



Prescription Management: The Tough Cases Western Canada PD Days

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A review of ancient history

- ❑ my recruitment interview with the Chief of Medicine (also a nephrologist) for a faculty position working in PD at Toronto Western Hospital
- ❑ **Me:** *I would love this job in PD, but I have never done PD before*
- ❑ **Chief:** *Don't worry, you can learn PD in 20 minutes*

What are “The Tough Cases”?

- ☐ the patient with ultrafiltration failure (I will discuss tomorrow)
- ☐ the patient with recurrent heart failure
- ☐ the anuric patient
- ☐ the rapid transporter
- ☐ the obese patient or one with a crowded abdomen

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James W – True Story

71 year old man with type II DM and ischemic cardiomyopathy

recurrent episodes of diuretic-resistant CHF necessitating admission to CCU for parenteral diuretics and dobutamine infusion

one episode of HD for ultrafiltration

6 hospitalizations in the previous year

GFR approximately 20 ml/min

James W (2)

agreed to a trial of PD to attempt to manage ultrafiltration and avoid hospitalization

PD catheter inserted without incident

prescribed night cyclor 2L exchanges X 3 over 8h, day dry

average UF 500-800 ml

James W (3)

no episodes of CHF, but rapid decline in RKF to almost anuria over 6 months

icodextrin day dwell added, average UF 200-400 ml

years 1,2: NO admissions to hospital for CHF

- one admission for coag neg staph peritonitis, resolved quickly

James W (4)

Year 3: worsening of peripheral arterial disease, gangrene of feet
arterial stenting unsuccessful
patient refused amputation
died of sepsis likely from the necrotic feet

The Cardiorenal Syndrome (CRS)

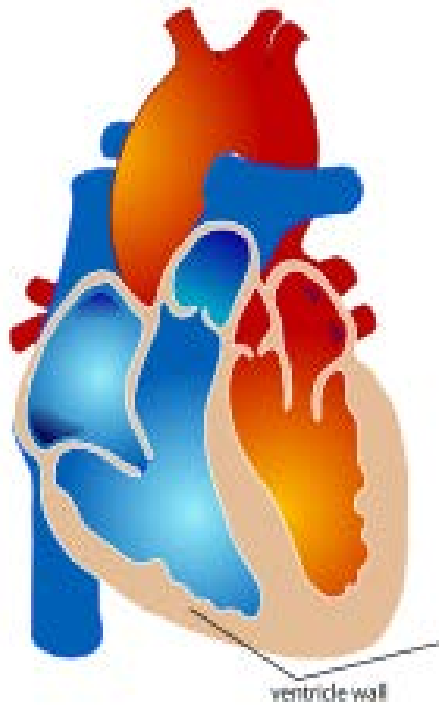
puts a name to something we see very often

“acute or chronic dysfunction in one organ may induce acute or chronic dysfunction in the other organ”

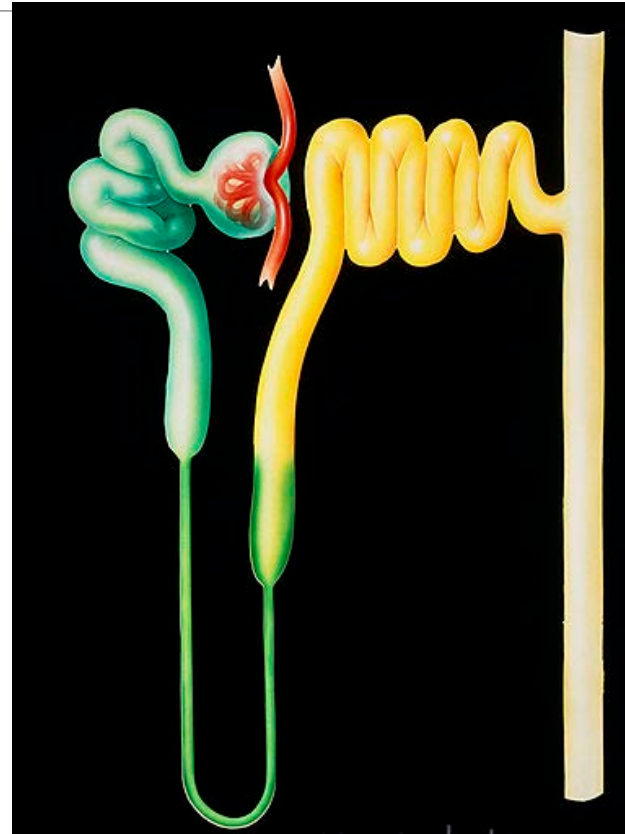
- (Ronco et al Blood Purif 2009)

we will focus on CRS Type 2 (chronic heart failure leading to CKD)

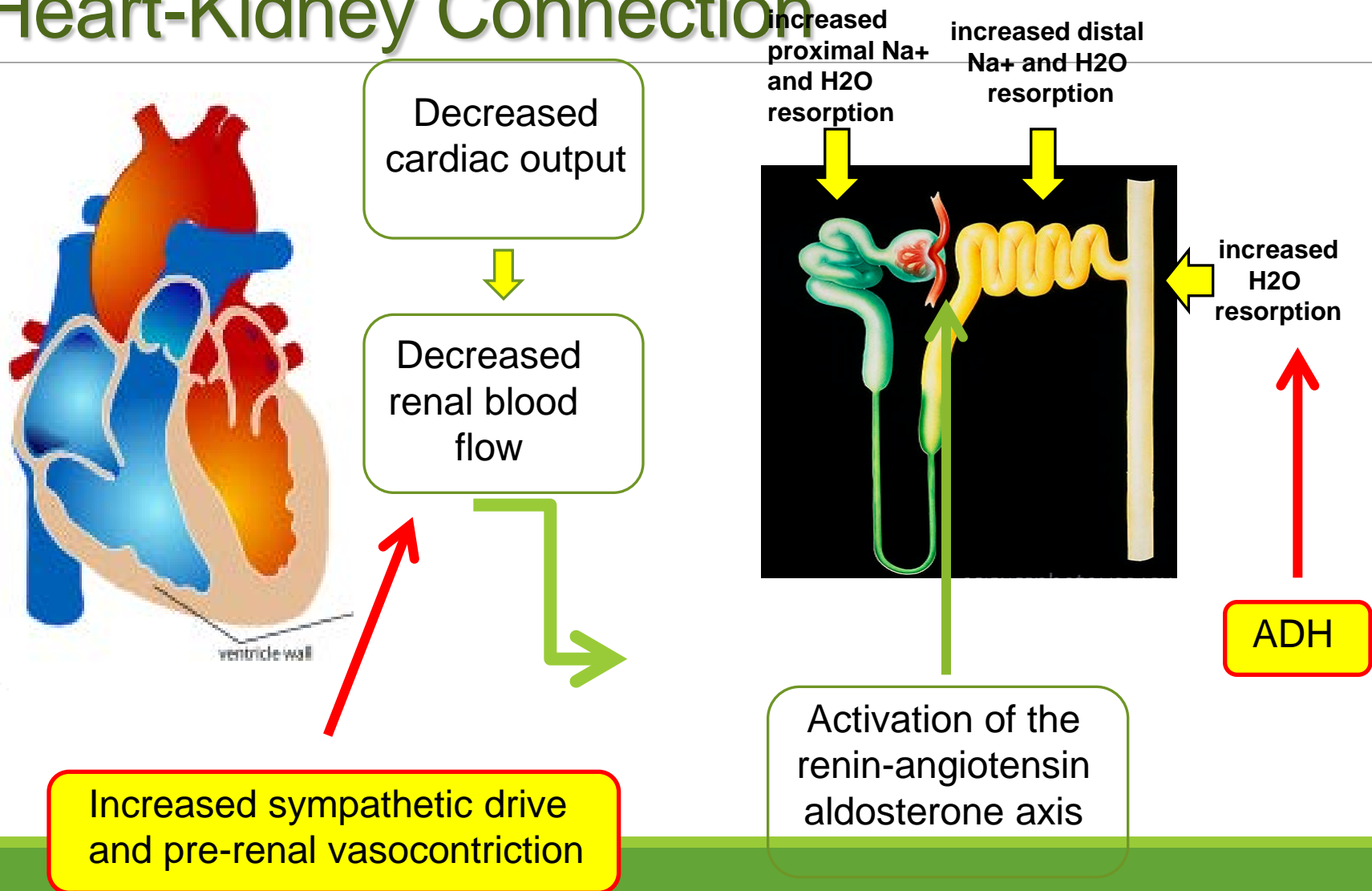
The Heart-Kidney Connection



Decreased
cardiac output



The Heart-Kidney Connection



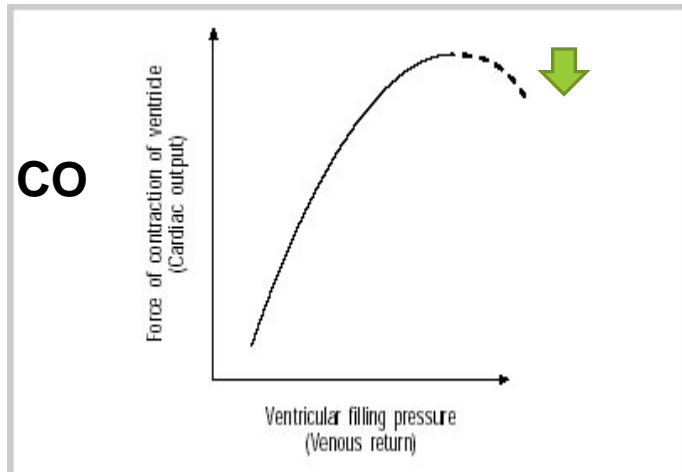
The Cardiorenal Syndrome

- ❑ these maladaptive responses lead to salt and water retention
 - edema
 - congestive heart failure
- ❑ chronic hypoperfusion leads to functional, and then fixed decrease in GFR

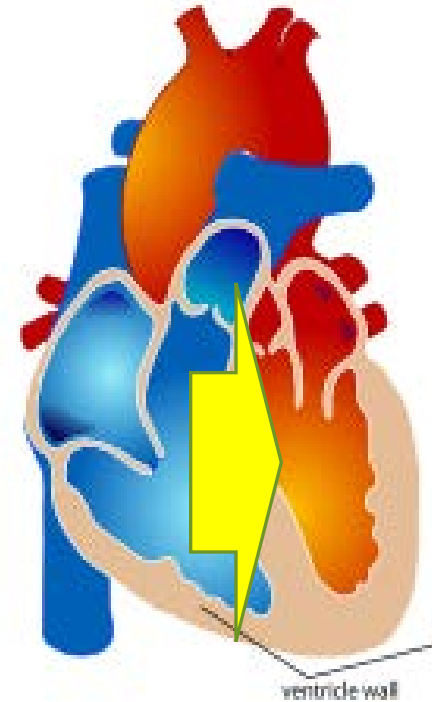
“Hypoperfusion Nephropathy”

- ☐ gradual decline in GFR
- ☐ gradual shrinkage of kidney mass
- ☐ oscillation of serum creatinine
- ☐ episodes of acute on chronic kidney injury

Salt and Water Retention Further Worsens Cardiac Output

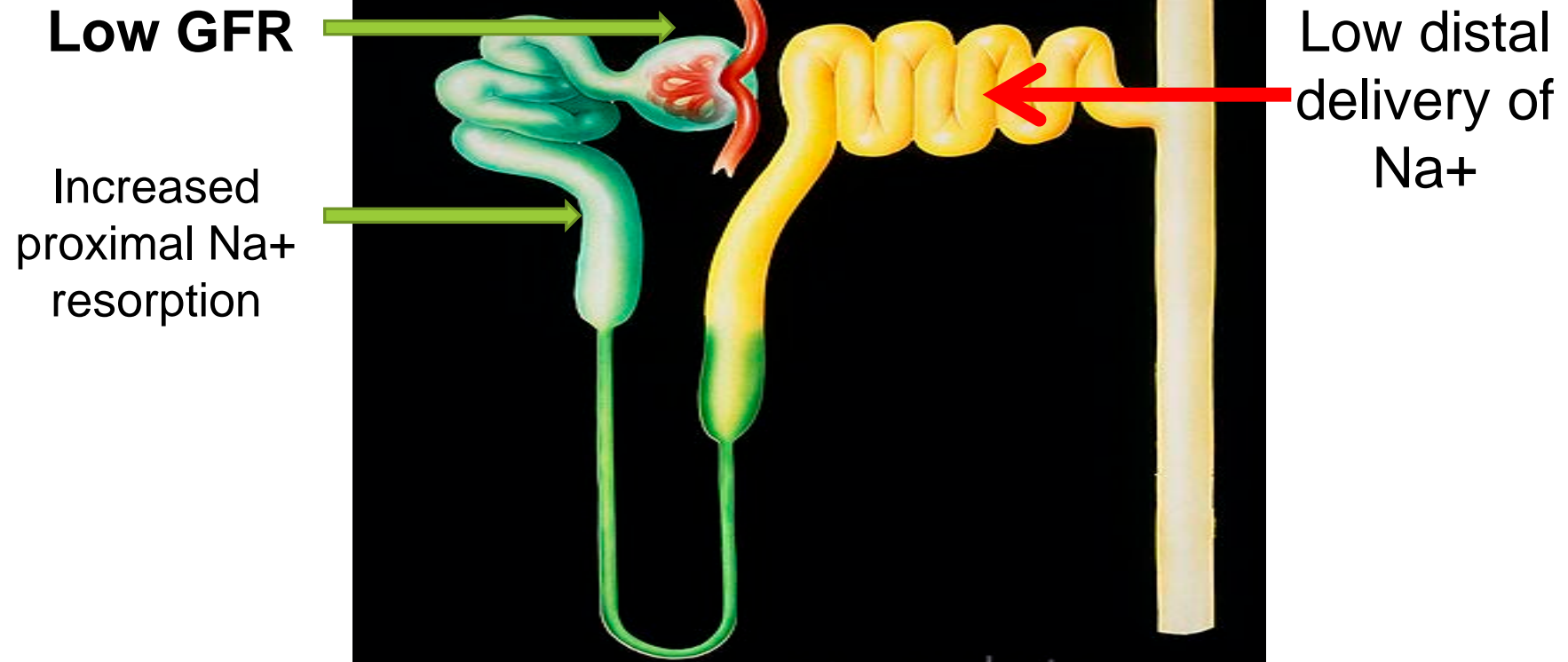


The Frank-Starling Curve:
increased ventricular filling
pressure leads to decreased
cardiac output



Expansion of the right ventricle
Impairs left ventricular filling

Diuretic Resistance



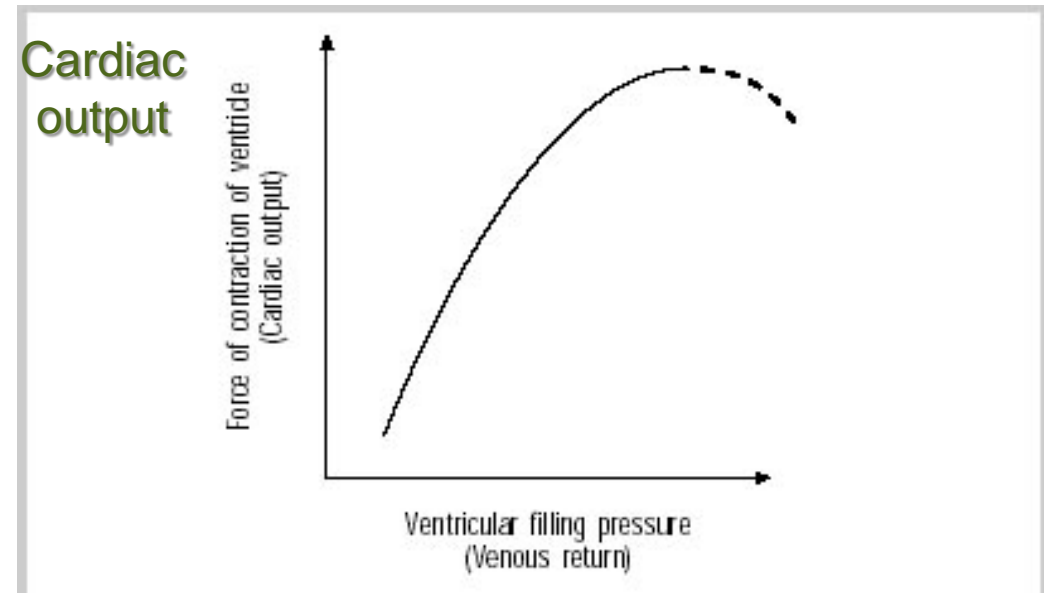
Rationale for Ultrafiltration in General

- ❑ Treat symptoms of extracellular fluid volume overload
 - congestive heart failure
 - peripheral edema
- ❑ to decrease sympathetic drive
- ❑ removal of cardiotoxic or negative inotropic factors?

Rationale for Ultrafiltration in General (2)

Restore diuretic responsiveness

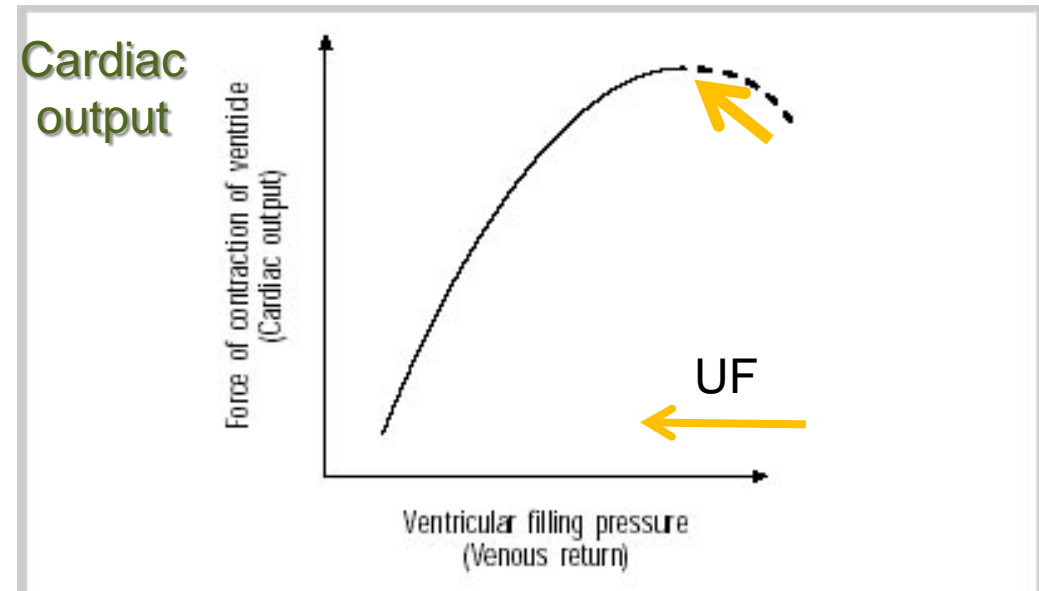
- move LV back up the Frank-Starling curve
- reduce preload and right ventricular impingement of left ventricle
- improve cardiac output
- improve GFR



Rationale for Ultrafiltration in General (2)

Restore diuretic responsiveness

- move LV back up the Frank-Starling curve
- reduce preload and right ventricular impingement of left ventricle
- improve cardiac output
- improve GFR



Rationale for PD in Particular

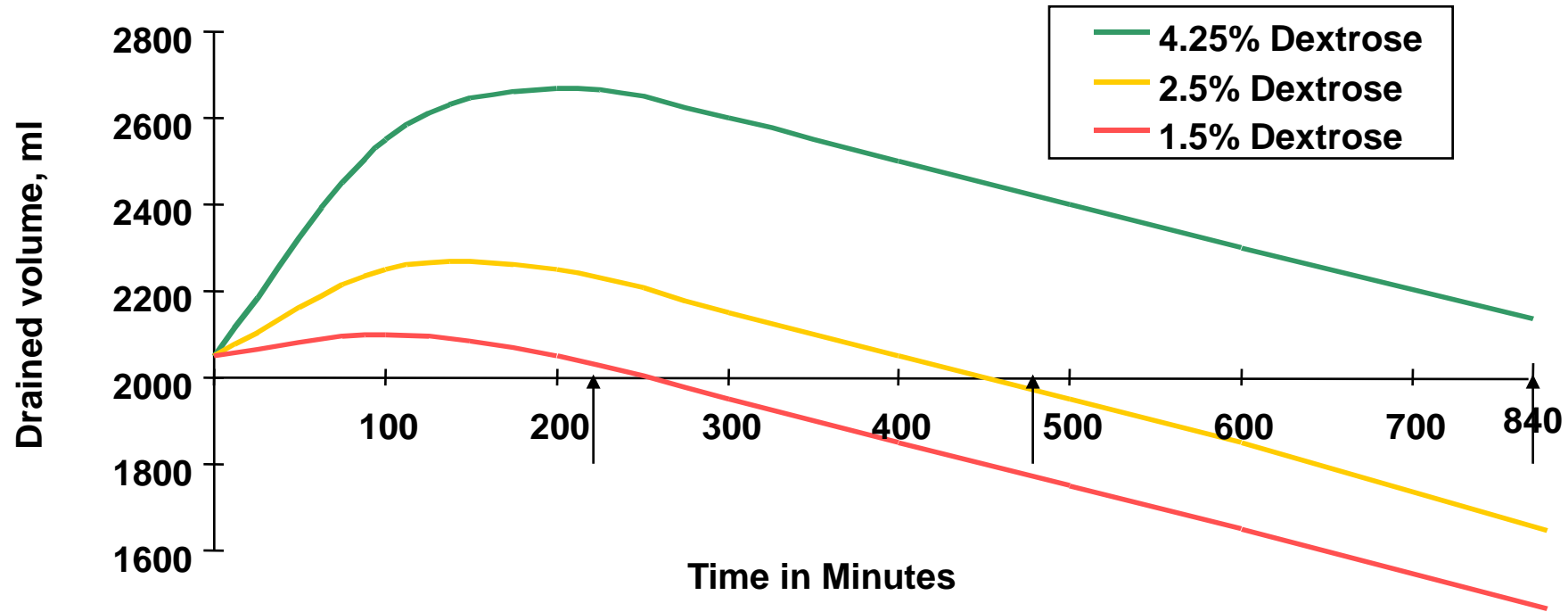
- ☐ continuous therapy, or at least daily therapy
- ☐ better tolerated than HD in the hypotensive patient
- ☐ no extracorporeal circuit to fill up
- ☐ slow, gentle ultrafiltration
- ☐ no myocardial stunning

Other Advantages of PD for Cardiorenal Syndromes

- ❑ no need for arteriovenous access
 - high flow fistulas can increase cardiac work and exacerbate heart failure
- ❑ dextrose-based solutions ultrafilter more water than sodium
 - correction of hyponatremia
- ❑ very low risk of bacteremia compared to HD
 - important if there is a pacemaker or LVAD in place

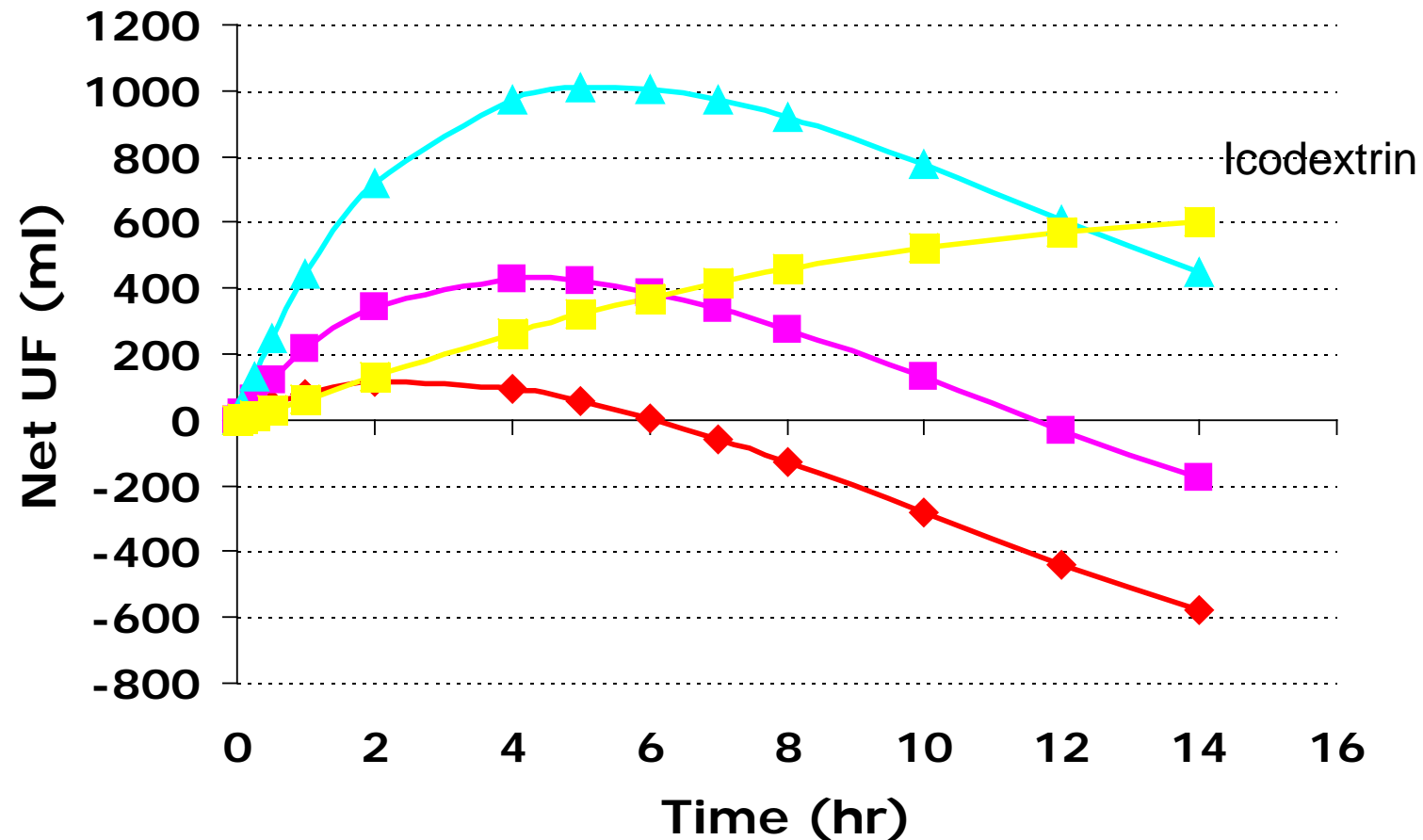
(Thomas et al Perit Dial Int 2012)

Good Ultrafiltration with PD



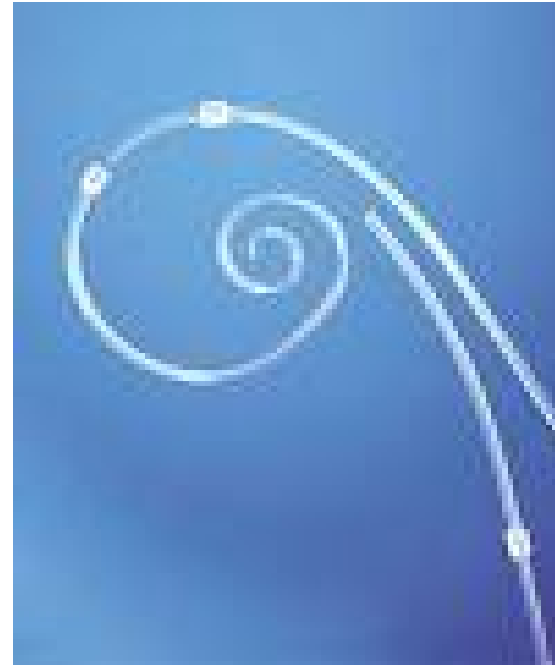
- typical UF with a 4.25% dextrose solution is 1000 ml over 4 hours
= 250 ml/hour !

Icodextrin Produces Slow and Steady UF Over the Long Dwell



Disadvantages of PD

- ❑ may be harder to get a PD catheter inserted than a venous catheter
 - availability of OR time
 - surgical expertise
 - less of a problem for radiologic or bedside insertions

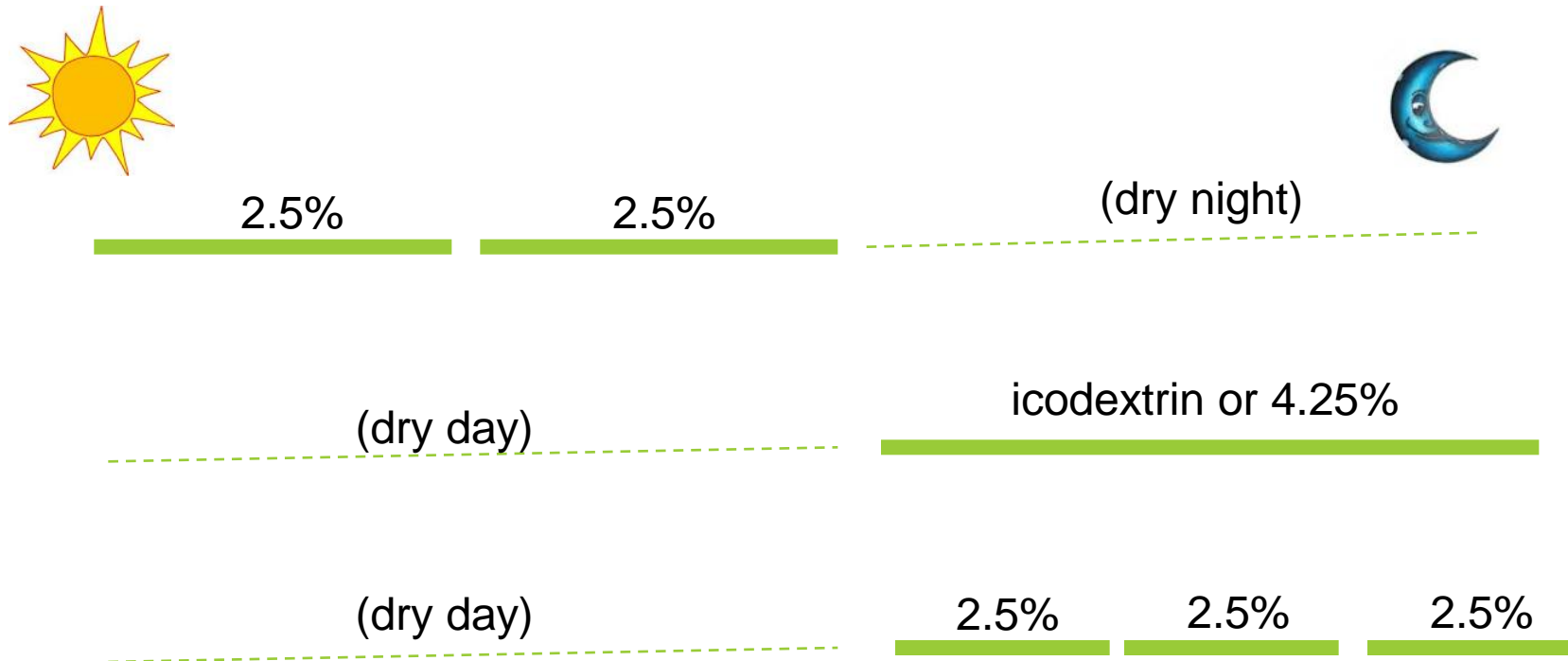


Disadvantages of PD

- ❑ the catheter may not work
- ❑ it may stop working
 - constipation, constipation, constipation
- ❑ it may leak
- ❑ in chronic CRS, patient or caregiver has to be taught the technique
- ❑ ultrafiltration is not predictable and may vary over time
- ❑ risk of peritonitis

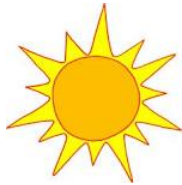
What Kind of PD Prescription?

Scenario 1: Adequate Solute Clearance by Residual Kidney Function



What Kind of PD Prescription?

Scenario 2: Need for both solute clearance and fluid removal



2.5%

2.5%

(2.5% or icodextrin)



(2.5%)

(1.5%)

(2.5%)

icodextrin or 4.25%

(icodextrin or 4.25%)

2.5%

2.5%

2.5%

Won't All that Glucose Harm the Peritoneal Membrane?

- ❑ the evidence for the association of glucose exposure and long-term peritoneal membrane function is tenuous
- ❑ these patients typically don't survive for a long time on dialysis anyway

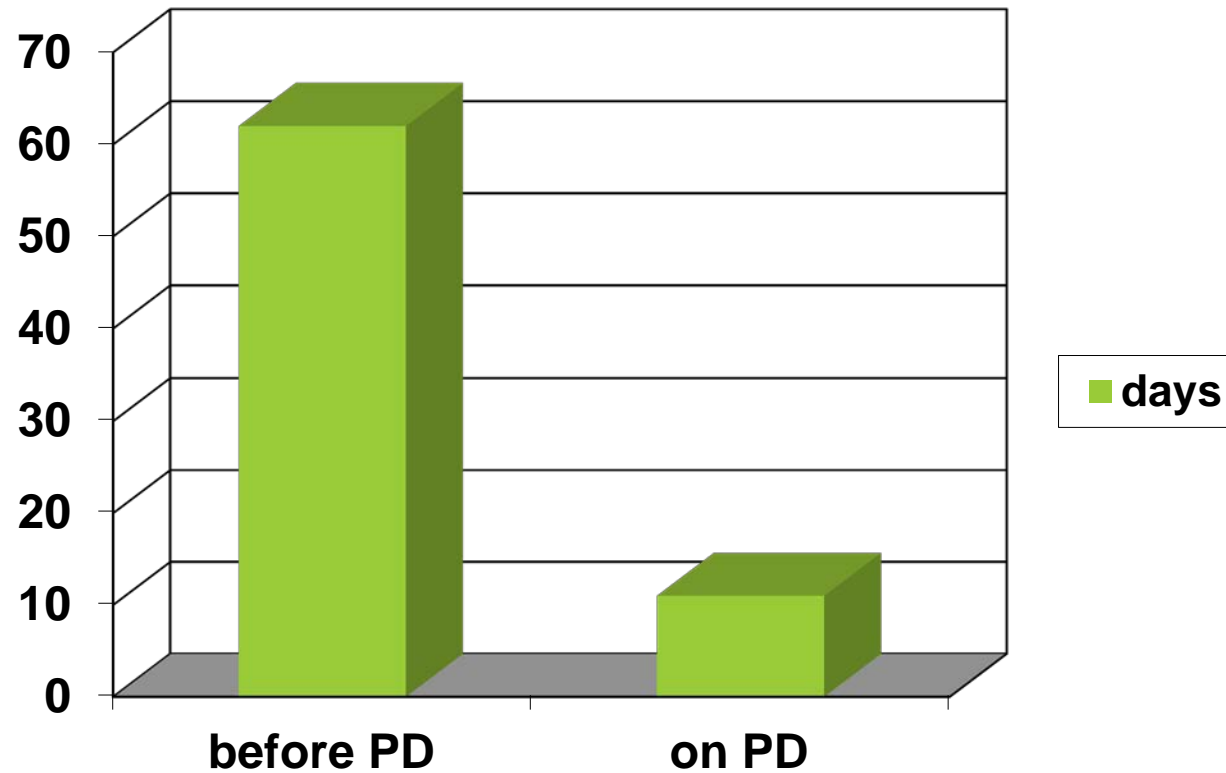
Add question icon

PD for CHF: Recent Studies

- mean daily peritoneal UF 670 +/- 225 ml
- GFR did not change over the study (mean F/U 15 months) (*surprising to me*)
- peritonitis very uncommon

Sanchez et al Neph Dial Transpl 2010

Days in Hospital/Year



Sanchez Neph Dial Transpl 2010

Change in Functional Status Before and During PD

NYHA Functional Class

4	4	3	3	4	3	3	4	4	4	4	3	4	4	3	3	4	Before PD
3	2	1	2	2	1	2	2	2	2	2	1	2	2	2	2	2	During PD

- 3 patients died of heart failure at 5, 12 and 16 months
- improved quality of life
- cost-effective

Sanchez Neph Dial Transpl 2010

Survival Comparisons

Median survival 16 months

- *Cnossen Neph Dial Transpl 2012*

Mean survival 17.3 months

- *Elhalel-Dranitzki Neph Dial Transpl 1998*

Mean survival 12.7 months

- *Ryckelynck Adv Perit Dialy 1997*

More Recent Studie



Bertoli (*Perit Dial Int 2013: 10 centers in Italy*)

- incremental dialysis for UF: 30/48 pts used 1 icodextrin overnight, 13 intermittent APD, 5 had 2 exchanges/day
- improved NYHA score
- hospitalizations went from 43 to 11 days/pt-year
- survival 56% at 2 years

Courivaud (*Perit Dial Int 2013: 2 centers in France*)

- improved LVEF over first year
- hospitalizations for decompensated heart failure improved from 40 to 4 days/pt-year
- 42% mortality in the first year

Rizkallah Clin Nephrol (*Clin Nephrol 2013 1 center Canada*)

- average 7 kg weight loss, restoration of diuretic responsiveness
- reduced hospitalizations and length of stay

Summary of PD for the Patient with Recurrent Heart Failure

- ❑ PD has many advantages for gentle continuous ultrafiltration
- ❑ there is probably more promise for its use in chronic (CRS 2) heart failure than for acute (CRS1) heart failure
- ❑ overall survival remains reduced due to cardiac and non-cardiac co-morbidities
- ❑ there is evidence for reduced hospitalization for CV-related events, and improved quality of life, even without improved left ventricular performance

What are “The Tough Cases”?

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- ☐ **The anuric patient**
- ☐ The rapid transporter
- ☐ The obese patient or one with a crowded abdomen

The Anuric Patient

- ☐ There seems to be an impression that these patients should be transferred to HD
- ☐ I don't understand or agree with this
- ☐ There is no evidence that they do any better on HD, and they likely will have a permcath
- ☐ But more attention has to be paid to the PD prescription, especially ultrafiltration

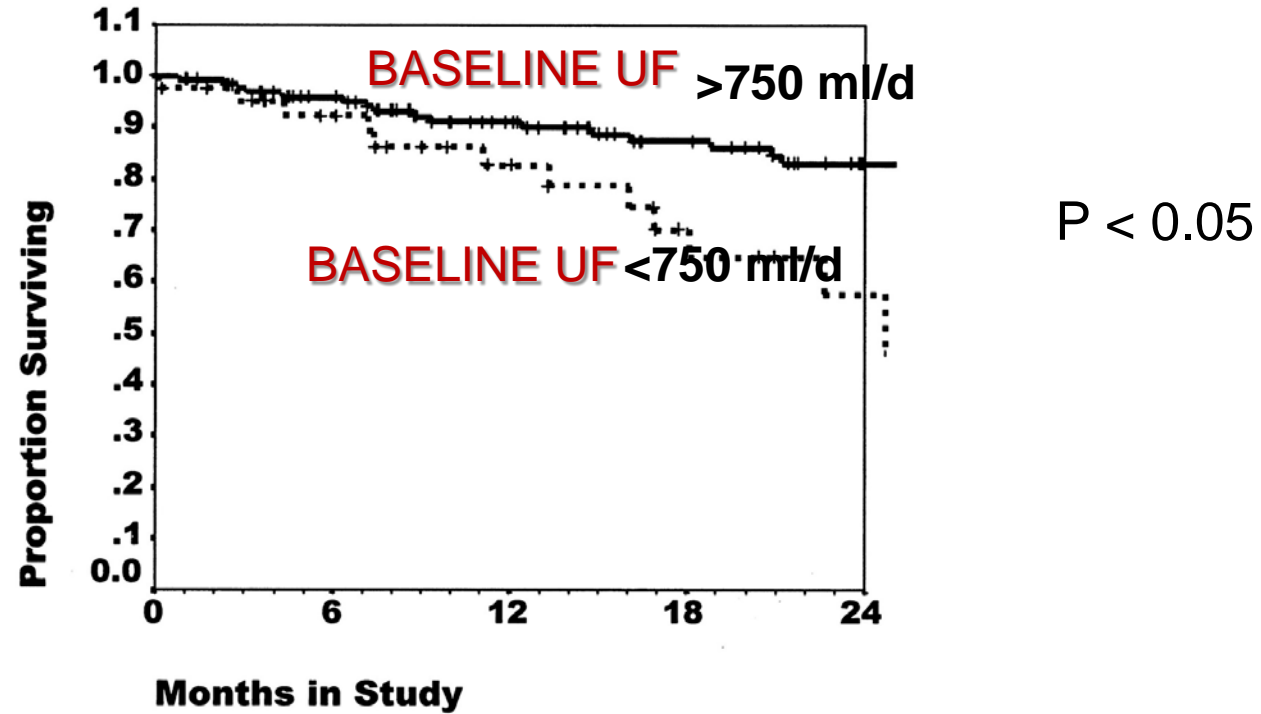
The Importance of Ultrafiltration: The EAPOS Study

- ❑ multi-centre study in Europe examining predictors of outcome in anuric APD patients
- ❑ small solute clearance parameters did not predict survival
- ❑ baseline ultrafiltration volume significantly predicted survival
- ❑ time-dependent ultrafiltration volume was also of borderline statistical significance

Brown et al, J Am Soc Nephrol 14:2948-2957, 2003

Fluid Removal and Survival

(The EAPOS Study)



Brown et al, J Am Soc Nephrol 14:2948-2957, 2003

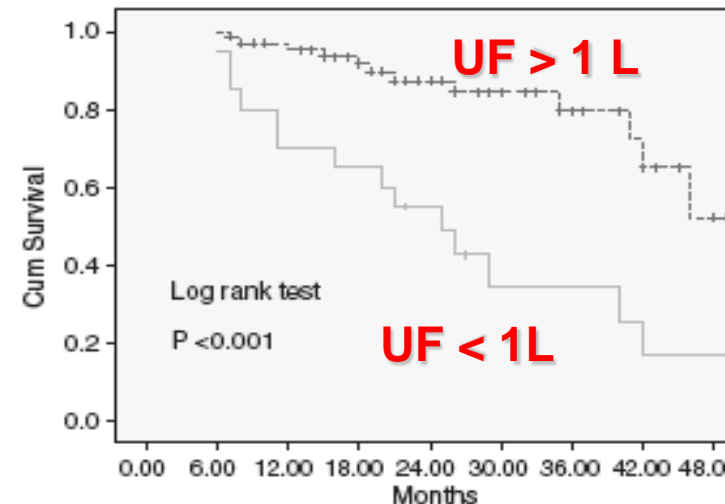
Predictors of Survival in Anuric PD Patients

- recent study of anuric PD patients in Shanghai
- like EAPOS, ultrafiltration volume was an important predictor of survival

Lin et al Neph Dial Transpl 2010

Table 4. Multivariate Cox regression analysis showing independent predictors of mortality in 86 anuric PD patients followed up for a median of 25.3 months (range, 6 to 54 months)

	RR	95% CI	P-value
Age (1 year)	1.064	1.019–1.111	0.005
Serum albumin (1 g/L)	0.850	0.744–0.973	0.018
UF(t) (100 ml/24 h)	0.800	0.709–0.901	0.000



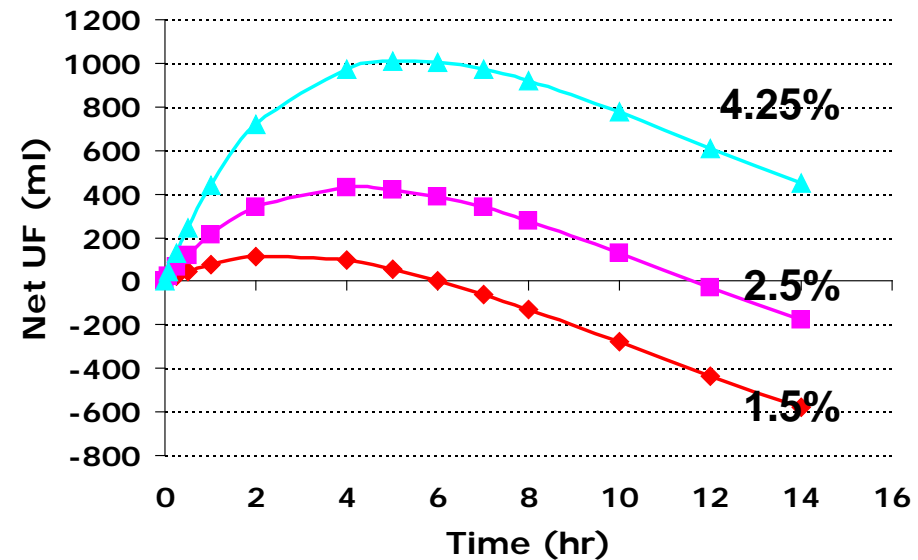


The Importance of Sodium and Water Removal

- evidence suggests that ultrafiltration volume and euvolemia are important for survival
- this makes sense physiologically, given risks of chronic volume overload
 - LVH
 - increased sympathetic tone
 - congestive heart failure

Hypertonic Dextrose-Based Solutions

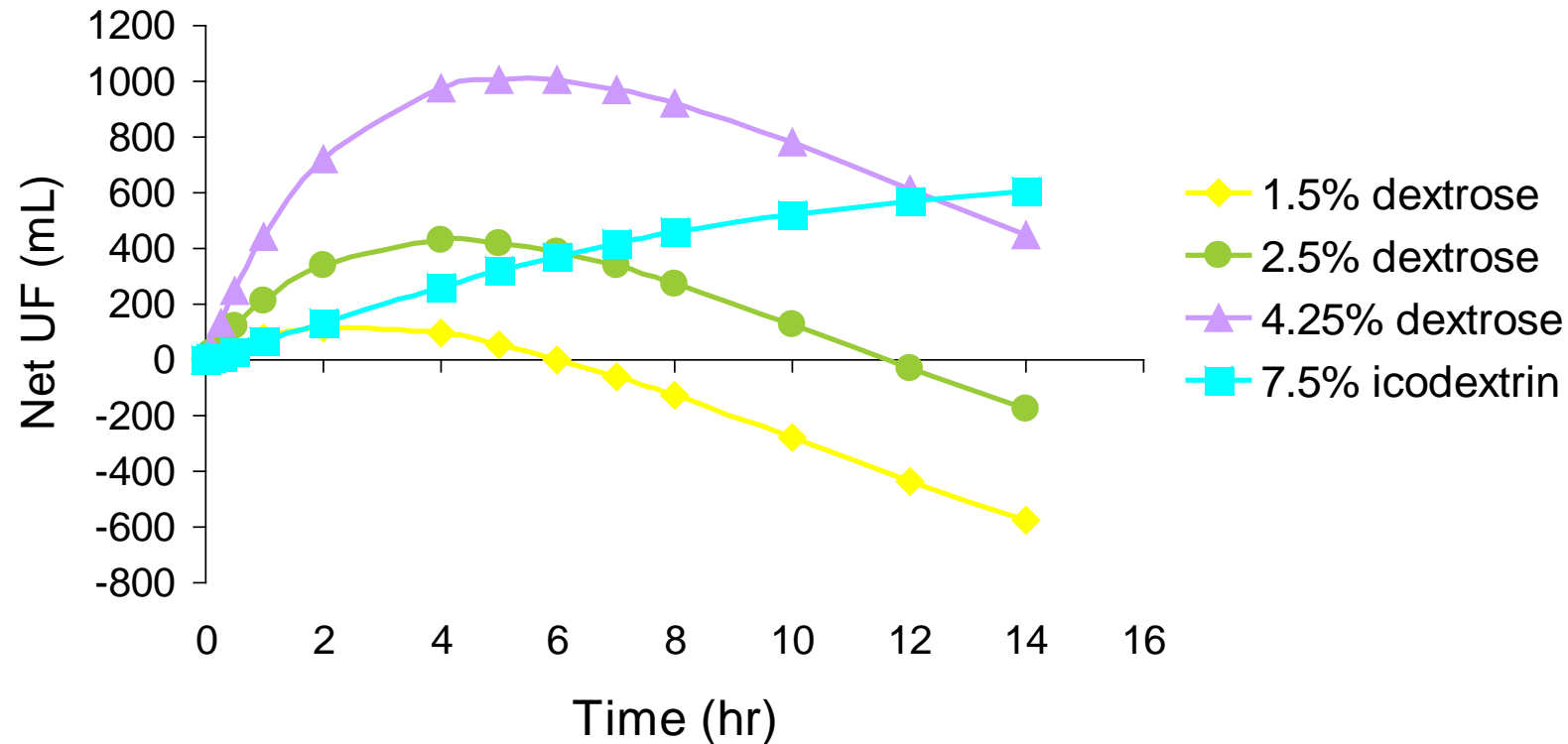
- ❑ To compensate for loss of RKF, hypertonic dialysate will result in more UF and convective removal of solute



Hypertonic Dextrose-based solutions

- ❑ The downside to this is
 - increased caloric load
 - abnormal lipid profile
 - unmasking or exacerbation of diabetes
 - potential for damage of the peritoneal membrane

Sustained Ultrafiltration With Icodextrin



Extended Technique Survival With Icodextrin

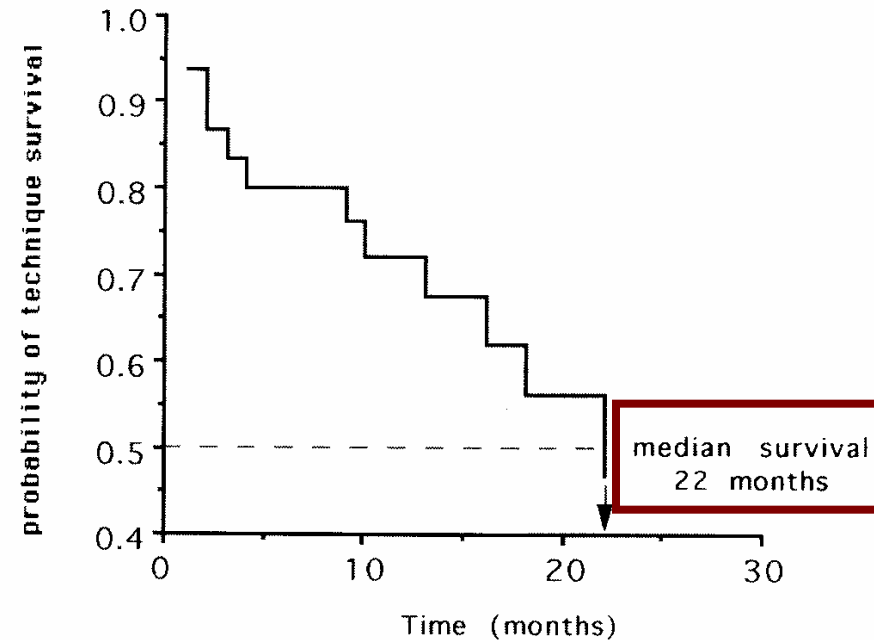


Figure 1 — Extension of peritoneal dialysis technique survival in 33 CAPD patients with ultrafiltration failure using icodextrin. The broken line indicates median survival.

Use of Icodextrin to Achieve Euvolemia in the Anuric PD Patient

- ❑ more ultrafiltration with reduced “metabolic cost” compared to dextrose-based solutions
- ❑ more costly (but cheaper than changing to HD?)
- ❑ associated with extended technique survival
- ❑ 2 icodextrins/day (off-label!) associated with more UF but higher blood concentrations of icodextrin metabolites

My Opinion: What Works for UF in Anuric Patients - CAPD



CAPD

2.5%

1.5%

2.5%

Icodextrin

CAPD

1.5%

2.5%

1.5%

2.5%

Icodextrin

My Opinion: What Works for UF in Anuric Patients - APD



APD	Icodextrin	<u>2.5%</u>	<u>2.5%</u>	<u>2.5%</u>	<u>2.5%</u>
APD	Icodextrin	<u>2.5%</u>	<u>2.5%</u>	<u>2.5%</u>	<u>2.5%</u>

and maybe...

APD	Icodextrin	Icodextrin	<u>2.5%</u>	<u>1.5%</u>	<u>2.5%</u>
	(off label!)				

What Is Sufficient Solute Clearance in the Anuric PD Patient?

- ❑ who knows?

- ❑ studies are urea-based

- 2 studies have found that a weekly Kt/V urea of 1.8 was the “break point,” above which there was no improvement in survival

- ❑ doesn't address whether patient would be better served with HD

When to Transfer to HD

- ❑ keep in mind the quality of life issues, especially if the transfer is to in-center HD
- ❑ it is a major change in the patient's lifestyle
 - independent at home to powerless in the HD unit
 - the tunneled line: are we doing them any favours?
- ❑ this is an important decision and *should not be made lightly*



The assembly line

When to Transfer the Anuric PD Patient to HD: A Personal View

- ultrafiltration failure and persistent significant volume overload
 - in some countries these patients are treated with combination HD (for UF) and PD

Summary of The Anuric PD Patient

- ❑ once the patient is anuric, the PD (and HD) patient should be considered “high risk” and thought should be put into the dialysis prescription
- ❑ the patients need to be monitored for uremia and volume overload
- ❑ there is no good evidence to support transferring a thriving anuric PD patient to HD

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What's the Deal with the Rapid Transporter?

- ❑ CAPD-based studies showed reduced survival for rapid transporters
- ❑ many postulated mechanisms:
 - reduced ultrafiltration and chronic fluid overload
 - more glucose absorption and worsened metabolic indices
 - more albumin loss into the peritoneal fluid
 - ** rapid transport status reflects systemic inflammation**
 - the reduced survival is because of the systemic inflammation
- ❑ the association is less robust for patients on APD

Prescriptions for the Rapid Transporter

- ❑ stay tuned for tomorrow's lecture
- ❑ in brief:
 - ❑ you may not have to do anything if there is a lot of residual kidney function
 - ❑ keep dwells short and use dry abdomen if there is residual kidney function
 - ❑ APD is not a panacea
 - ❑ sure, short dwells overnight is great, but what about the long day dwell?
 - ❑ icodextrin is very helpful for the long dwell
 - ❑ don't forget about dietary salt restriction and diuretics

A rapid transporter with declining residual kidney function and persistent volume overload should be advised about transitioning to hemodialysis

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PD for the Big Patient

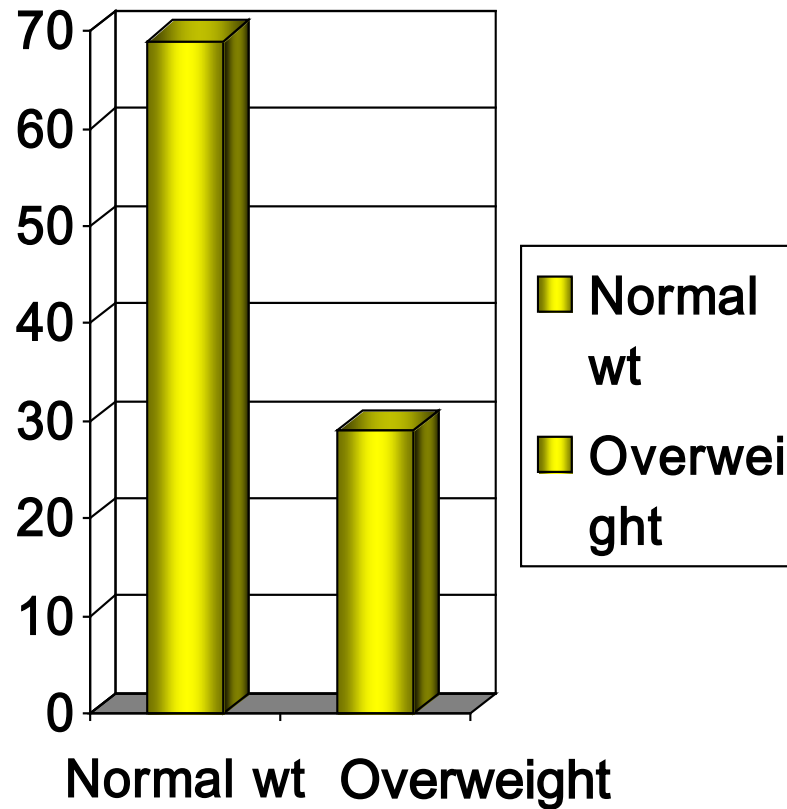
- ❑ Kt/V urea will be a trap for the big patient on PD
- ❑ most “big” patients are big because they are fat, not muscular

The Trap of Kt/V: The Obese Patient

- the use of total body weight to calculate “V” in Kt/V will include fat weight
- fat is anhydrous, so is not part of the true volume of distribution of urea
- the incorrectly big “V” will make Kt/V a smaller number, so obese patients will appear “underdialyzed” by urea kinetics



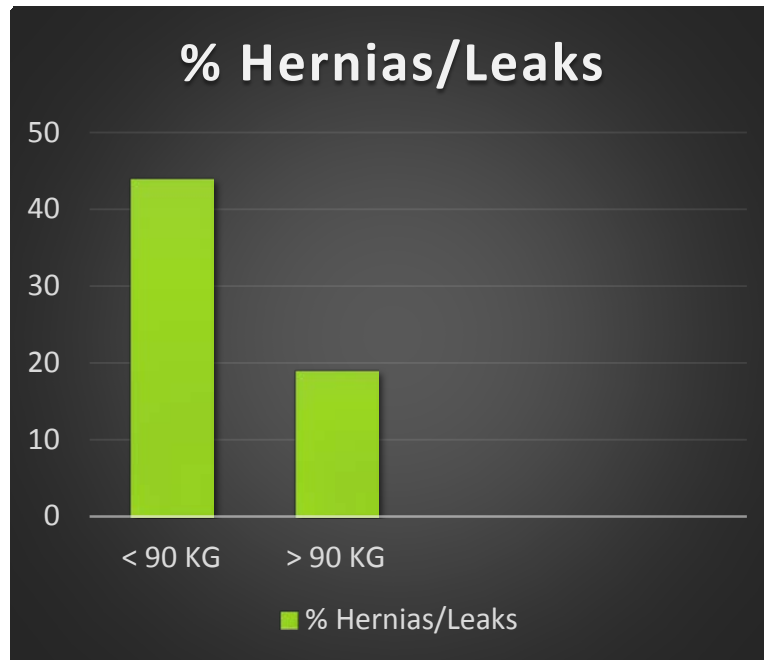
Obesity Confers a Survival Advantage in PD Patients



- 3 year follow-up of PD patients with BMI 20-27.5 or BMI > 27.5
- survival advantage for the high BMI group (HR 0.09, $p < 0.05$)

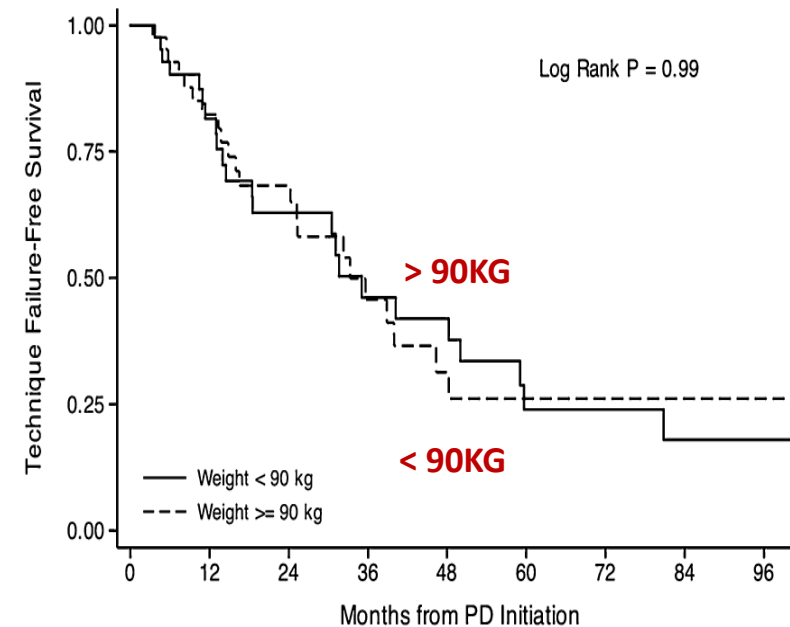
Outcome of a Modern Cohort at Our Center

IDENTICAL SURVIVAL AND FEWER
HERNIAS AND LEAKS IN THE PATIENTS >
90 KG



Ananthakrishnan et al Int Urol Nephrol 2013

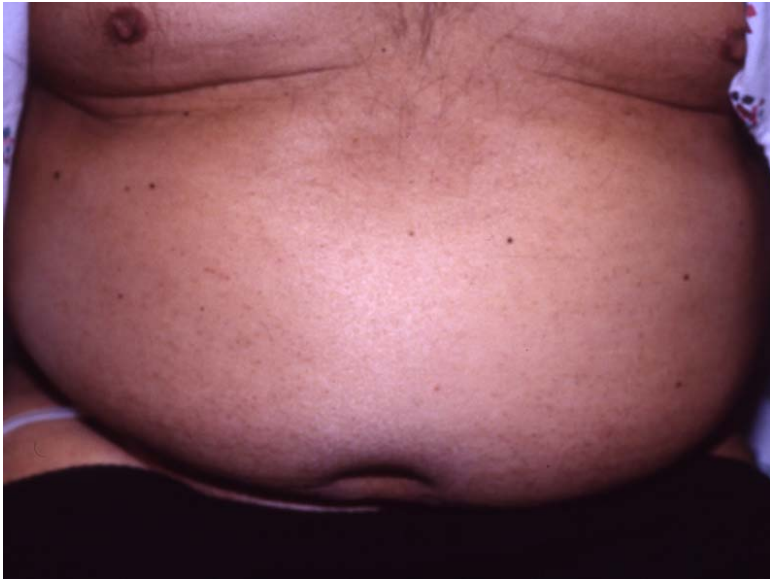
TECHNIQUE SURVIVAL



Catheter Placement in the Obese Patient

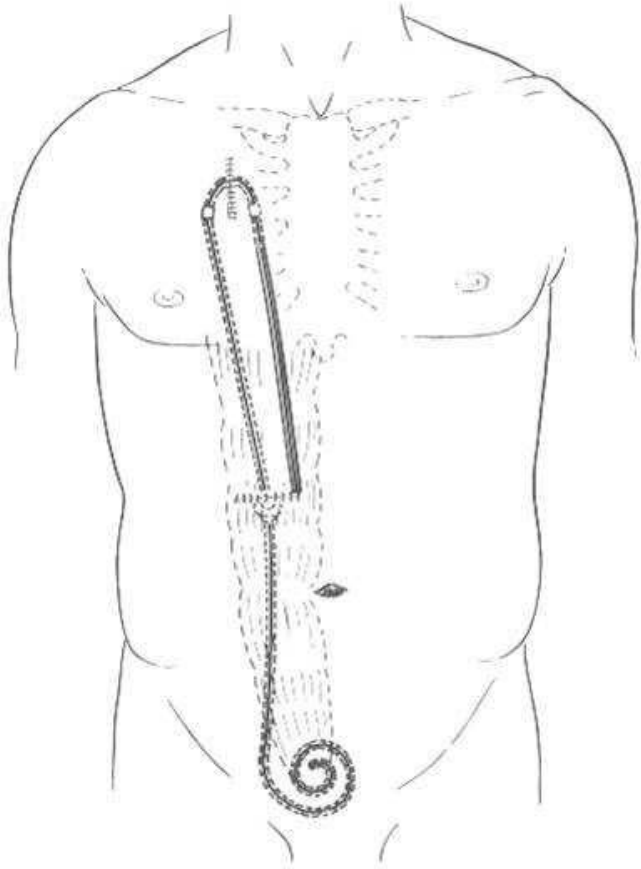
- ☐ estimate length of catheter needed
 - may need longer catheter or a connector
- ☐ select the catheter exit site ahead of time
- ☐ have the patient sitting when the exit site is marked
 - allows better visualization of abdomen, including fat rolls

Poorly-Placed Catheter Exit Sites

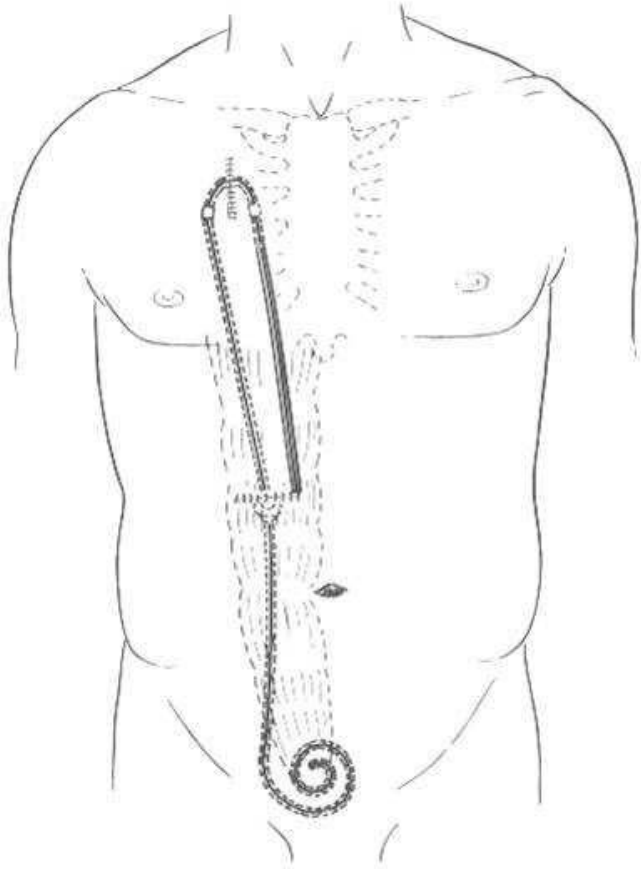


Photos courtesy of Dr. J. Crabtree

The Pre-Sternal Catheter



The Pre-Sternal Catheter



My Patient with an Upper Abdominal Catheter



Prevention and Treatment of Hernias in the Obese PD Patient

if a hernia does occur:

- surgical repair
- abdominal mesh may be helpful
- dialyze post-repair with small volumes, supine position
- encourage night cycler dialysis with smaller day volumes
- for example
 - 2.5 L X 4 overnight, 1.5 L last fill, 1.5 L day exchange

If Kt/V Urea is Misleading, How Will You Know if Your Patient is Adequately Dialyzed?

What happened to clinical judgement?

- how do they look?
- are they eating well?
- serum albumin?
- ESA responsive?

if you must use Kt/V urea, use fat-free body weight

Other crowded abdomens



- 55 year old woman with PCKD and massive polycystic liver
- night cyclor PD with day dry
- excellent results and she eventually received a deceased donor renal transplant

Polycystic Kidney Disease and PD

- ❑ not all PCKD is the same
- ❑ some kidneys are humungous and the belly is already stretched over them – I wouldn't suggest PD in that circumstance
- ❑ otherwise, even patients with enlarged kidneys do very well on PD
- ❑ there is predisposition to hernias
- ❑ try to prescribe a low-pressure regimen
 - ❑ I would encourage cycler with larger volumes at night
 - ❑ dry or smaller dwell volumes during the day
 - ❑ drain for activities or exercise

Summary of the Obese Patient or Crowded Abdomen

- ❑ obese patients have similar technique and improved overall survival
- ❑ the continuous glucose loading may make them more obese
- ❑ planning is needed for implantation of the PD catheter
- ❑ try to prescribe a “low-pressure” regimen, typically taking advantage of night cyclers

One More Patient – Because I Get Asked this All the Time

- endstage liver patient receiving regular paracenteses
- worsening renal function (hepatorenal syndrome)

So let's do PD! 



www.diseasepictures.com

PD in the Patient with Ascites

- leaking from the PD catheter
- large drain volumes
- massive protein loss
- enteric peritonitis (“spontaneous bacterial peritonitis” equivalent?)

PD works more smoothly when the cause of ascites is right heart failure, rather than liver failure

Prescription Management – Not so Tough?

- ❑ there are challenging patients in whom the prescription has to be given some thought
- ❑ even these patients can thrive on PD
- ❑ this leads to better quality of life – for both the patient and the medical/nursing staff