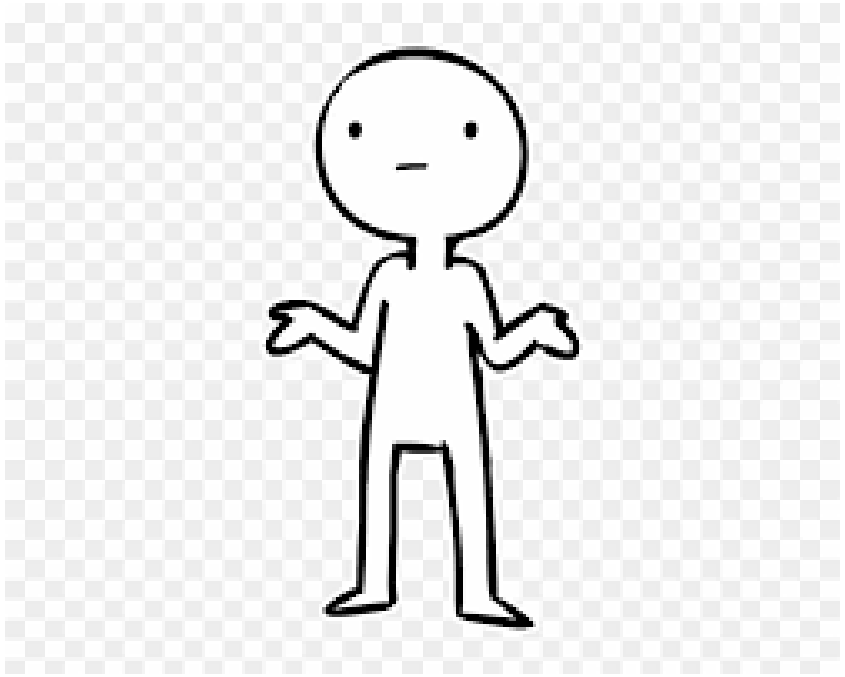
- dextrose-based
- icodextrin

Adequacy of PD

Approach to volume management

The “Rapid Transporter” – *so what*?

- 67 year old woman with type II diabetes starts on peritoneal dialysis
- two months later, peritoneal equilibration test (PET) shows that the D/P creatinine at 4 hours is 0.90 (“high” or “rapid” transporter)



Which ONE of the following statements about D/P creatinine is TRUE?

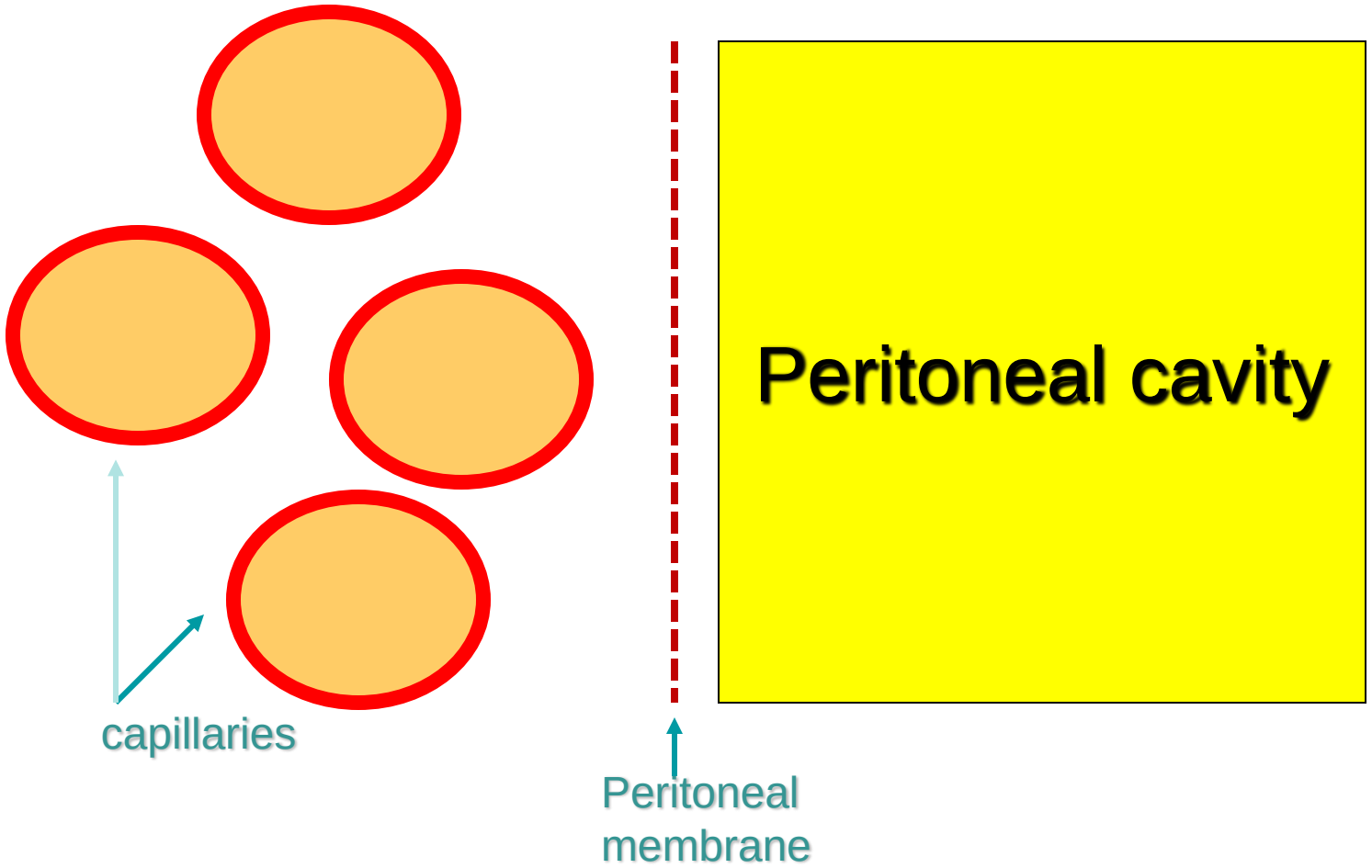
A. The D/P creatinine is an important predictor of dialysis adequacy.

B. The PET test was performed too soon after the start of PD.

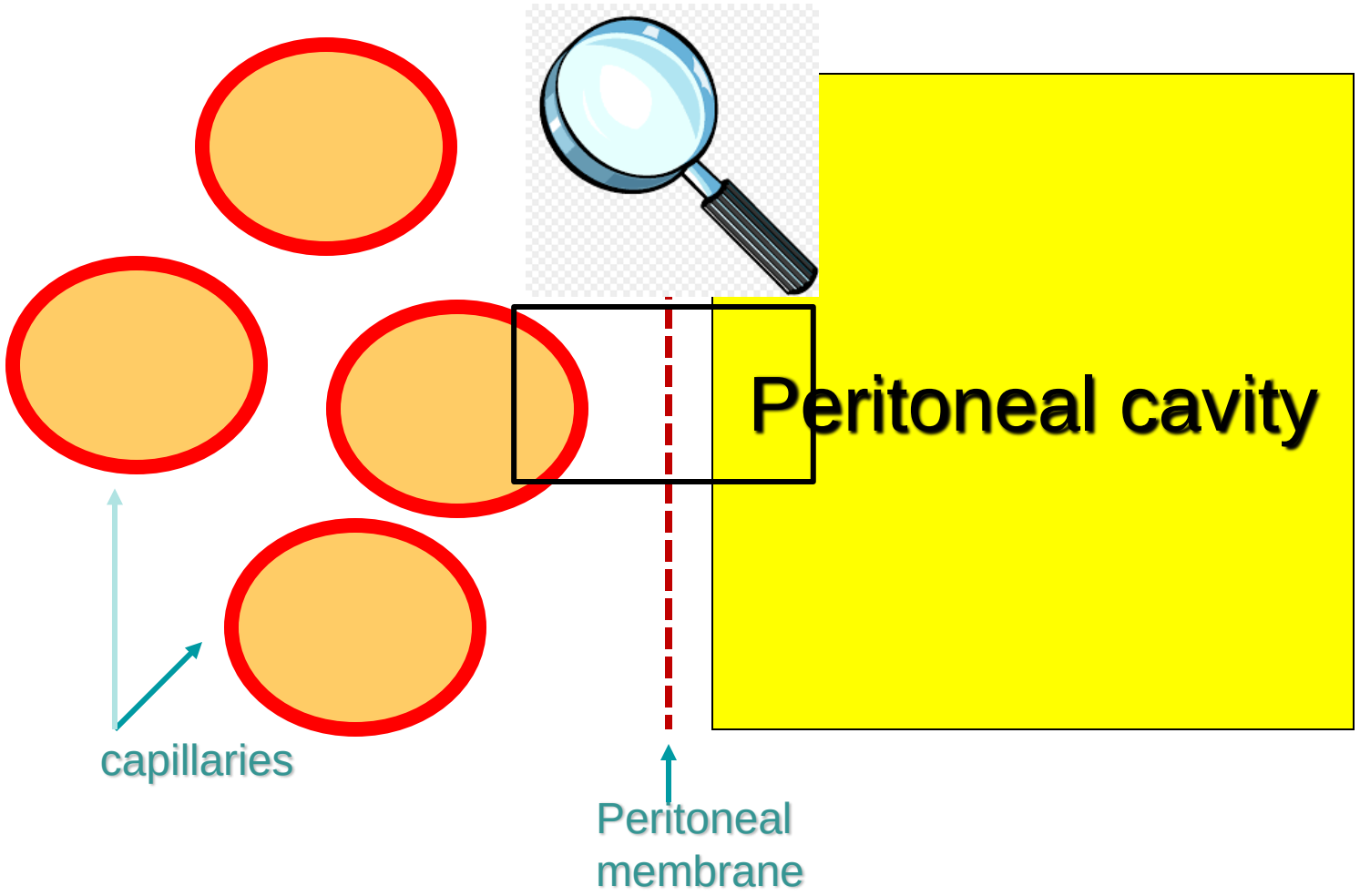
C. There may be problems with ultrafiltration, especially during the long dwell of dialysate.

D. Icodextrin is not useful for this high or rapid transporter

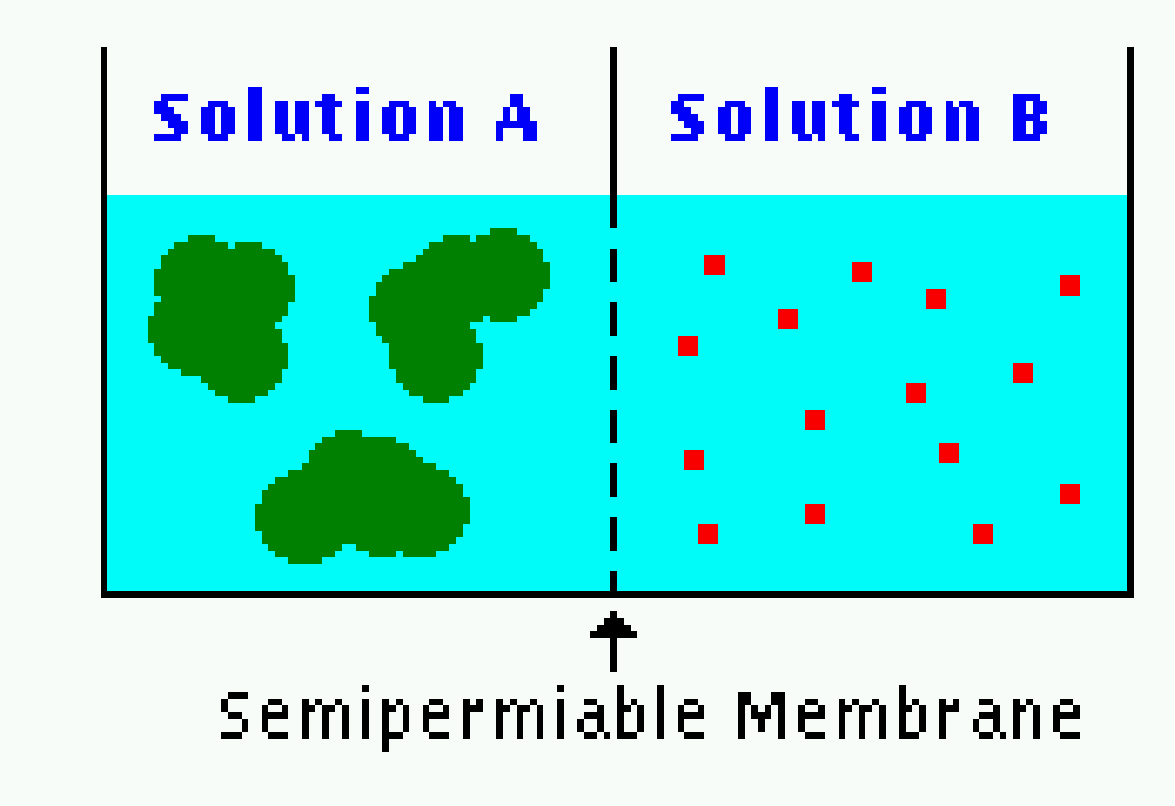
How PD Works: The Peritoneal-Vascular Interface



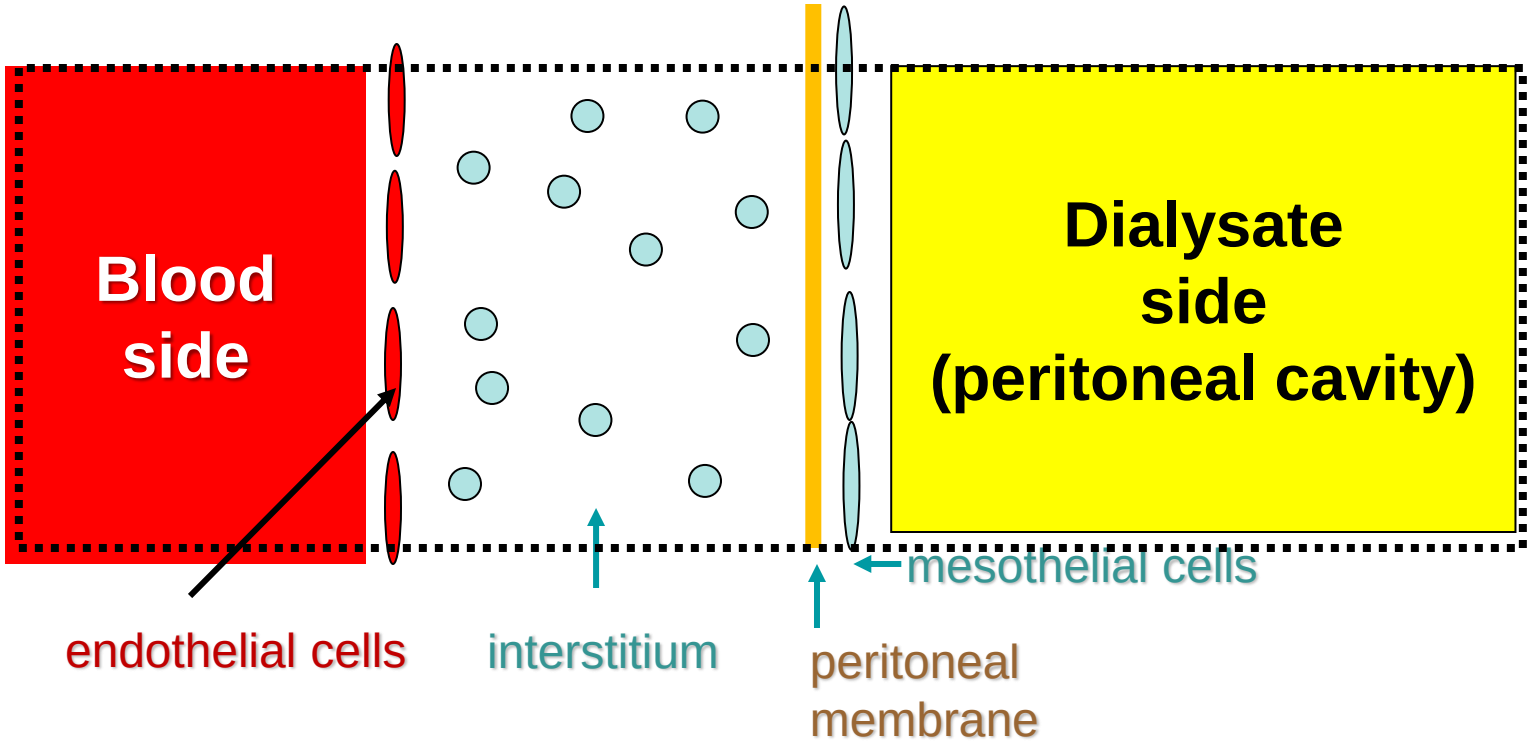
How PD Works: The Peritoneal-Vascular Interface



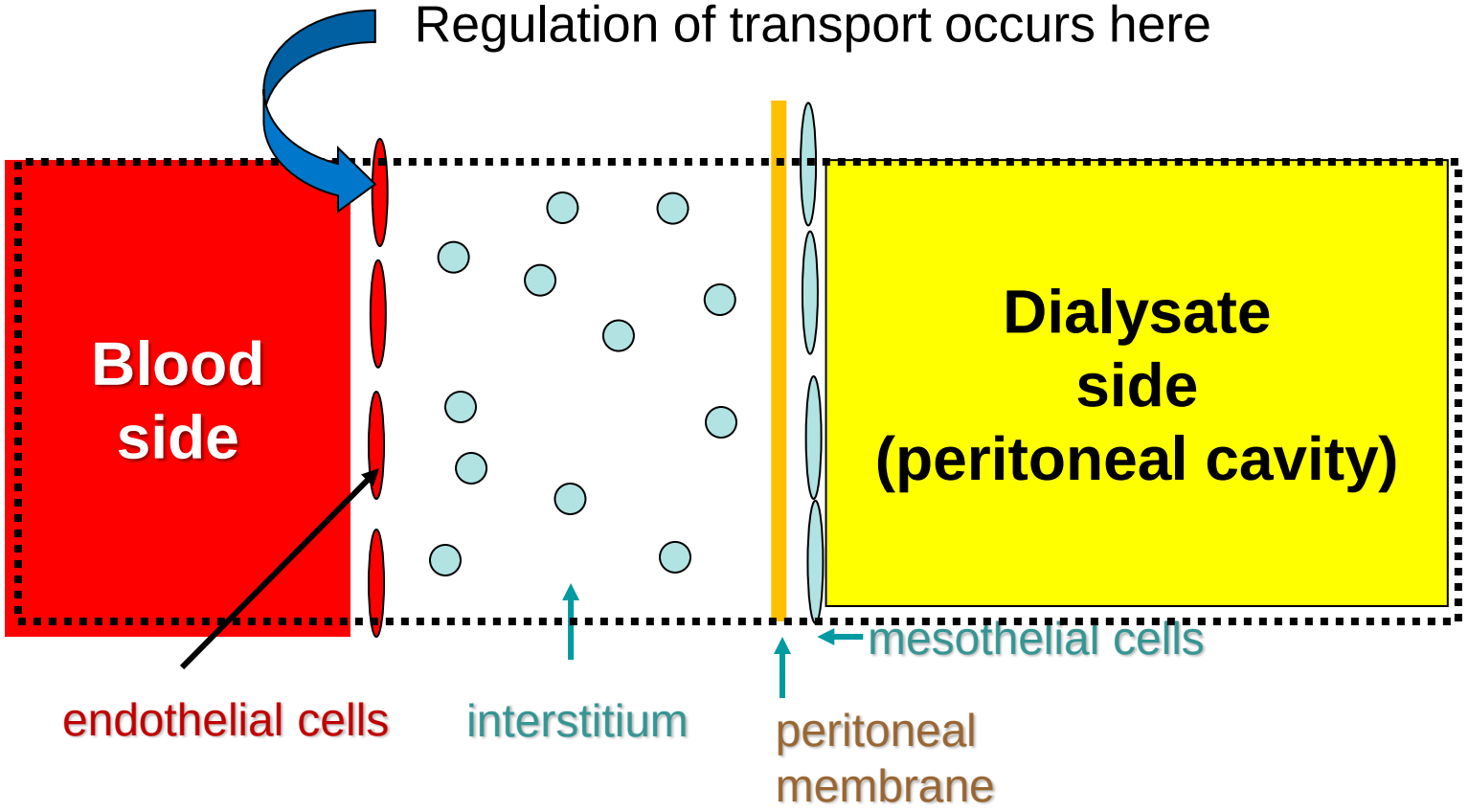
Remember Your Grade 12 Chemistry Experiments?



The Peritoneal-Vascular Interface



The Peritoneal-Vascular Interface



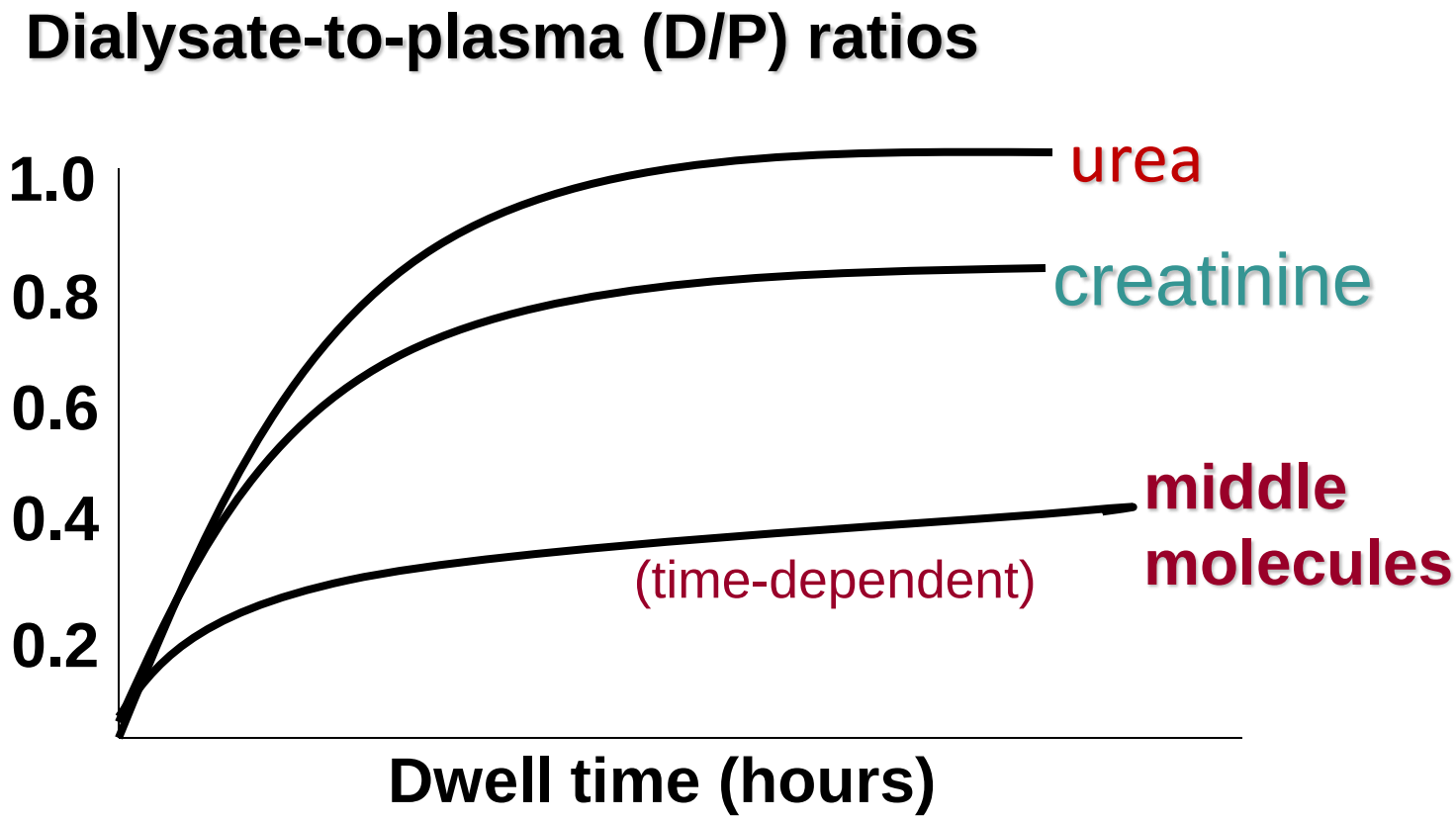
Solute Transport in PD: How Does Solute Get from the Blood to the Peritoneal Fluid?

I. Diffusion
II. Convection (during ultrafiltration)

Diffusion Kinetics - *from blood to dialysate*

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

Diffusion Curves – a Schema



Diffusion Kinetics – *A Two-Way Street*

Diffusion goes in both directions.
What can you add to dialysate that ends up in the blood?

- antibiotics (not just for peritonitis)
- insulin
- KCl (up to 10 mEq/l)
- xylocaine, NaHCO3 (infusion pain)

Ultrafiltration in PD

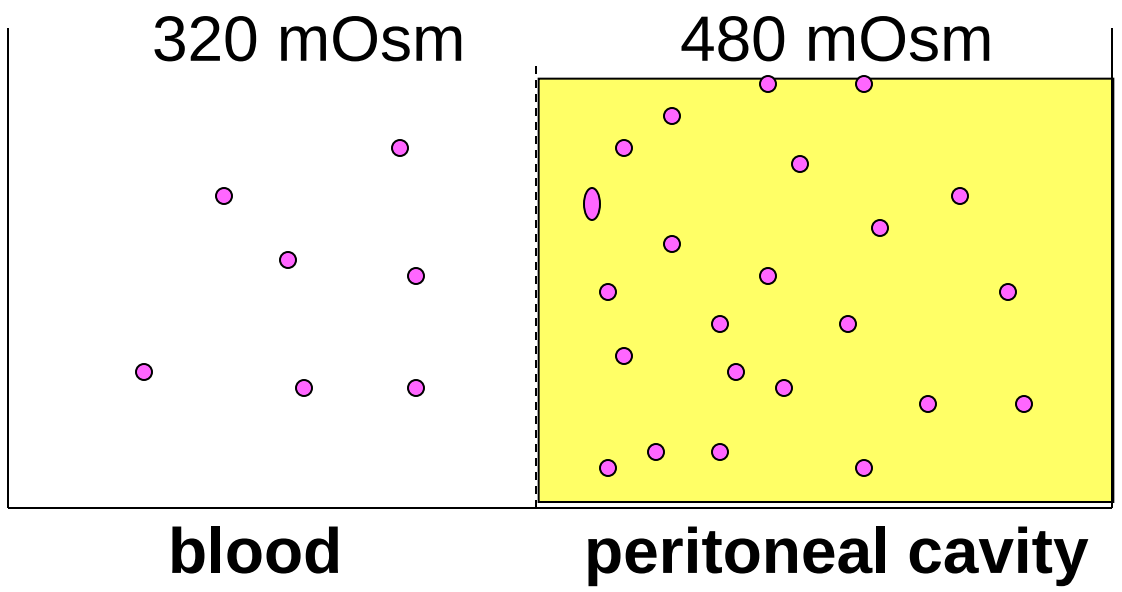
- result of *osmotic* pressure (compared to HD where result of *hydraulic* pressure)
- results of ultrafiltration:
  - fluid removal
  - convective removal of solutes, especially middle molecules

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 (more hypertonic)

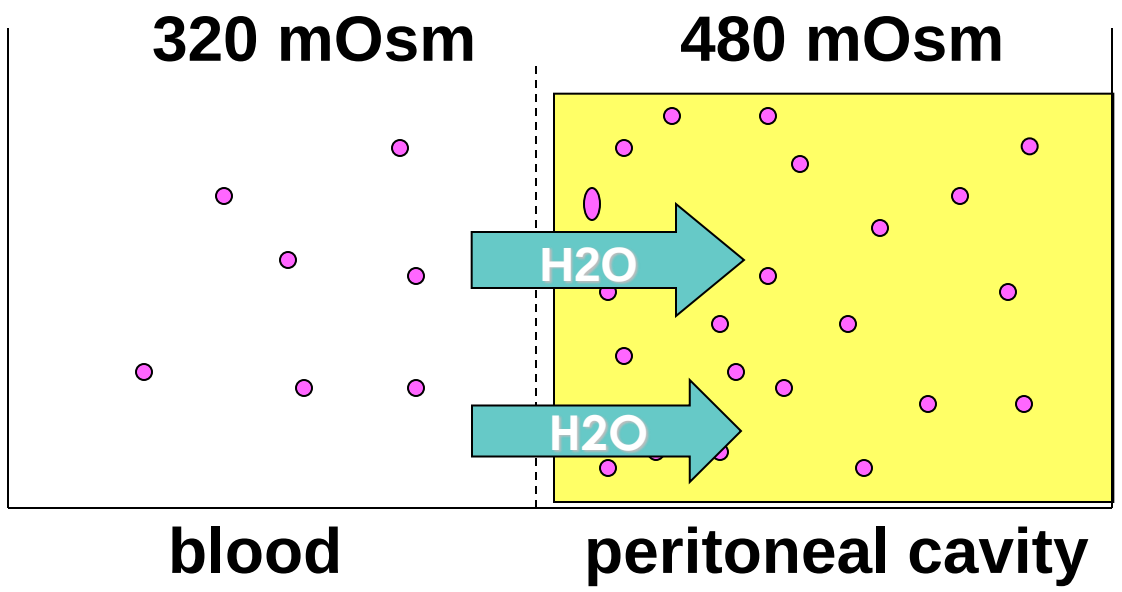
Ultrafiltration in Peritoneal Dialysis

Example: 4.25% dextrose dialysate



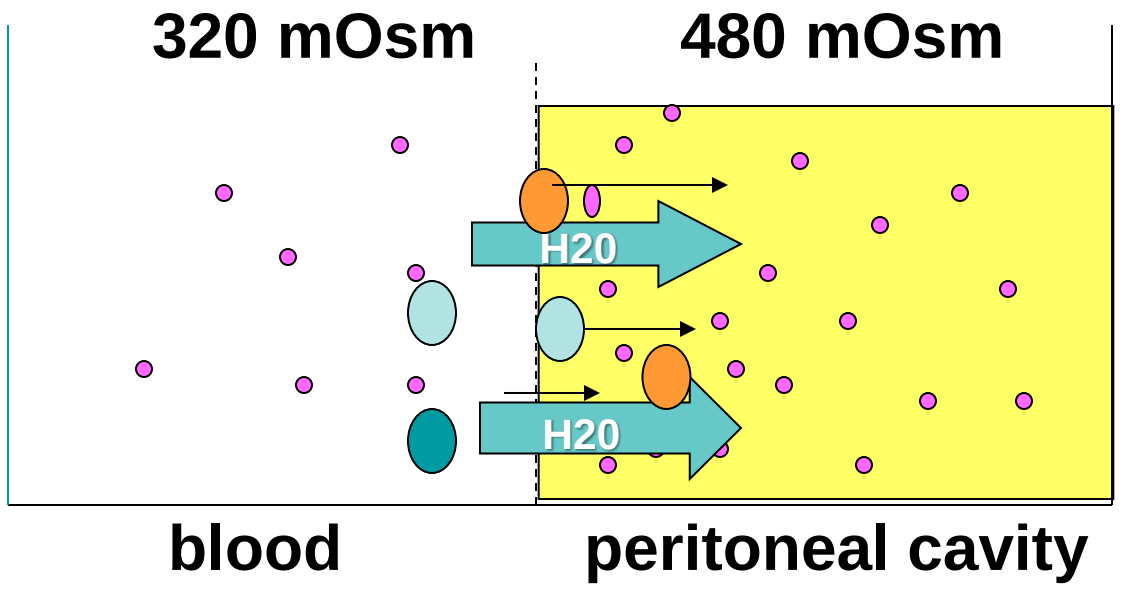
Ultrafiltration: 4.25% Dialysate

Water will move from lower to higher osmolality



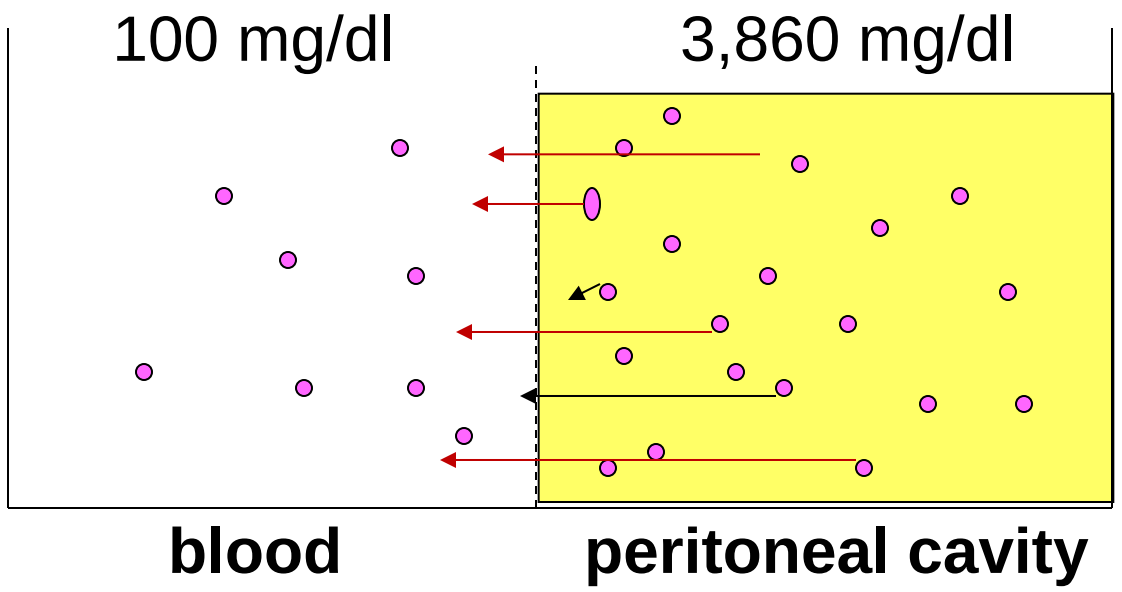
Ultrafiltration: 4.25% Dialysate

Water will move from lower to higher osmolality and take solute with it

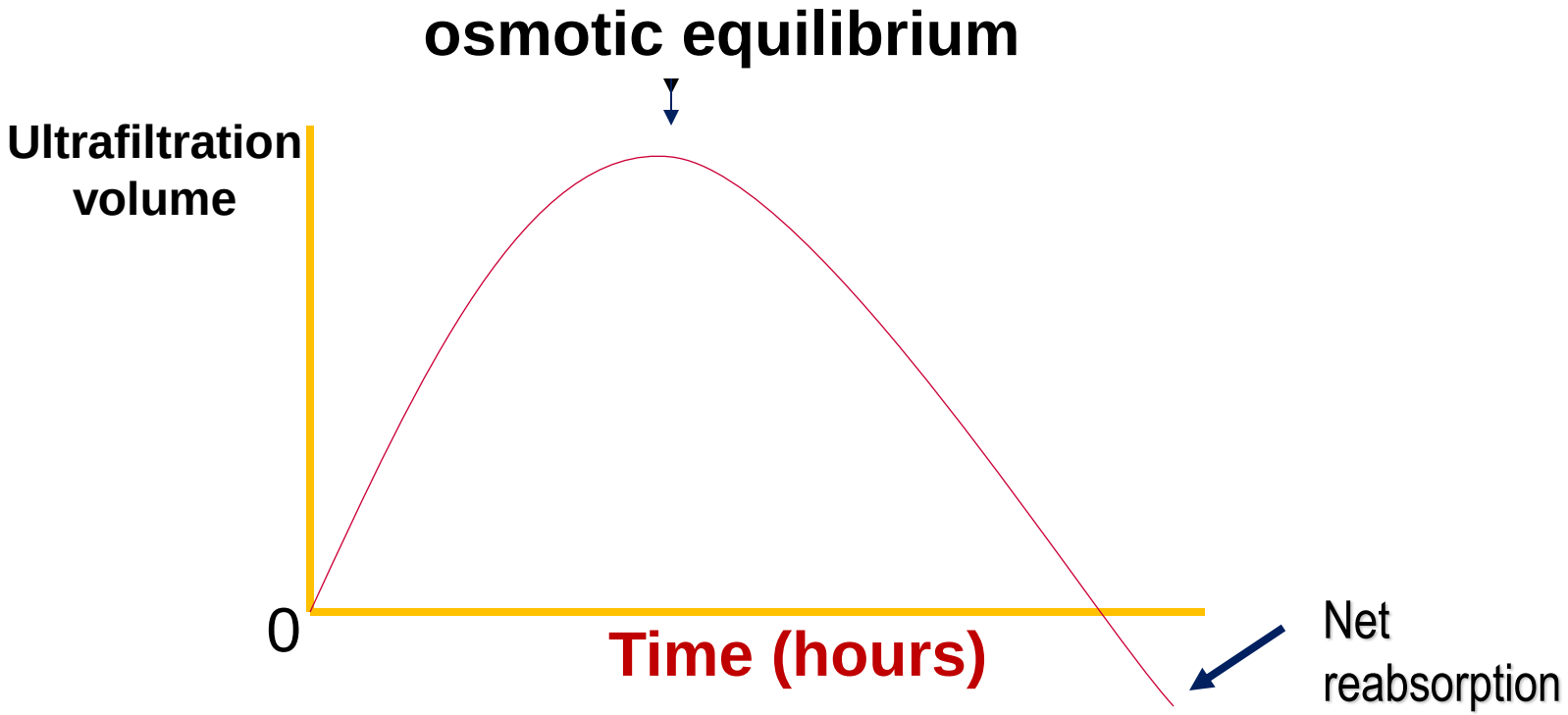


Ultrafiltration in PD: The Bad News

The glucose itself diffuses out of peritoneal cavity along its own concentration gradient



Ultrafiltration in PD is Time-Dependent



Typical Ultrafiltration Values in PD

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

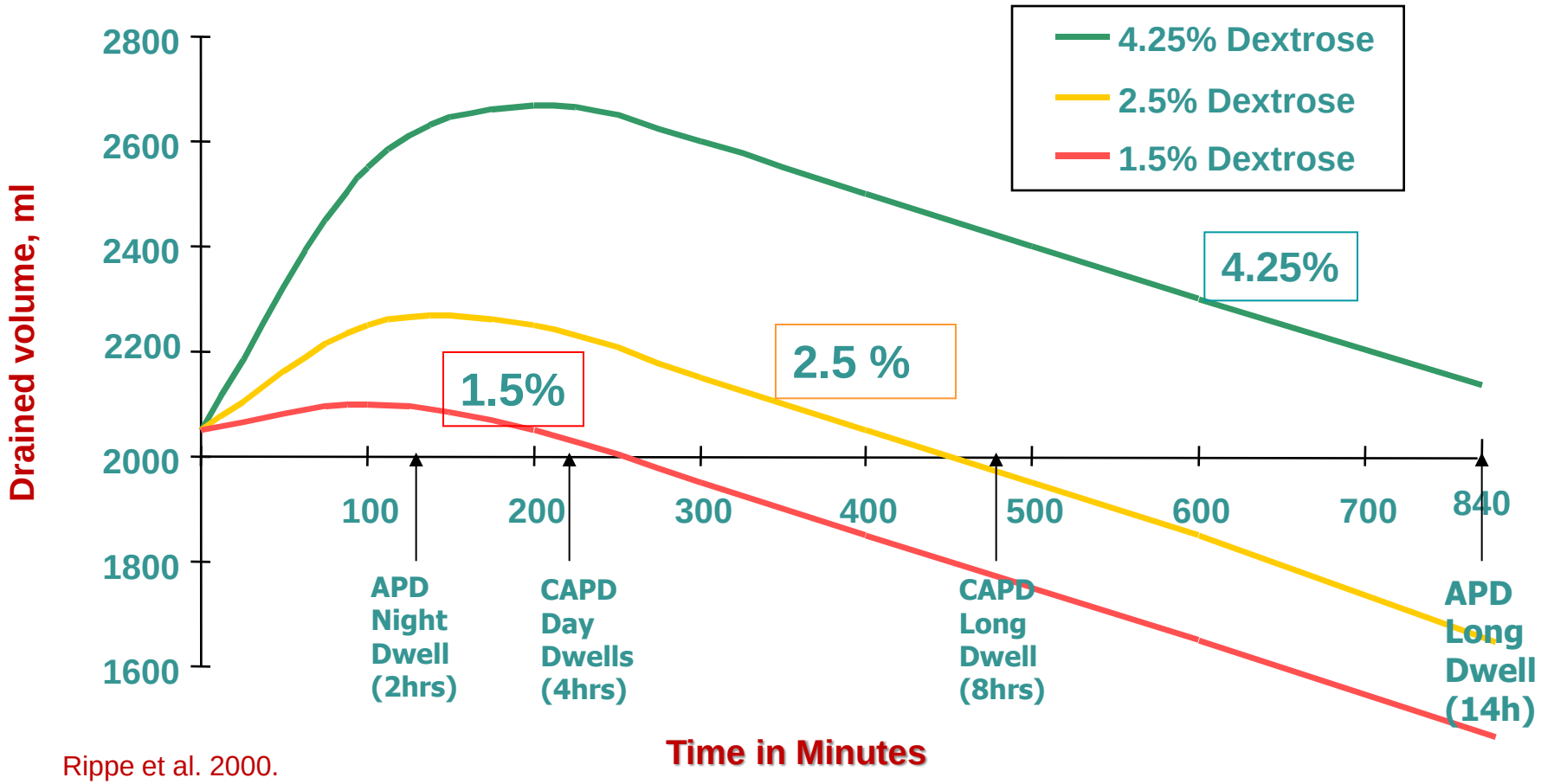
Snap Quiz

A 4.25% solution typically leads to 1L of UF over 4h (=250 ml/hr), so:

Why are PD patients switched to HD for fluid removal if they end up in ICU?

Beats me…

Typical Ultrafiltration Curves for Each Strength of Dialysate



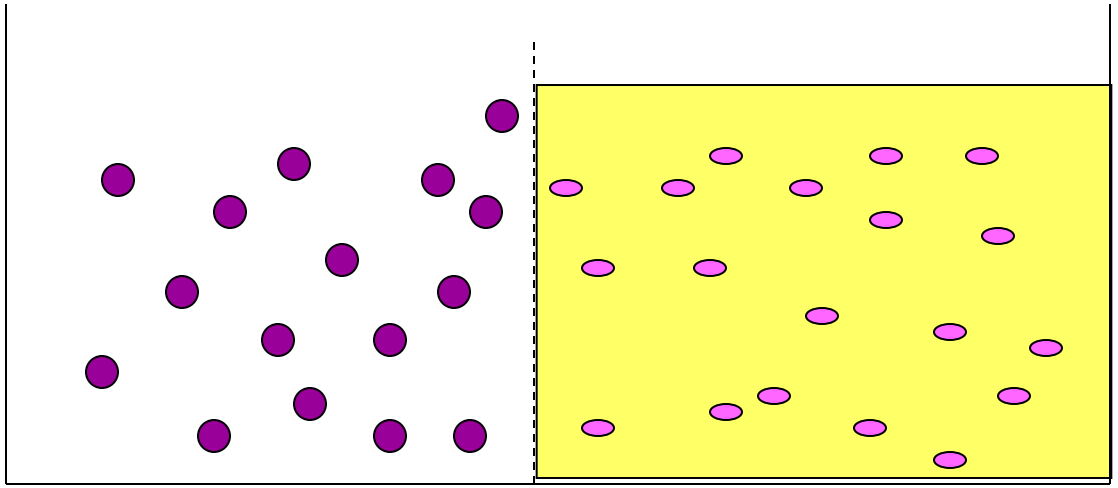
Rippe et al. 2000.

The Amount of UF Depends on 3 Main Factors

- tonicity of dialysate
  - 4.25% > 2.5% > 1.5%
- duration of dialysate dwell
  - after osmotic equilibration, fluid starts to be absorbed
- permeability of peritoneal membrane to glucose
  - osmotic gradient dissipates faster across a more permeable membrane

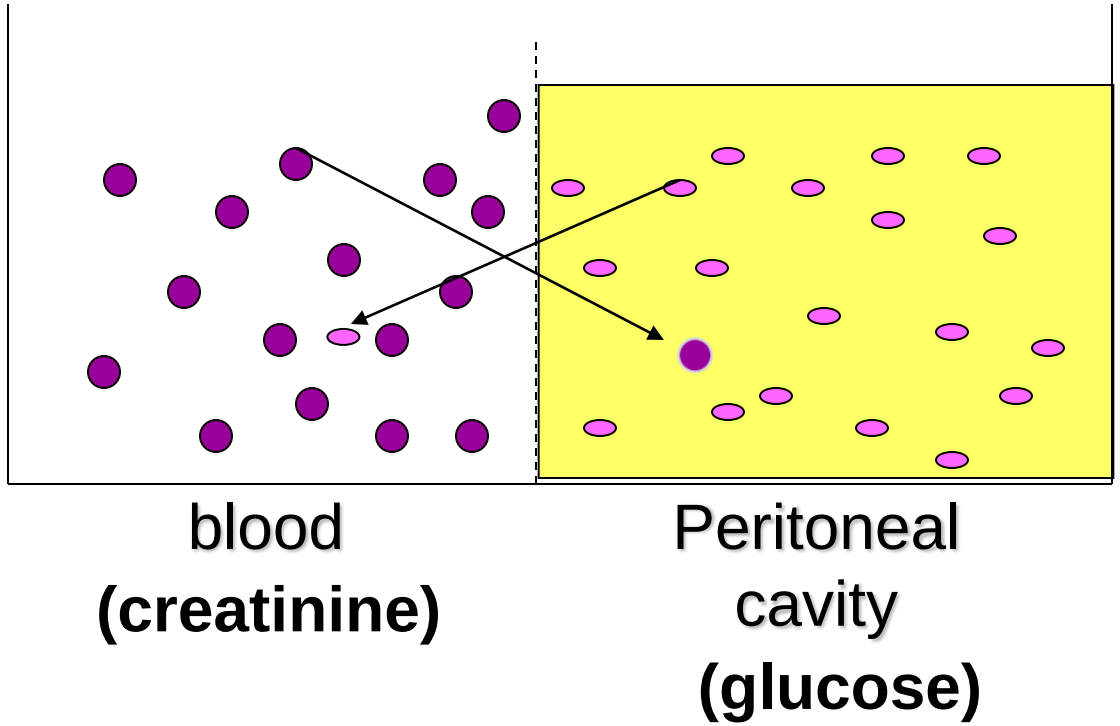
The Peritoneal Equilibration Test (PET):
A Way to Characterize the Peritoneal Membrane

At time t = 0:



The Peritoneal Equilibration Test (PET):
A Way to Characterize the Peritoneal Membrane

Solutes diffuse along their concentration gradient:



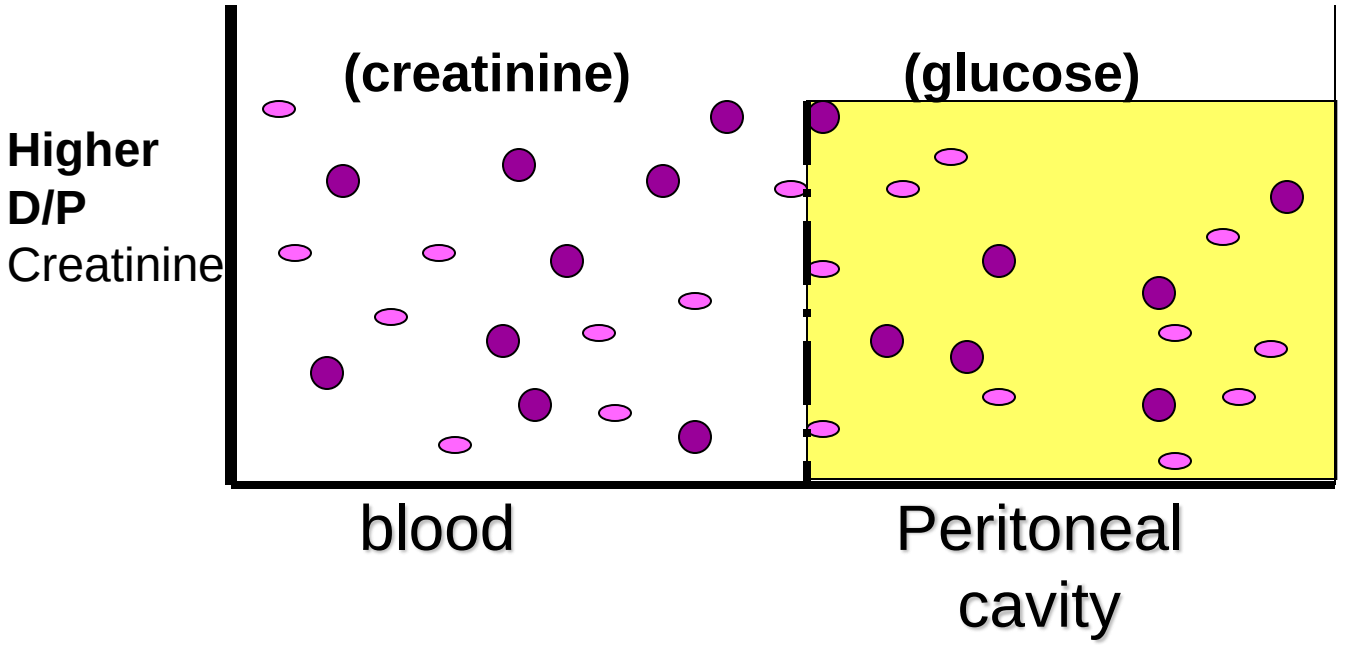
The Peritoneal Equilibration Test

How *easily* does creatinine cross from blood to the peritoneal cavity?

- quantified as $\frac{\text{Dialysate [creatinine]}}{\text{Plasma [creatinine]}}$ or D/P creatinine (at T = 4 hours)
- the “leakier” the peritoneal membrane, the ***higher*** the D/P creatinine

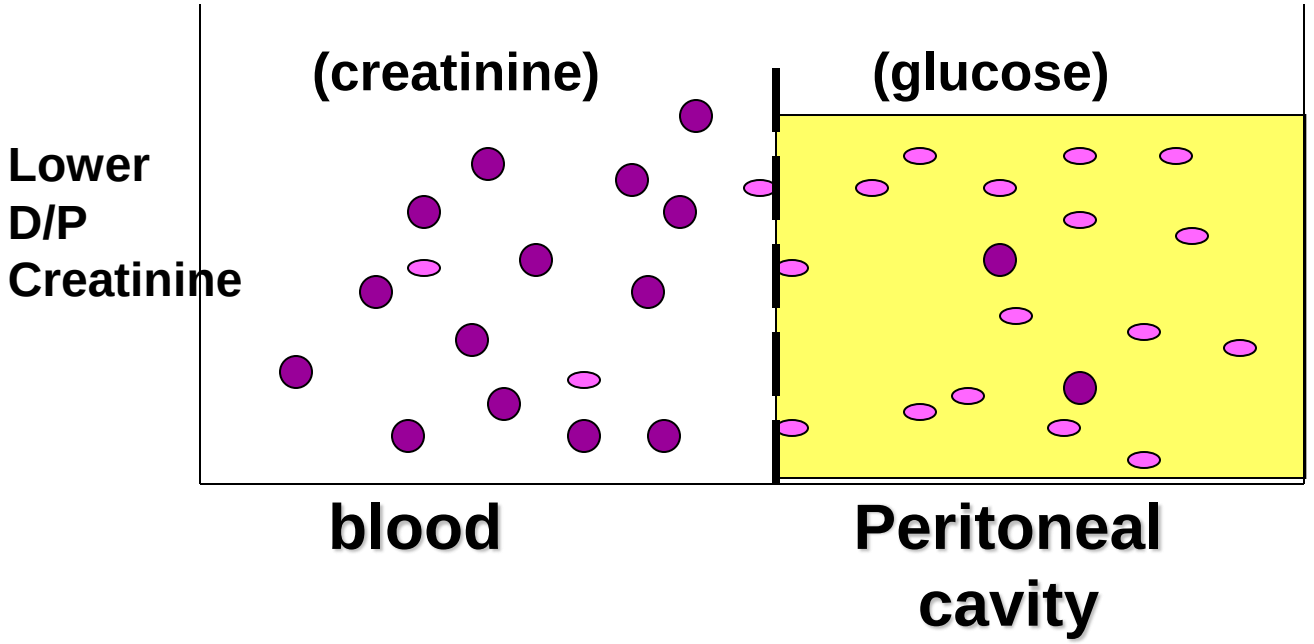
The Peritoneal Equilibration Test (PET):
A Way to Characterize the Peritoneal Membrane

"leaky" peritoneal membrane
(rapid transporter)

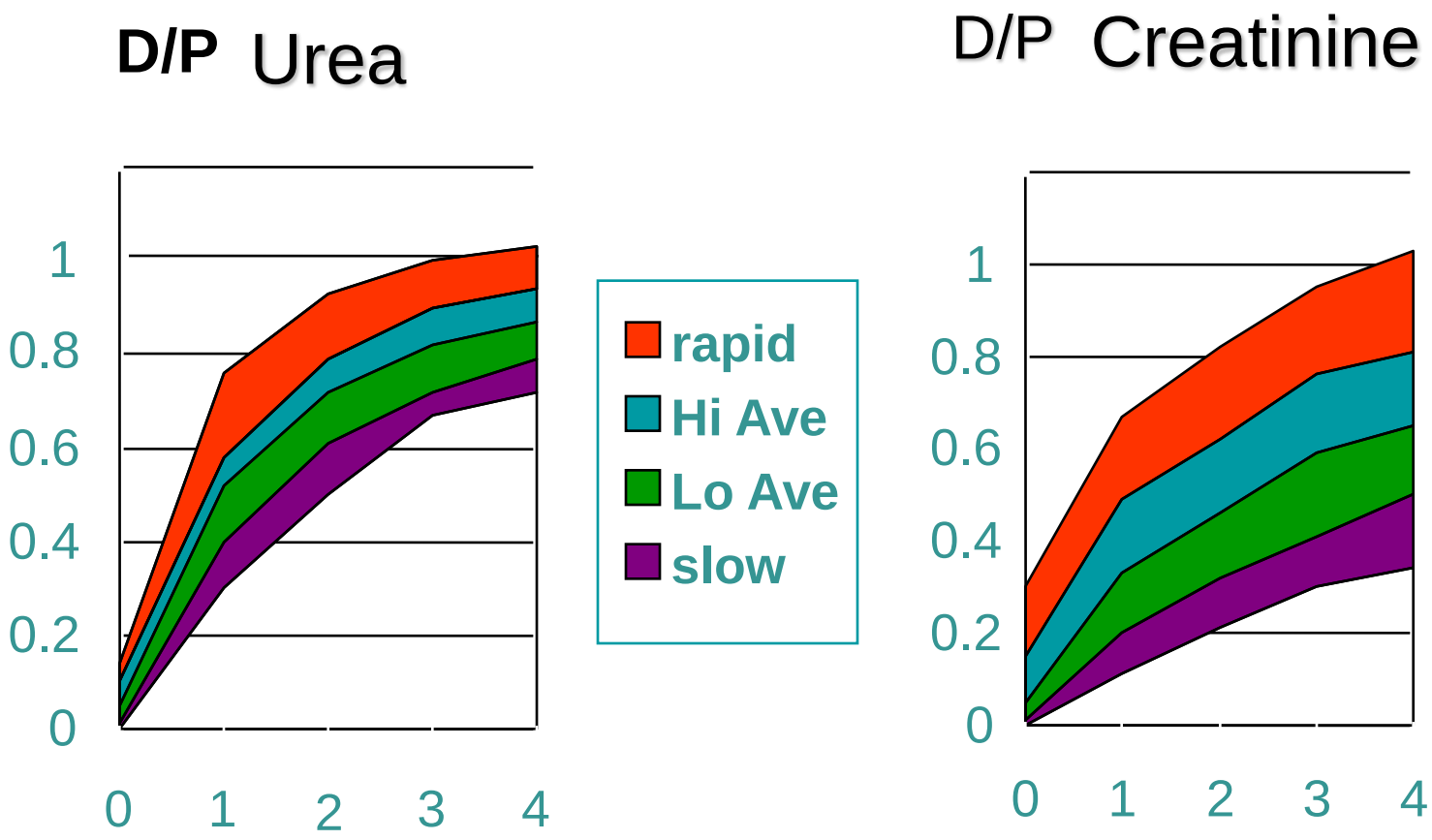


The Peritoneal Equilibration Test (PET):
A Way to Characterize the Peritoneal Membrane

"tight" peritoneal membrane
(slow transporter)



Peritoneal Equilibration Test



Twardowski et al. Blood Purif 1989

Membrane Permeability and Ultrafiltration "rapid transporters"

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

↓

the faster the glucose will diffuse out of the peritoneal cavity

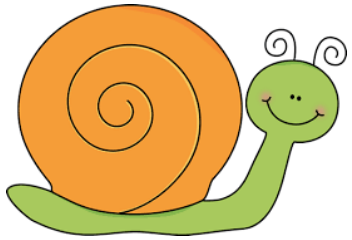
↓

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 is seen even 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 (fewer open vascular beds)

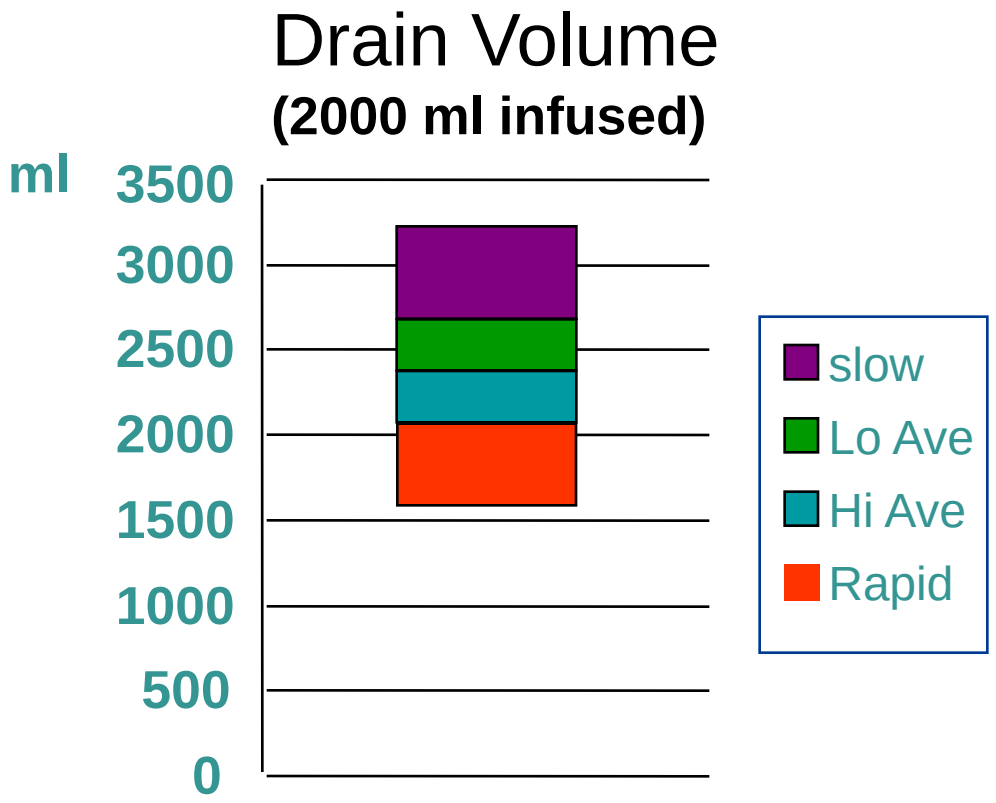
↓

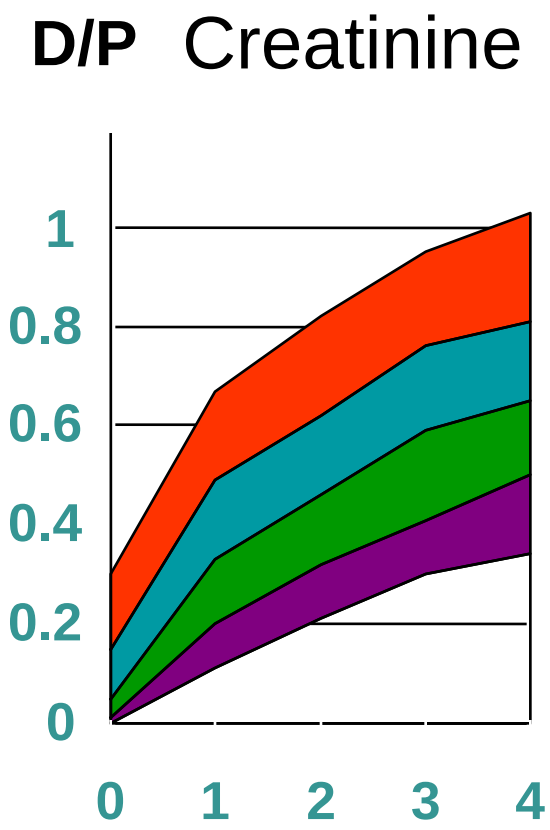
the slower glucose will diffuse out of the peritoneal cavity

↓

the osmotic gradient will be maintained longer

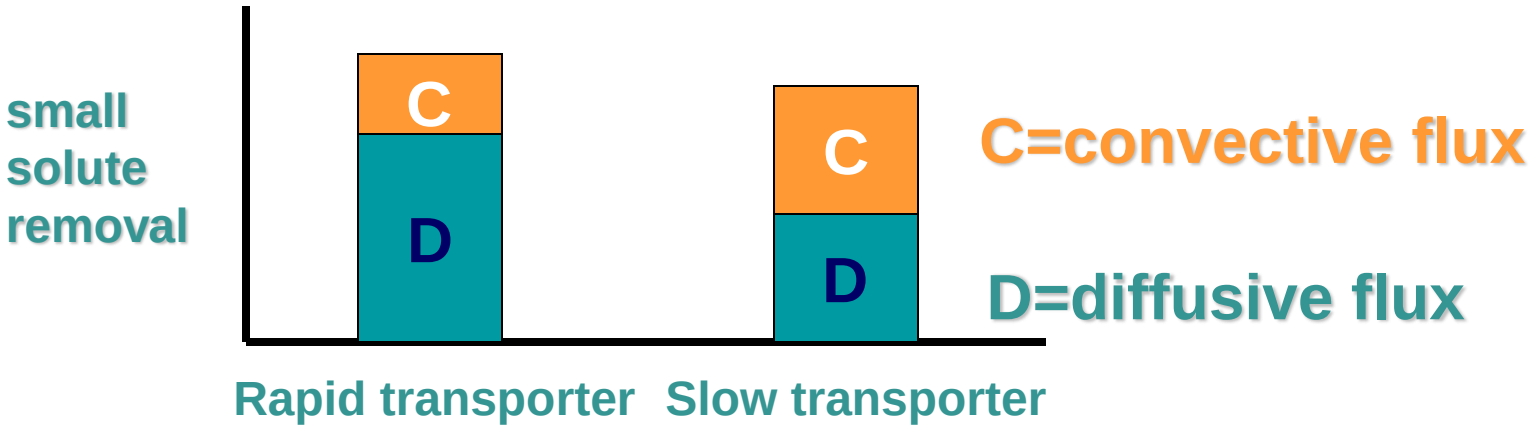
MembraneTransport Status – Implications for Ultrafiltration





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

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



Back to Our Patient:

Which ONE of the following statements about our “rapid transporter” is TRUE?

A. The D/P creatinine is an important predictor of dialysis adequacy.

B. The PET test was performed too soon after the start of PD.

C. There may be problems with ultrafiltration, especially during the long dwell of dialysate.

D. Icodextrin is not useful for this high or rapid transporter

Explanation

- glucose diffuses out of the peritoneal dialysis fluid over time into the systemic circulation
- during a long dwell, the loss of glucose in the dialysis fluid leads to dissipation of the osmotic gradient and ultrafiltration will stop
- this all happens faster in the rapid transporter

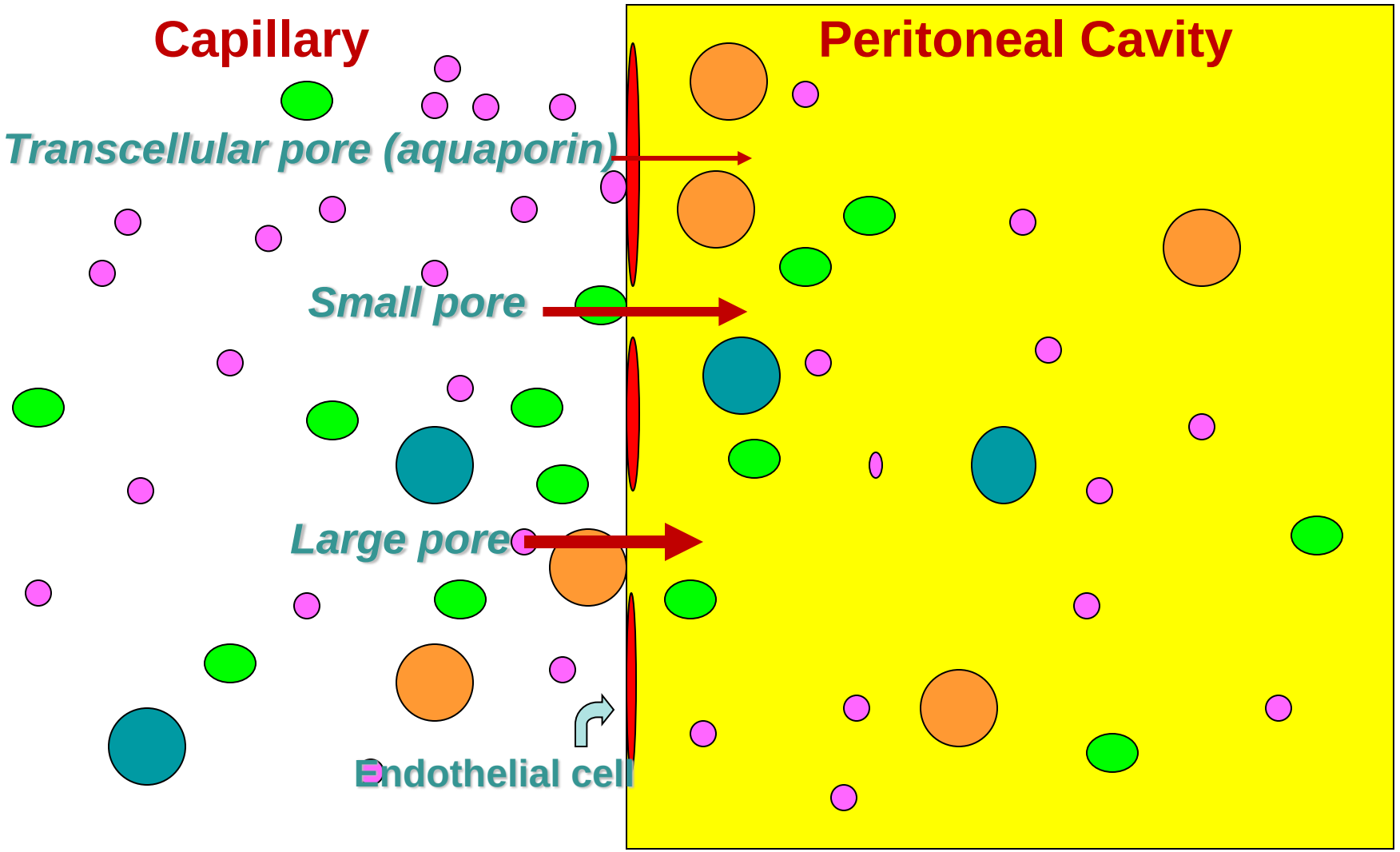
Thirsty in the Morning – Why?

- a 42 year old woman with IgA nephropathy is on night cycler PD
- the nephrologist wants to impress the administrator and CMS with a high Kt/V urea and prescribes 5 cycles over 9 hours, 2.5% dialysate
- The patient complains of marked thirst in the morning and has to drink several glasses of water

What is the One Best Answer?

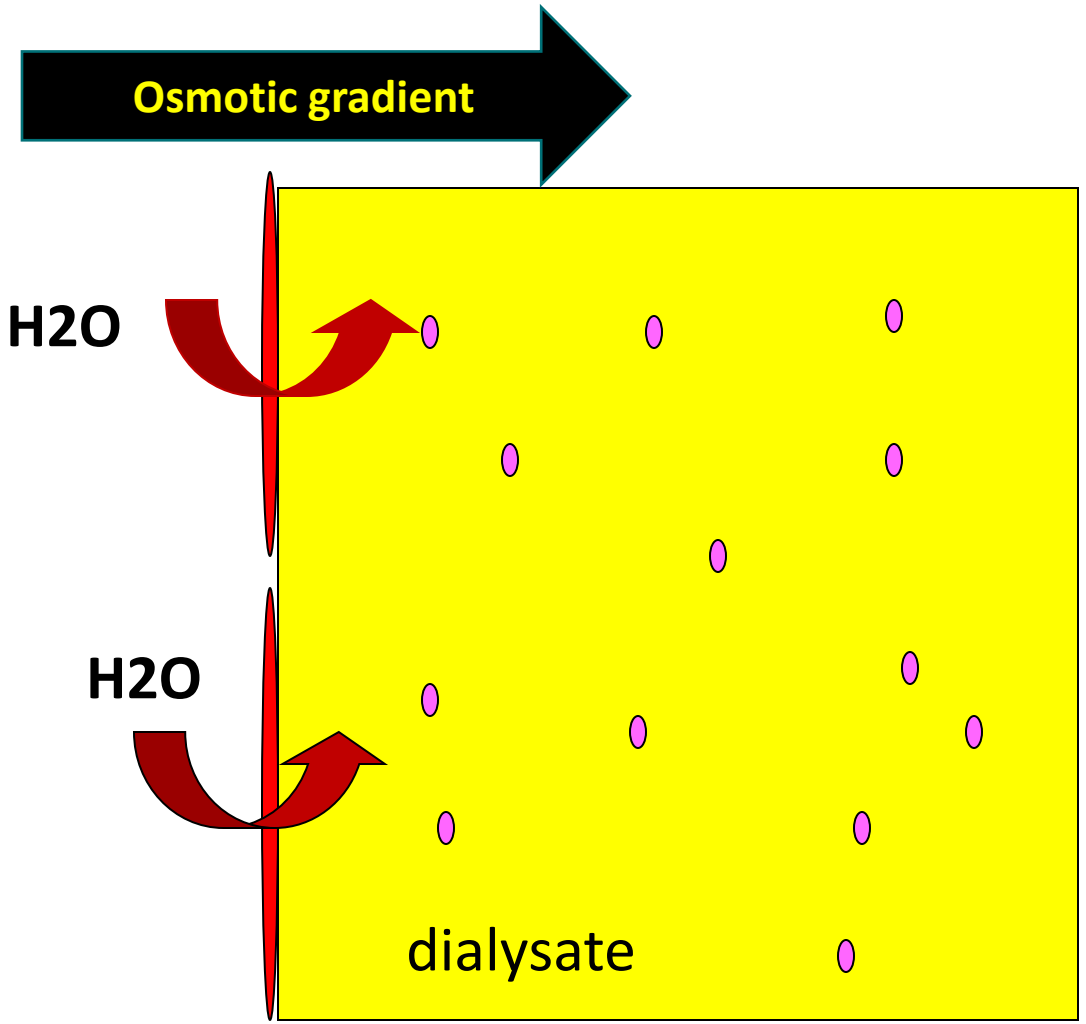
A. The sleep apnea syndrome seen in dialysis patients leads to mouth breathing and thirst.
B. The patient may be hypernatremic in the morning because of sodium sieving on PD.
C. The glucose absorption increases the serum osmolality and drives thirst.
D. The morning thirst is the result of resetting of the osmostat because of the cycling PD.

Transport in Peritoneal Dialysis
The Three Pore Model



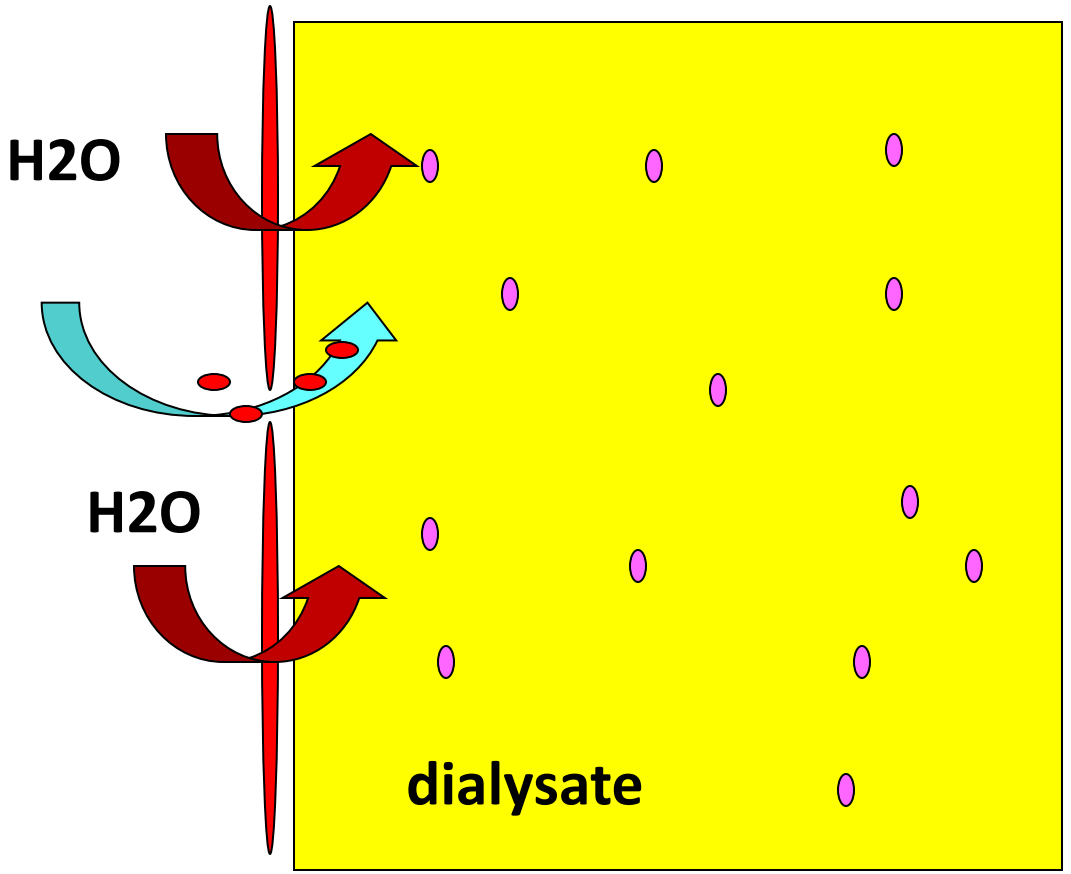
Sodium Sieving in Peritoneal Dialysis

1. Water movement through aquaporins



Sodium Sieving in Peritoneal Dialysis

2. Na^+ and H_2O movement through small pores



Sodium Sieving

- more water than sodium moves into the peritoneal cavity at the beginning of UF
- sodium is held back or "*sieved*" at the aquaporin
- sodium diffuses into the dialysate more slowly via the intercellular pores
- short dwells will lead to more water than sodium removal

PD Patients in the US Get a Lot of Exchanges!

Giles et al Clin J Am Soc Nephrol 2024

Table 2. Summary of day 120 peritoneal dialysis prescriptions (*N*=11,659)

Prescription Information	Nocturnal APD Patients (*n*=10,037, 86%)	Daytime+Nocturnal APD Patients (*n*=1622, 14%)
	Mean±SD or *No* (%)	Mean±SD or *No.* (%)
Weekly frequency of PD treatments		
≤6	232 (3)	14 (1)
7	9774 (97)	1608 (99)
Estimated dry weight, kg	83.9±21.5	90.2±23.4
Total number of cycles[a]	4.9±1.3	6.4±1.6
Total treatment volume,[b] L	9.3±2.5	11.4±3.1
Total dwell time,[c,d] min	420 (360–570)	1440 (555–1440)

Thirsty in the Morning: Choose the Best Answer

A. The sleep apnea syndrome seen in dialysis patients leads to mouth breathing and thirst.

B. The patient may be hypernatremic in the morning because of sodium sieving on PD.

C. The glucose absorption increases the serum osmolality and drives thirst.

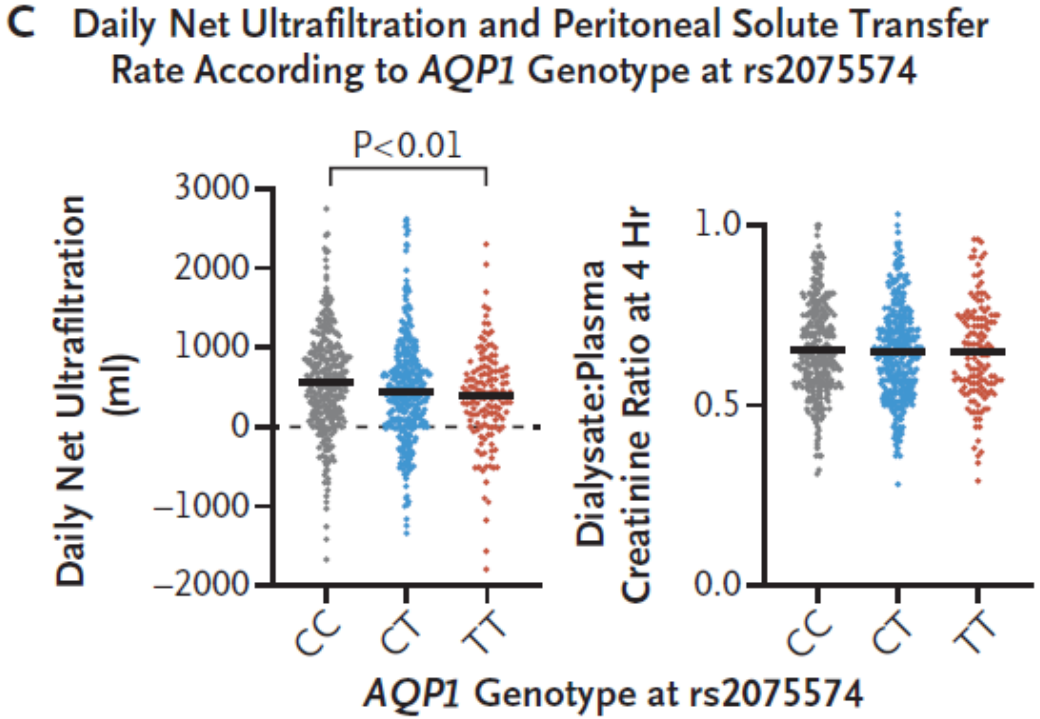
D. The morning thirst is the result of resetting of the osmostat because of the cycling PD.

Explanation

- *Aqua*porins allow only *aqua* to cross the endothelial membrane
- Rapid exchanges with hypertonic dialysis fluid will lead to more water removal compared to sodium removal
- The result will be hypernatremia, a powerful drive for thirst

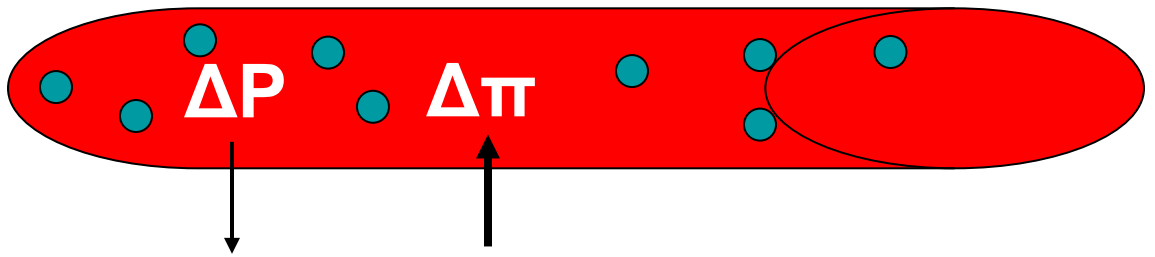
The Plot Thickens: There are Different Aquaporin Genotypes *(Morelle N Eng J Med 2021)*

- there are genetic variants of aquaporins leading to different amounts of ultrafiltration
- Registry studies *suggest* that these changes may impact survival



Icodextrin – Mechanism of Action

Colloid osmosis - analogous to the Starling force of albumin causing fluid flux from the interstitial to vascular compartment



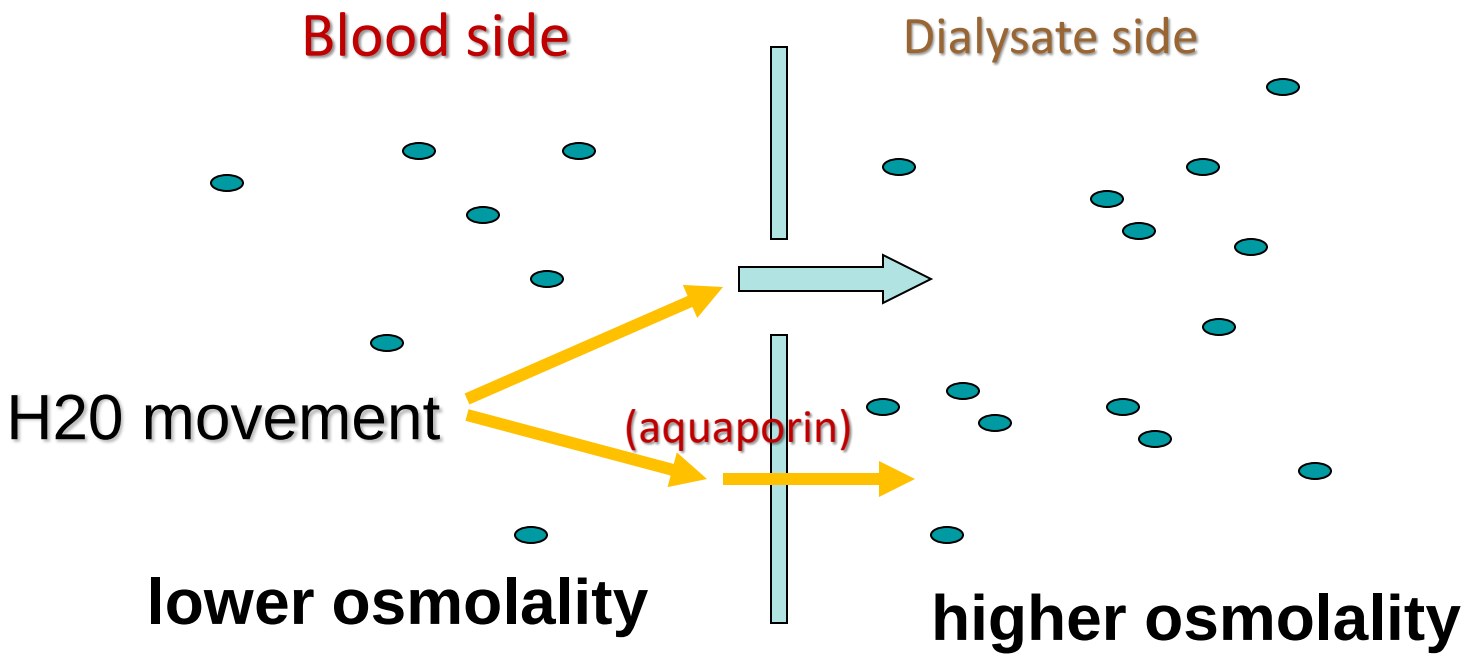
Plasma osm

=

Interstitial osm

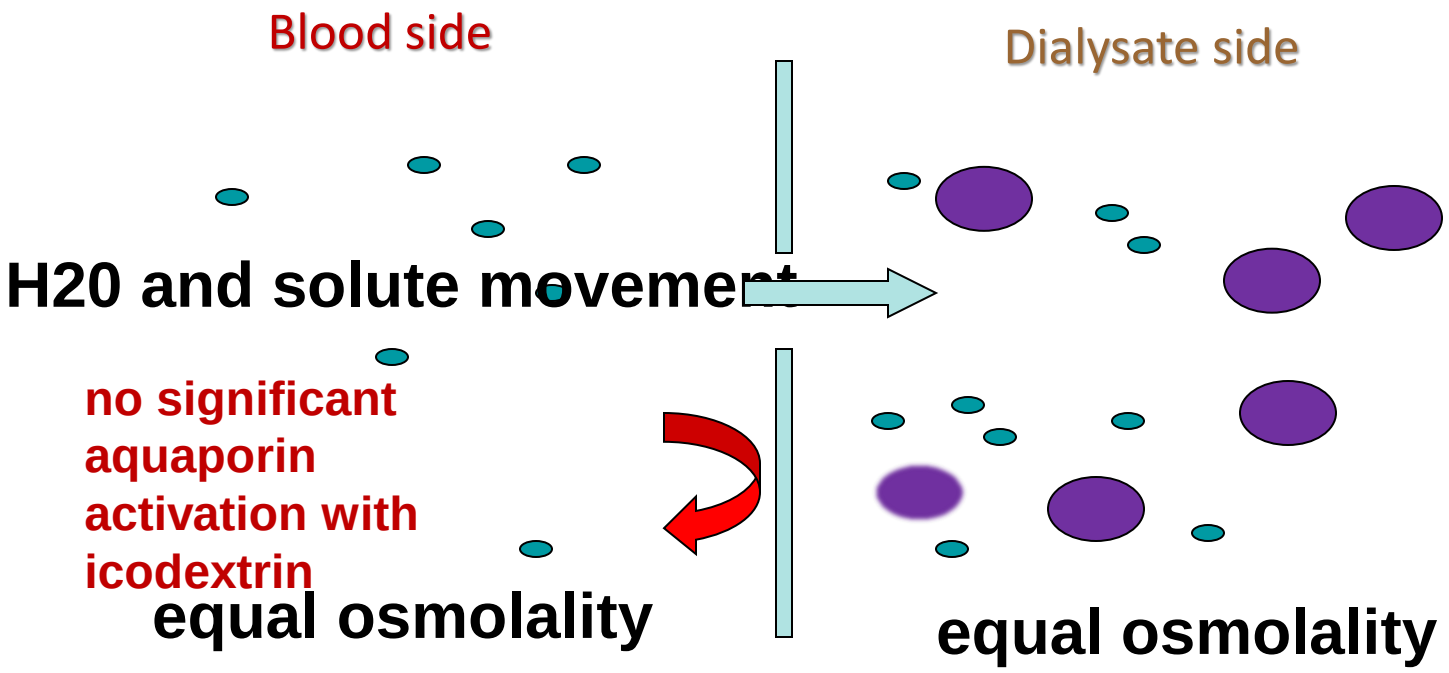
Dextrose vs Icodextrin

Crystalloid osmosis with dextrose

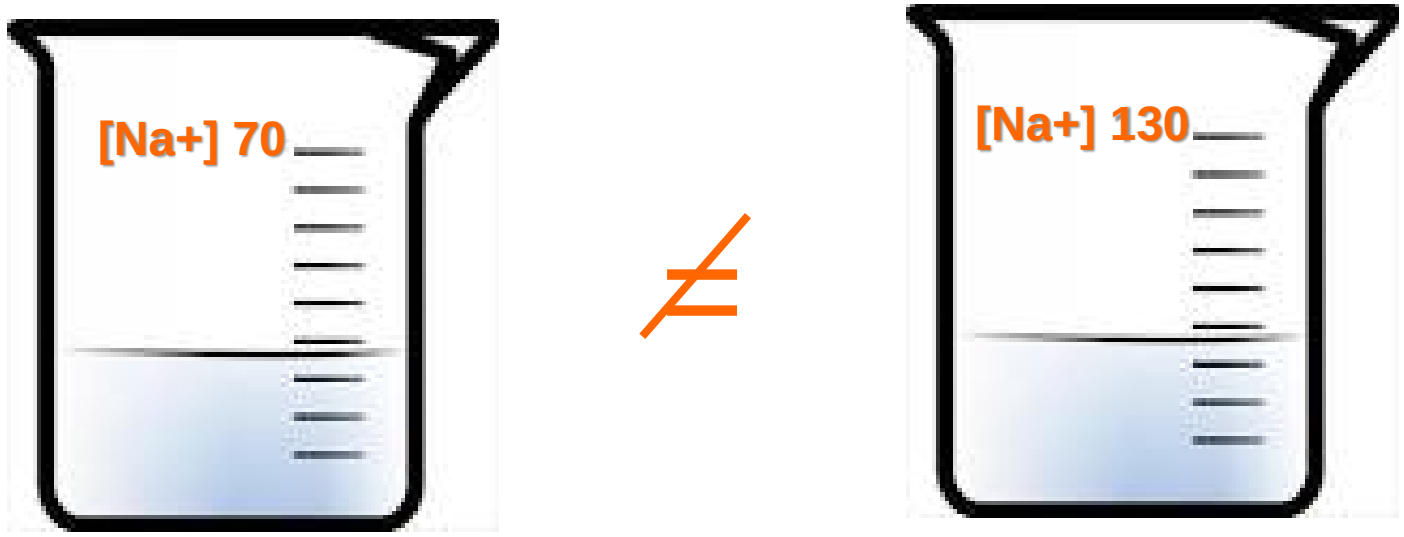


Dextrose vs Icodextrin

Colloid osmosis with icodextrin



No Sodium Sieving with Icodextrin: So Not all Ultrafiltrate is the Same



1 Liter of UF with dextrose

1 Liter of UF with icodextrin

Marvin on APD (Part I)

- Marvin is a 35 year old man with chronic GN who starts on APD, 2.0L X 3 exchanges over 8 hours at night, last fill 2L.
- Residual kidney function is GFR 9 ml/min, U_{out} 960 ml/24h.
- Typical UF on the cycler is 800 ml, average initial drain volume of his day dwell is 1700 ml when he goes on the cycler at night.

Which ONE Statement is FALSE?

a) He is protected from ECF volume overload in part by the residual urine volume.
b) He probably has borderline adequacy and should have his dialysis prescription increased, or be converted to hemodialysis.
c) He should be advised to avoid nephrotoxic insults, such as NSAID's and COX-2 inhibitors.
d) Eight hours of APD is appropriate for many patients.

Which ONE Statement is FALSE?

a) He is protected from ECF volume overload in part by the residual urine volume.
b) He probably has borderline adequacy and should have his dialysis prescription increased, or be converted to hemodialysis.
c) He should be advised to avoid nephrotoxic insults, such as NSAID's and COX-2 inhibitors.
d) Eight hours of APD is appropriate for many patients.

Explanation

- Marvin is on a reasonable PD regimen (8.0 L/day)
- in addition, he has a lot of residual kidney function
- there should be no question of adequacy issues at this point
- (he would probably even do fine with a lower dose of PD)

Adequacy of Peritoneal Dialysis

The strength of PD lies in

- continuous therapy 24/7
- preservation of residual kidney function (RKF) compared to HD
- good middle molecule clearance (by RKF and the peritoneal membrane)

None of these is captured by Kt/V urea

Adequacy of Dialysis in PD

Guidelines

PERITONEAL DIALYSIS INTERNATIONAL

Peritoneal Dialysis International
2020, Vol. 40(3) 244–253

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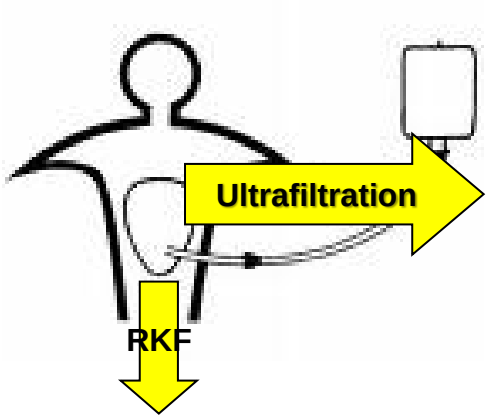
International Society for Peritoneal Dialysis practice recommendations: Prescribing high-quality goal-directed peritoneal dialysis

High-Quality, Goal-Directed PD ISPD Guidelines 2020

- Shared decision-making
- Take into consideration life goals
- Minimize symptoms and the burden of therapy
- Preserve residual kidney function
- Focus also on
  - nutrition
  - volume status

Fluid Balance in Peritoneal Dialysis

Intake		Output
Na+ and water	=	**Urine and UF**



Volume Overload in PD

Intake

- excessive salt and water consumption

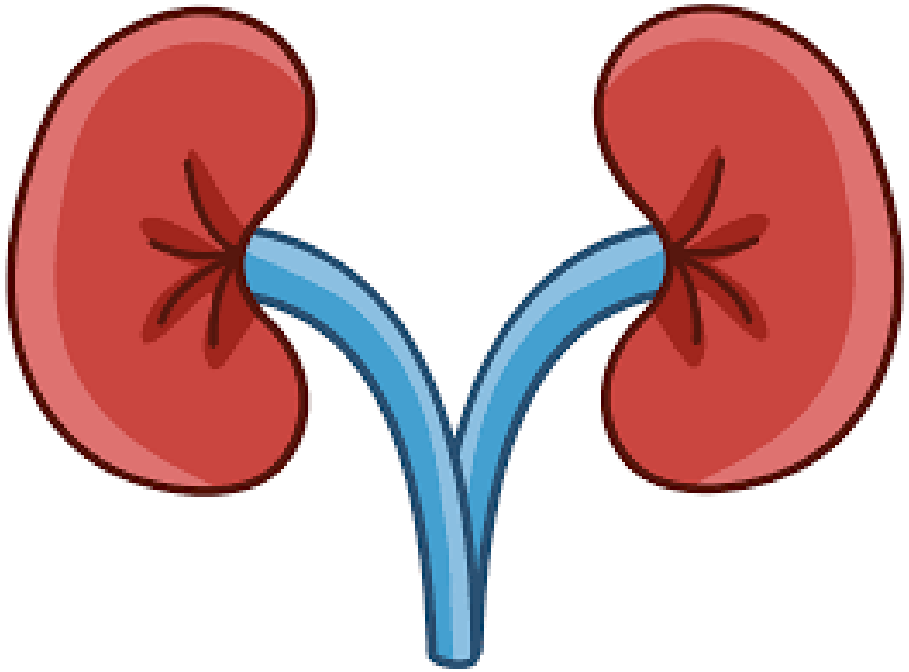
Output

- loss of residual kidney function
- use of the wrong dialysis fluid
- failure of peritoneal membrane to respond (true ultrafiltration failure)
- mechanical problems like leaks

Volume Overload in PD

Output: Loss of Residual Kidney Function

- probably the commonest cause of progressive fluid overload
- rate of loss of RKF is variable and unpredictable from patient to patient
- use diuretics to augment urine Na^+ & water output
  - eg furosemide, metolazone



Try to Protect the Kidney Function

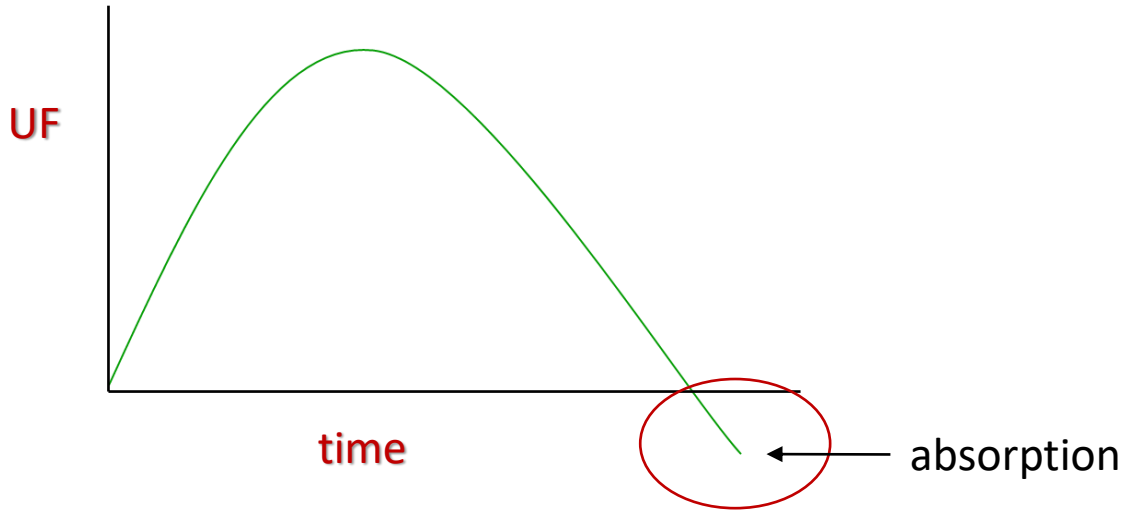
- avoid NSAID's, COX 2-inhibitors, dye studies, aminoglycosides, volume depletion
- continue immunosuppression for failed transplant kidneys that still have function

Treat your dialysis patient with RKF just like you would your CKD 3 or 4 patient

Volume Overload (continued)

Use of the wrong type of PD fluid

- usually this means failure to account for the risk of fluid absorption during the long dwell



Volume Overload (continued)

Tackling the long dwell:

1. use icodextrin or a more hypertonic dialysate (e.g. 2.5%)
2. break up the long dwell
   - day dry (only if there is a lot of RKF)
   - “mid-day” exchange in APD
   - drain out day exchange in APD after a few hours

Fluid Absorption During the Long Dwell

Or, it may not need any intervention

if there is a lot of urine volume, may compensate for fluid absorption

- e.g. patient on APD
  - last fill 2L
  - initial drain 1.5 L (so .5L fluid absorption)
  - urine output 1.0 L
  - patient is clinically euvolemic

No Need to Change the Prescription

Volume Overload in PD

Output dependent

- failure of the peritoneal membrane to allow ultrafiltration (membrane failure)
- mechanical failure of dialysis procedure (leaks, etc)

True Peritoneal Membrane Failure

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

or

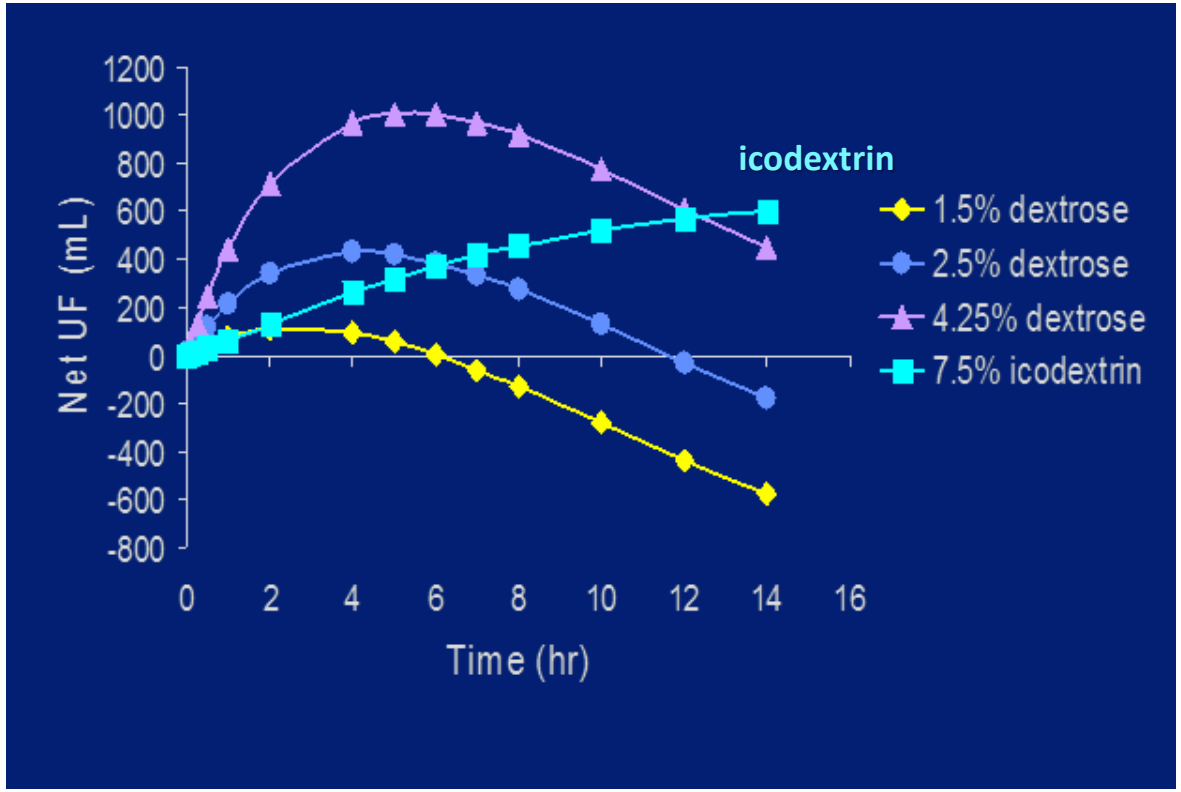
Failure to ultrafilter > 400 ml using a 4.25% bag for 4 hours (the Rule of 4's)

True Peritoneal Membrane Failure

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

Management of Rapid Transporters (I)

- reinforce salt and water restriction
- use more hypertonic dialysate
- icodextrin can be quite helpful here (as effective in high transporters as other transport types)



Management of Rapid Transporters (II)

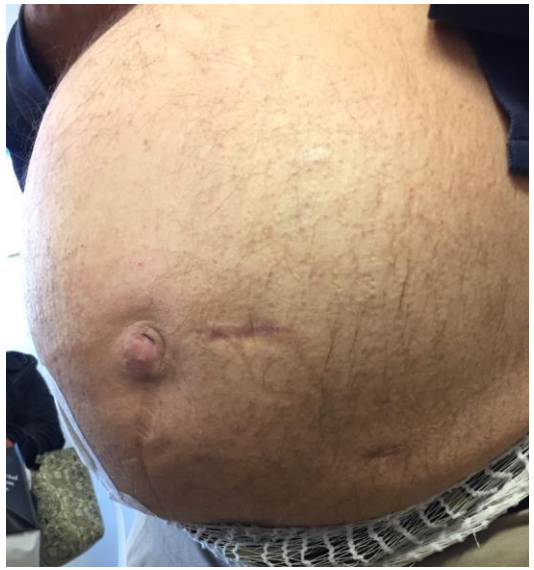
- “push” residual urine output (diuretics)
- APD with dry day, or drain out last fill at lunch (if enough RKF)
- once anuric, watch closely for volume overload

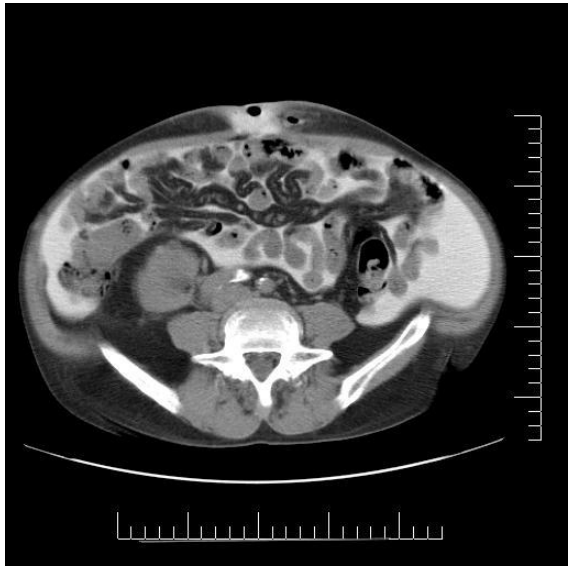
Consider transfer to hemodialysis if patient is chronically overloaded
(start talking about vascular access placement with the patient)

Volume Overload (continued)

Output dependent

- mechanical failure of dialysis procedure





Part II – Marvin Gets Puffy

- 1 year later, Marvin comes to clinic complaining of increasing ankle edema. The BP, which had been normal, is now 150/100.
- The dialysis prescription is unchanged. Serum creatinine, which had been 10.6 mg/dl at the start of dialysis, is now 13.8 mg/dl.

Which ONE Statement fits Marvin BEST?

a) The increased serum creatinine reflects a failure of solute transport across the peritoneum.
b) He most likely has peritonitis and the acquisition of a high transporter state.
c) The new onset hypertension is likely the result of acquired renal cystic disease.
d) Both the increased serum creatinine and peripheral edema can be explained by decreased residual kidney function.

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Explanation

- a decrease in RKF (both solute clearance and salt and water excretion) would explain the changes in Marvin over the past year
- an increase in serum creatinine is much more likely to be the result of a decrease in kidney creatinine clearance than to membrane changes
  - peritoneal membranes tend to become more, not less, permeable to solutes over time

Part II – Marvin Gets Puffy

How to help Marvin (APD 2.5L x3, 2L last fill)

- dietary salt restriction
- use high dose diuretics
- last fill:
  - mid-day exchange, or
  - icodextrin last fill, or
  - both (icodextrin X 10h, 2.5% X 6h)

Summary of Important Points (I)

Peritoneal Equilibration Test

- The “rapid transporter” has increased peritoneal vascularity and transports small solutes quickly; but loses the glucose osmotic gradient quickly and may have problems with ultrafiltration
- The “slow transporter” has slower removal of small solutes but better ultrafiltration

Summary of Important Points (II)

- short hypertonic PD dwells lead to removal of more water than sodium, leading to hypernatremia
  - avoid short dwells except in rapid transporters
- residual kidney 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
  - RKF
  - volume status
  - burden of therapy
  - and quality of life

References

1. Perl J, Dember LM, Bargman JM et al
   The Use of a Multidimensional Measure of Dialysis Adequacy – Moving Beyond Small Solute Kinetics
   Clin J Am Soc Nephrol 2017. 12(5): 839-47
2, Rodriguez-Carmona A and Perez Fontan M
   Sodium removal in patients undergoing CAPD
   Perit Dial Int 22: 705-13, 2002
3. Bargman JM
   Mistakes in Dialysis: We Use Kt/V As a Measure of Adequacy of Dialysis
   Semin Dial 29(4): 258-9, 2016
4. ISPD Guidelines: Prescribing High Quality Goal-Directed Peritoneal Dialysis
   Perit Dial Int 40 (3): 244-253, 2020
5. Giles HE, Parameswaran V, Lasky R et al
   Trends in automated Peritoneal Dialysis Prescriptions in a Large Dialysis Organization in the United States
   Clin J Am Soc Nephrol 19: 723-731, 2024

Clinical Trials

- Paniagua R, Amato D, Vonesh E et al
  Effect of increasing peritoneal clearance on mortality rates in peritoneal dialysis: ADEMEX, a prospective randomized controlled trial
  J Am Soc Nephrol 13: 1307-20, 2002
- Churchill D et al
  Adequacy of Dialysis and Nutrition in Continuous Peritoneal Dialysis: Association With Clinical Outcomes
  J Am Soc Nephrol 7: 198-207 1996
- Bargman J et al
  Relative Contribution of Residual Renal Function and Peritoneal Clearance to Adequacy of Dialysis: A Re-Analysis of the CANUSA Study
  J Am Soc Nephrol 12 (10): 2158-2162 2001
- Yan H et al
  Three versus 4 Daily Exchanges and Residual Kidney Function Decline in incident CAPD Patients: A Randomized, Controlled Study
  Am J Kidney Dis 69 (4): 506-513, 2017