Peritoneal Dialysis Adequacy and Complications

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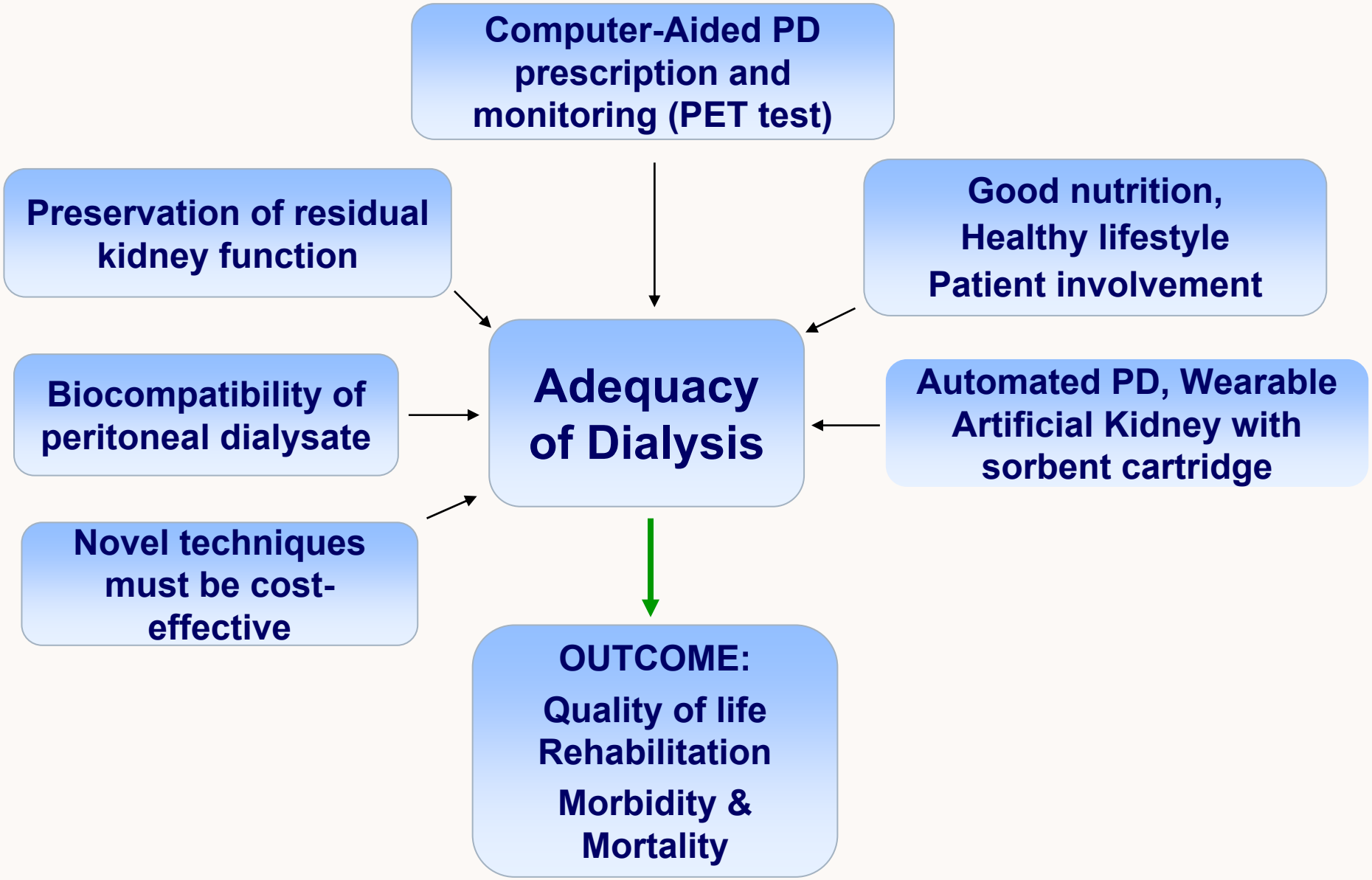
Monday, 08/31/2009 9:45-10:30

PD Adequacy


Computer-Aided PD prescription and monitoring (PET test)
Preservation of residual kidney function
Good nutrition, Healthy lifestyle Patient involvement
Biocompatibility of peritoneal dialysate
Adequacy of Dialysis
Automated PD, Wearable Artificial Kidney with sorbent cartridge
Novel techniques must be cost-effective
OUTCOME:
Quality of life
Rehabilitation
Morbidity & Mortality

PD Adequacy

1. Brief PD physiology
   - Anatomy of the peritoneum
   - Principles of solute and volume transport in PD
   - Some modalities of PD
2. Small solute transport
   - The PET test
   - Nutrition: protein equivalent of nitrogen appearance (PNA or PCR)
   - Modality selection (CAPD, CCPD, NIPD etc)
   - Studies of clinical outcomes with different weekly Kt/Vurea goals
   - Updated K-DOQI guidelines (2006)

Anatomy of the peritoneum

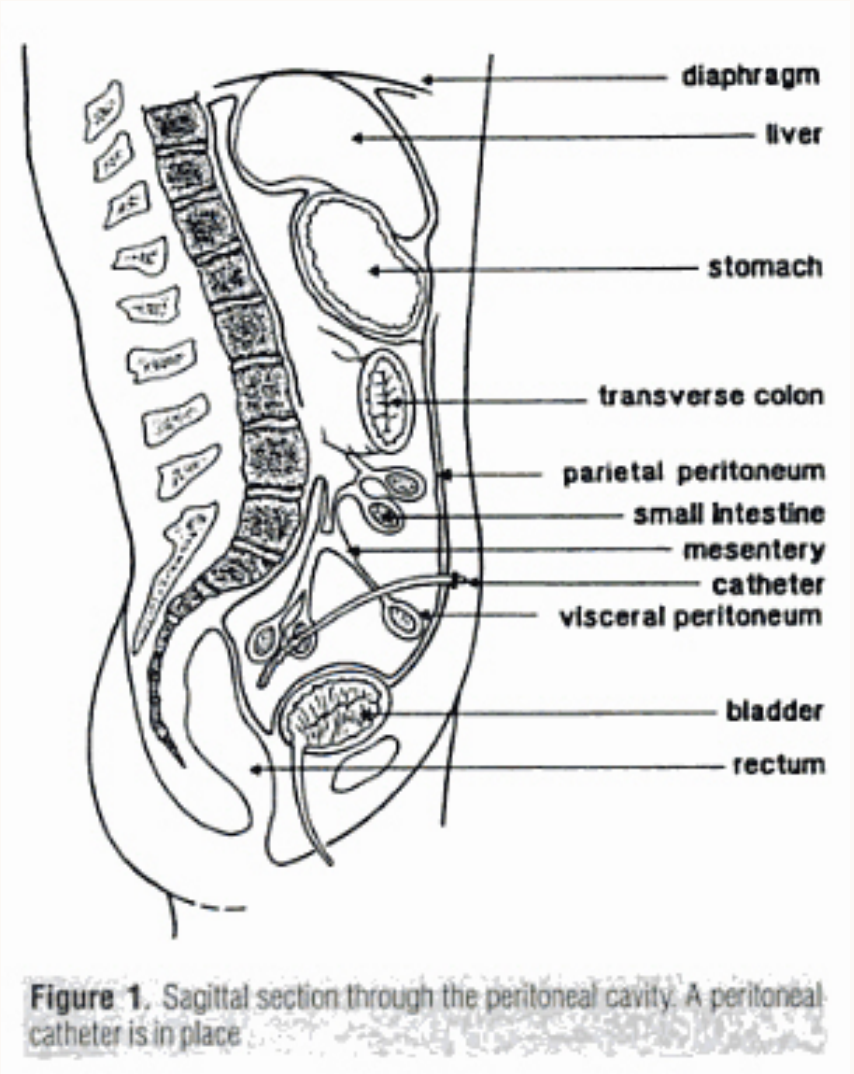
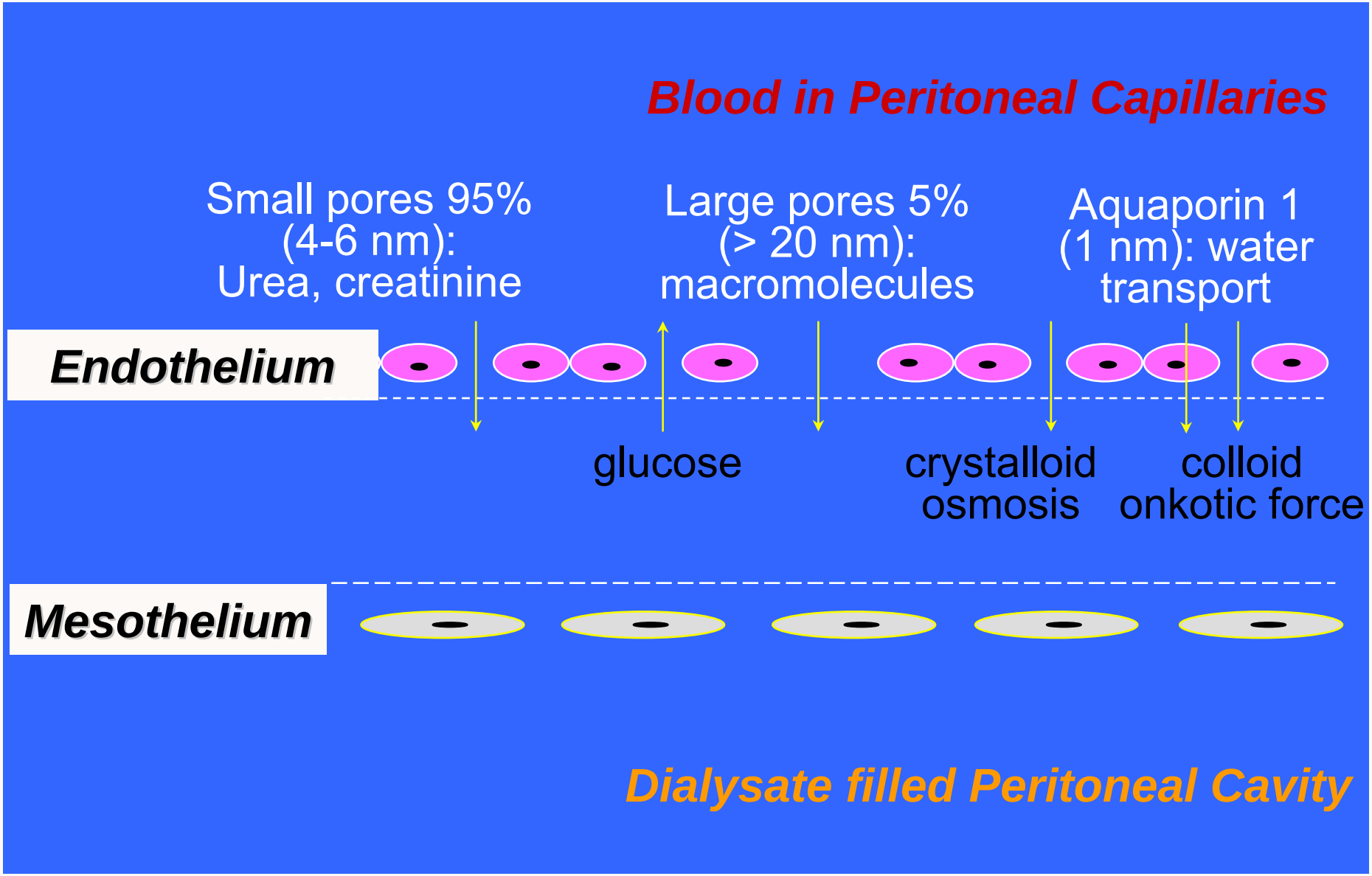


Figure 1. Sagittal section through the peritoneal cavity. A peritoneal catheter is in place

- Surface area 0.5-2 m^2
- Lined with mesothelial cells
- Blood flow ≈ 80 ml/min
- Changes with PD
  - Mesothelial cells (degeneration and hyperactivity)
  - Vascular changes (subendothelial hyalinization) – like DM
  - Collagen deposition

Krediet RT: Peritoneal anatomy and physiology during peritoneal dialysis; in Replacement of Renal Function by Dialysis, 5th edition; p116

3 Pores for Solute and Water Transport



Rippe B, Stelin G, Haraldsson B. Computer simulations of peritoneal fluid transport in CAPD.Kidney Int.1991;40:315-25.

Solute and Water transport in PD

I. Variable diffusive solute transport properties; may change with time for a specific patient
   - High transporter (1 STD above average;worse clinical outcomes)
   - High-average transporter
   - Low-average transporter
   - Low-transporter (1 STD below average)

II. Ultrafiltration/convection
   - Dependent on osmotic and colloid osmotic pressure
   - We cannot generate a negative hydraulic pressure in PD (compare with hemodialysis ultrafiltration)
   - Requires a favorable pressure gradient and functioning pores
   - Daily albumin losses are substantial but well-tolerated

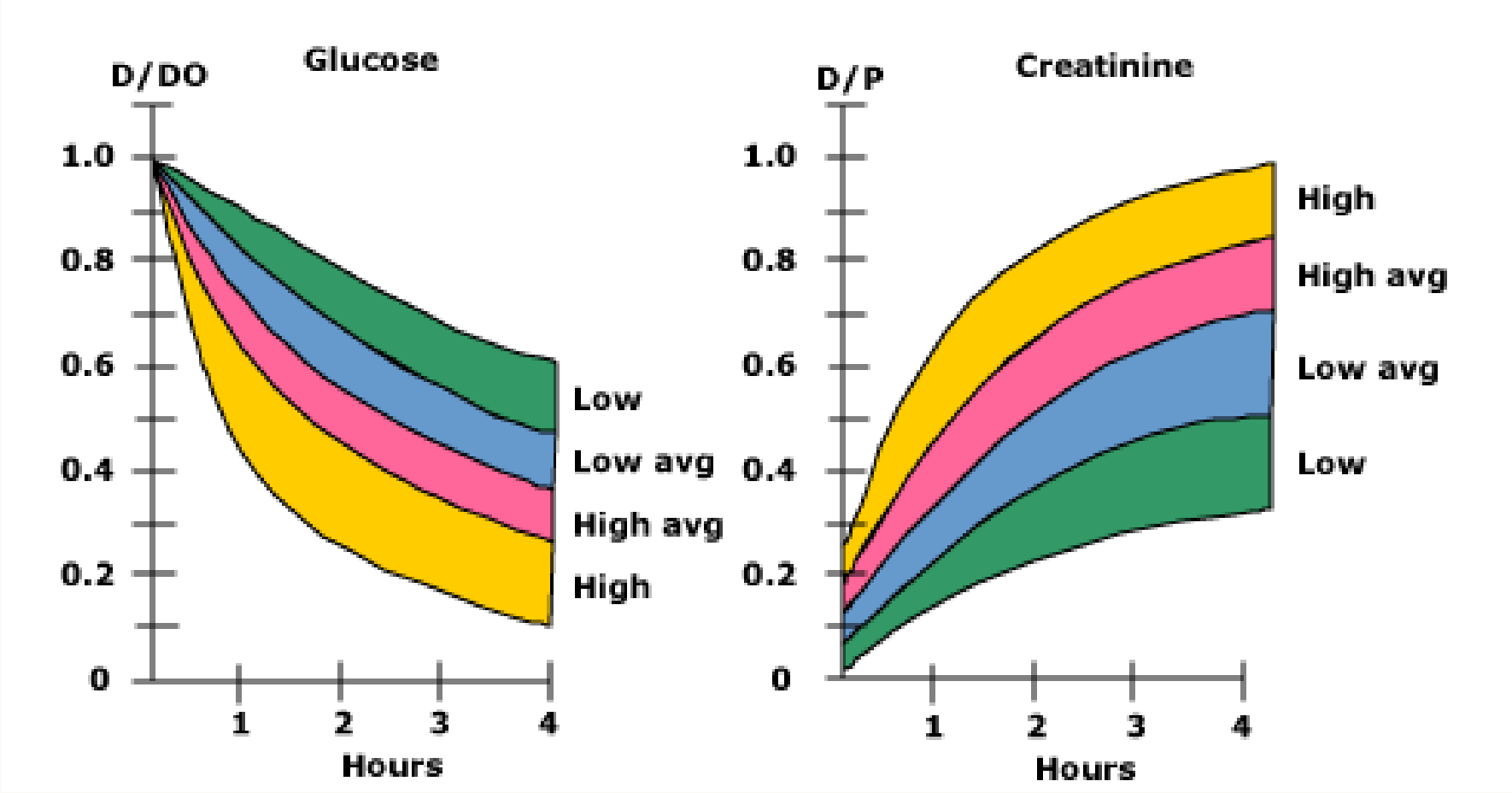
III. Lymphatic reabsorption
   - Patients may have variable rates of reabsorption

The PET Test 1

1. The peritoneal equilibration test (PET) is a semi-quantitative assessment of peritoneal membrane transport function:
   - After a long 10-12 h dwell, 2 liters of a 2.5% dextrose solution is infused for a 4-hour dwell
   - Highly standardized (inflow and drain duration, positions, serum and dialysate sampling, laboratory analysis
2. Information obtained
   - Dialysate to plasma ratios of solutes at 0, 120, 240 minutes (urea, creatinine, sodium, electrolytes, protein)
   - D(t)/D0 ratios for glucose are obtained from the dialysate
   - Drained volume helps evaluate ultrafiltration

1. Twardowski, ZJ, Nolph, KD, Khanna, R, et al. Peritoneal equilibration test. Perit Dial Bull 1987; 7:138.

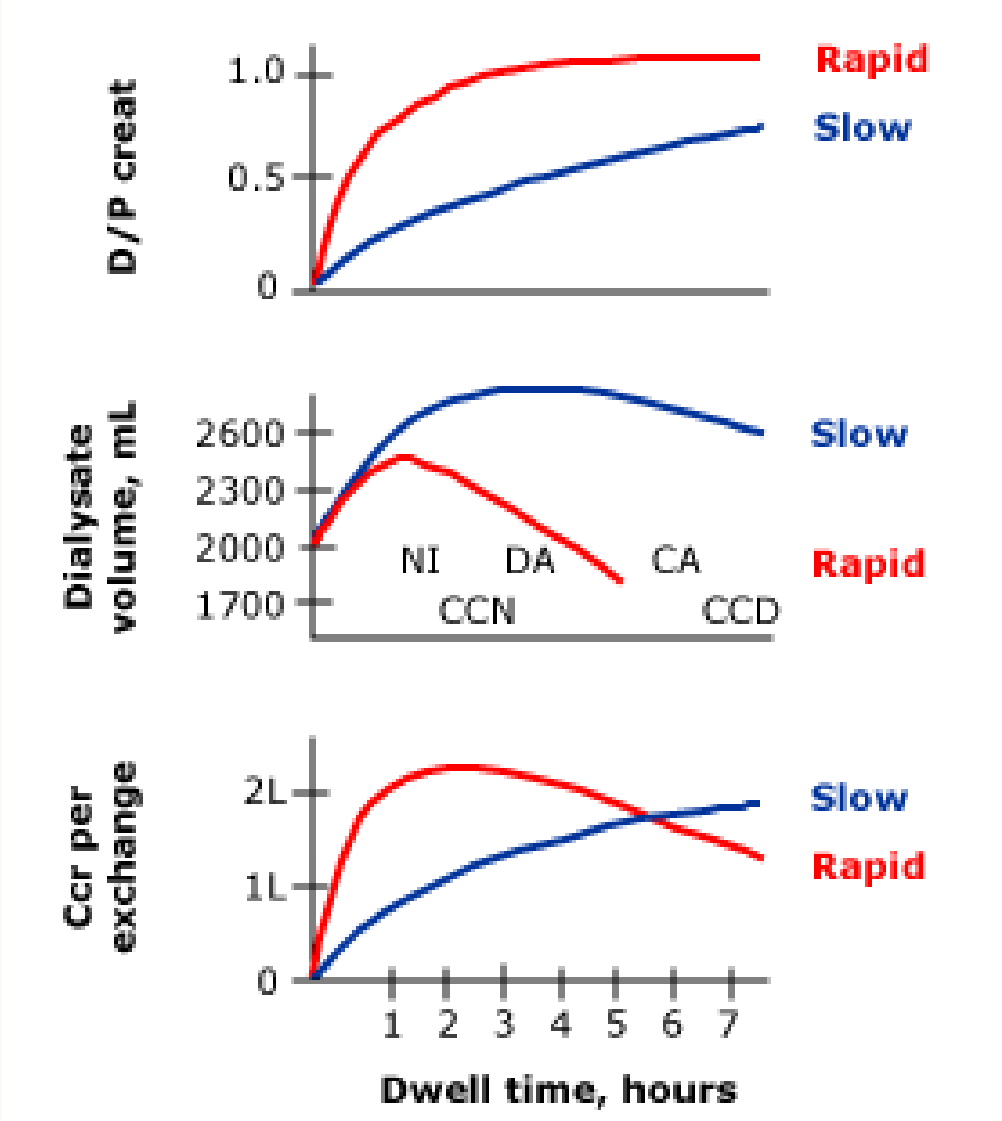
The PET Test 2



Time-dependent changes during peritoneal dialysis in dialysate (D) concentration of glucose (left panel) or creatinine (right panel) as a proportion of original dialysate glucose concentration (DO) or plasma creatinine concentration (P), respectively. High transporter have excessive glucose absorption and are at risk for ultrafilration failure and malnutrition due to amino acid losses. Low transporters are at risk of inadequate small solute removal.

1. ©UpToDate; Data from Twardowsky, ZJ, ASAIO Trans 1990; 36:8.

The PET Test 3



Differences between rapid and slow transporters during PD. Rapid transporters reach creatinine equilibration more quickly (dialysate-to-plasma creatinine equals one, top panel), have a gradual reduction in dialysate volume after two hours due to glucose absorption (middle panel), and have a reduction in creatinine clearance (Ccr) after four hours due to absorption of creatinine with the glucose and fluid (lower panel). Thus, short dwell times are most efficient in these patients. Values are shown for the major types of PD: nightly intermittent with short dwells (NI); daytime (DA) and continuous ambulatory (CA); and continuous cycling at night (CCN) with short dwells and during the long daytime dwell (CCD).

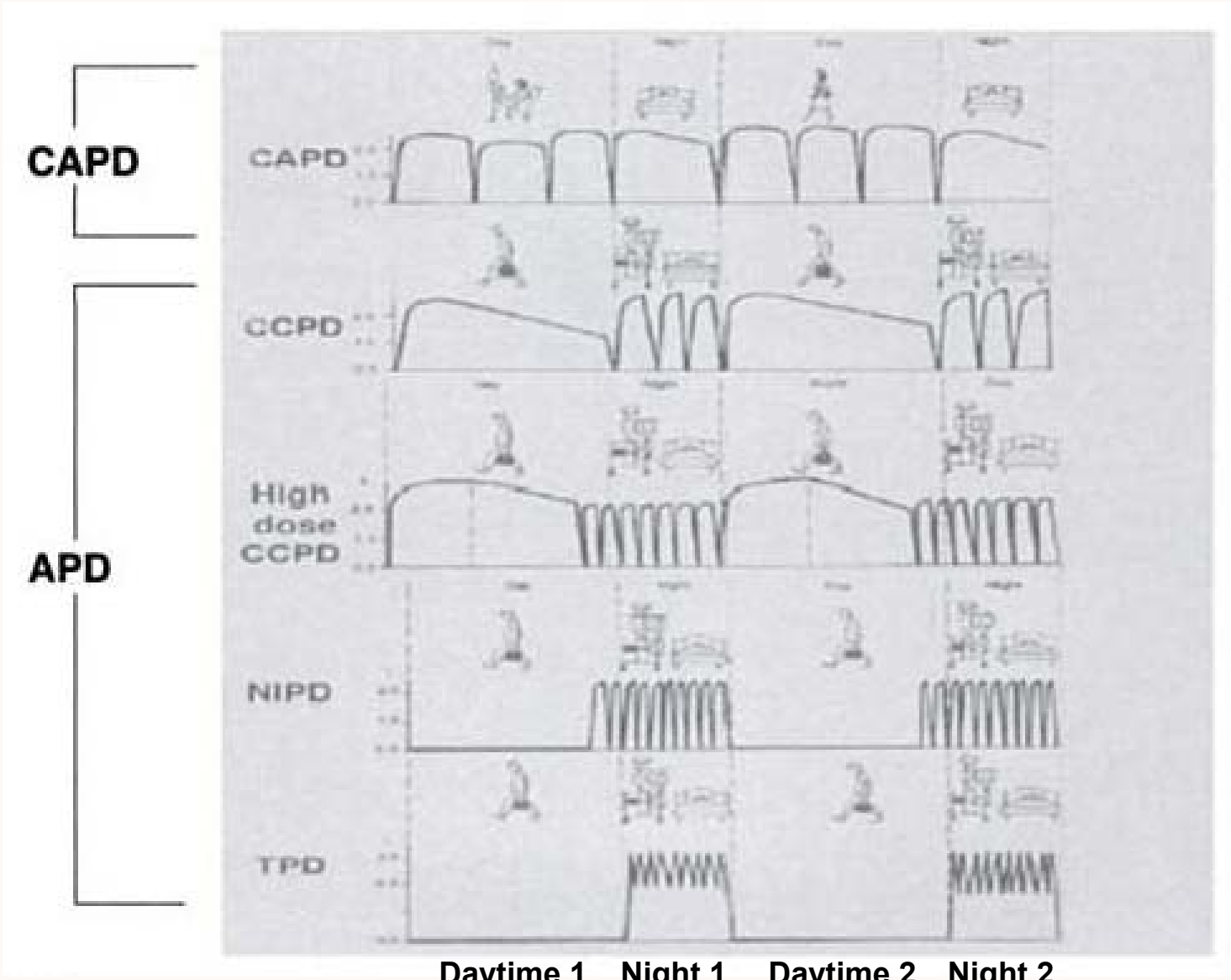
1. ©UpToDate; Data from Twardowsky, ZJ, ASAIO Trans 1990; 36:8.

Nutritional Assessment

1. Clinical assessment:
   - History, physical examination
   - Laboratory tests (albumin, etc)
2. Normalized protein equivalent of urea nitrogen appearance (nPNA) in PD
   - nPNA=6.25 x (Urea appearance + 1.81 + [0.031 x lean body weight, kg])
   - Urea appearance, g/day=(Vu x Cu)+(Vd x Cd)
   - A target of 1.0-1.2 g/kg per day or higher is recommended

1. Keshaviah, PR, Nolph, KD. Protein catabolic rate calculations in CAPD patients. ASAIO Trans 1991; 37:M400.

Various PD modalities



Continuous Ambulatory PD

Continuous Cycling PD

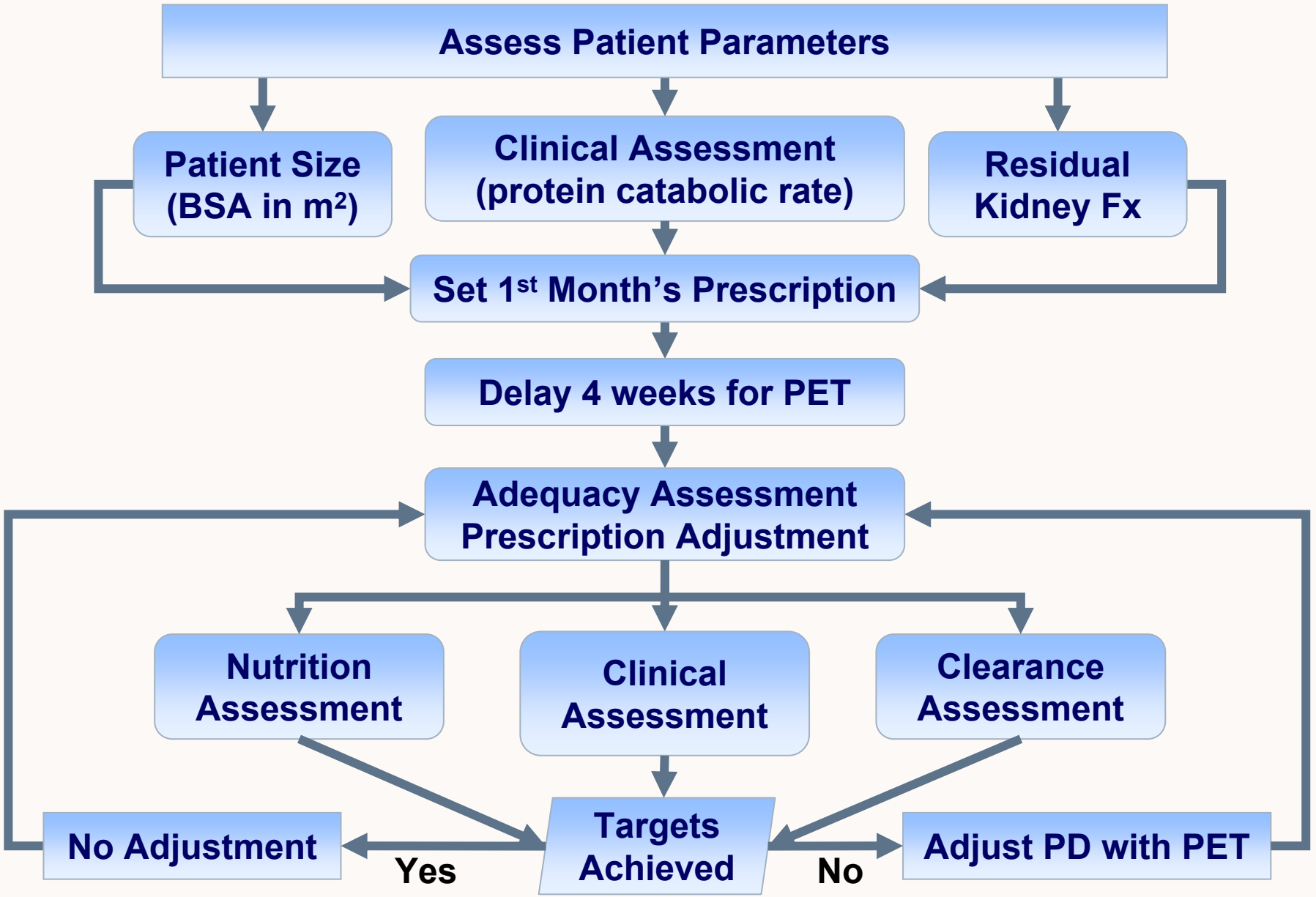
High Dose CCPD

Nocturnal Intermittent PD

Tidal PD

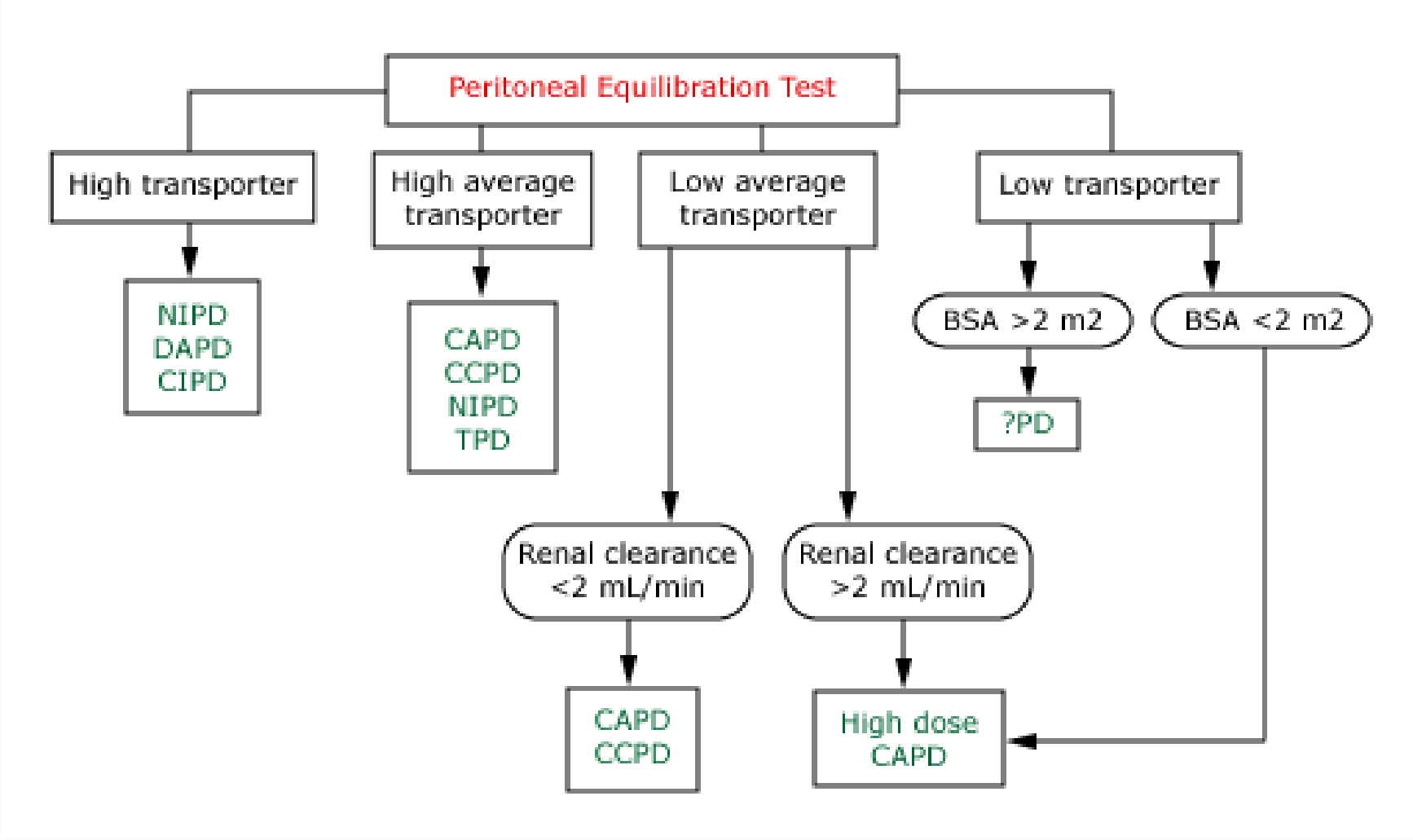
Gokal R: Dialysis techniques:Peritoneal Dialysis; in Replacement of Renal Function by Dialysis, 5th edition; p670

Selecting and adjusting a PD prescription



Adapted from Gokal R; in Replacement of Renal Function by Dialysis, 5th edition; p675

PET helps select PD modality



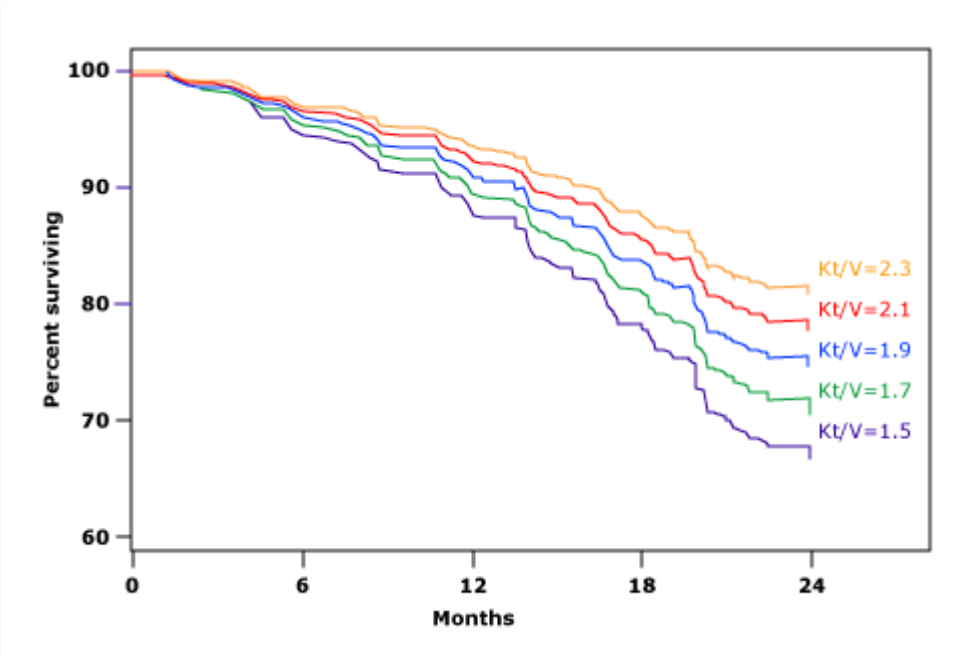
1. ©UpToDate; Misra M and Khanna R:PET Test

The CANUSA Study 1

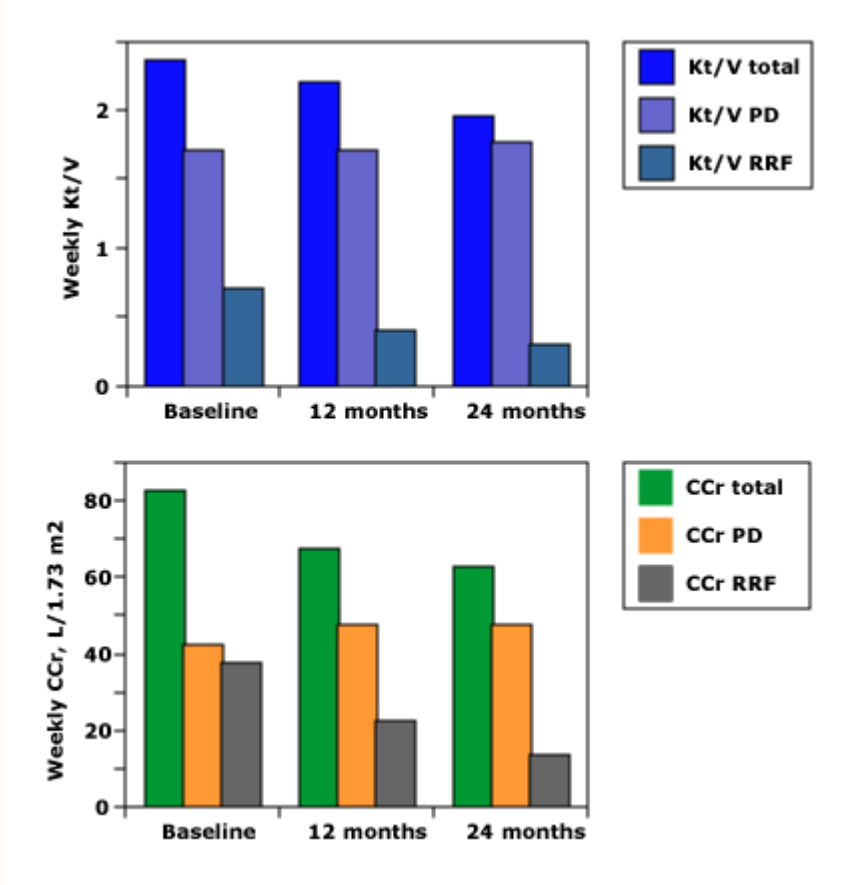
1. Prospective, cohort, multicenter observational study in Canada and the United States[1]
   - Each 0.1 unit decrease in total (PD and RRF) Kt/Vurea was associated with a 5% increase in the RR of death
   - A Kt/Vurea of 2.1 and a weekly creatinine clearance of 70 L/1.73 m2 body surface area were both associated with a 78 percent expected two-year survival rate
   - RRF and PD clearance were assumed equivalent
2. Reanalyzed to determine role of RRF versus PD Kt/V
   - Residual renal clearance then emerged as the most important predictor of mortality[2]

1. Adequacy of dialysis and nutrition in CAPD: association with clinical outcomes. Canada-USA (CANUSA) Peritoneal Dialysis Study Group. J Am Soc Nephrol 1996; 7:198.
2. Bargman, JM et al: Relative contribution of residual renal function and peritoneal clearance to adequacy of dialysis: A reanalysis of the CANUSA study. J Am Soc Nephrol 2001; 12:2158.

The CANUSA Study 2



Predicted probability of survival in patients treated with continuous peritoneal dialysis according to the weekly Kt/Vurea.[1]



Weekly Kt/Vurea and CCr in patients on CAPD.[2]

1. Bargman, JM et al: Relative contribution of residual renal function and peritoneal clearance to adequacy of dialysis: A reanalysis of the CANUSA study. J Am Soc Nephrol 2001; 12:2158.
2. ©UpToDate; Data from Burkart, JM, Schreiber, M, Korbet, SM, et al, Perit Dial Int 1996; 16:457.

The ADEMEX Study

1. Prospective, randomized, trial of different PD doses conducted in Mexico[1]
   - 965 patients assigned to 4 x 2 L PD or an increased prescription to achieve CCr > 60 L/1.72 m^2
   - Good separation of dose (Kt/Vurea 1.62 versus 2.13 and Ccr 46 versus 57 L/week/1.72 m^2)
2. Outcomes
   - There was no difference in survival between the two groups (68% versus 69%) at study end
   - There was no difference in quality of life
   - Survival was not different even in the subgroups of anuric patients

1. Paniagua, R et al: Effects of increased peritoneal clearances on mortality rates in peritoneal dialysis: ADEMEX, a prospective, randomized, controlled trial. J Am Soc Nephrol 2002; 13:1307.

The Hong Kong PD Study

1. Prospective, randomized, trial of different PD doses conducted in Hong Kong[1]
   - 320 new CAPD patients with < 1 renal Kt/Vurea were assigned to prescriptions to achieve 1.5-1.7 or 1.7-2 or >2 Kt/V urea
   - Dose separation took 1 year to achieve
2. Outcomes
   - There was no difference in survival, serum albumin or hospitalization rates
   - The lowest Kt/V group had more uremic symptoms and higher erythropoietin requirements

1. Lo, WK et al: Effect of Kt/V on survival and clinical outcome in CAPD patients in a randomized prospective study. Kidney Int 2003; 64:649.

Updated K-DOQI guidelines for PD adequacy (2006)

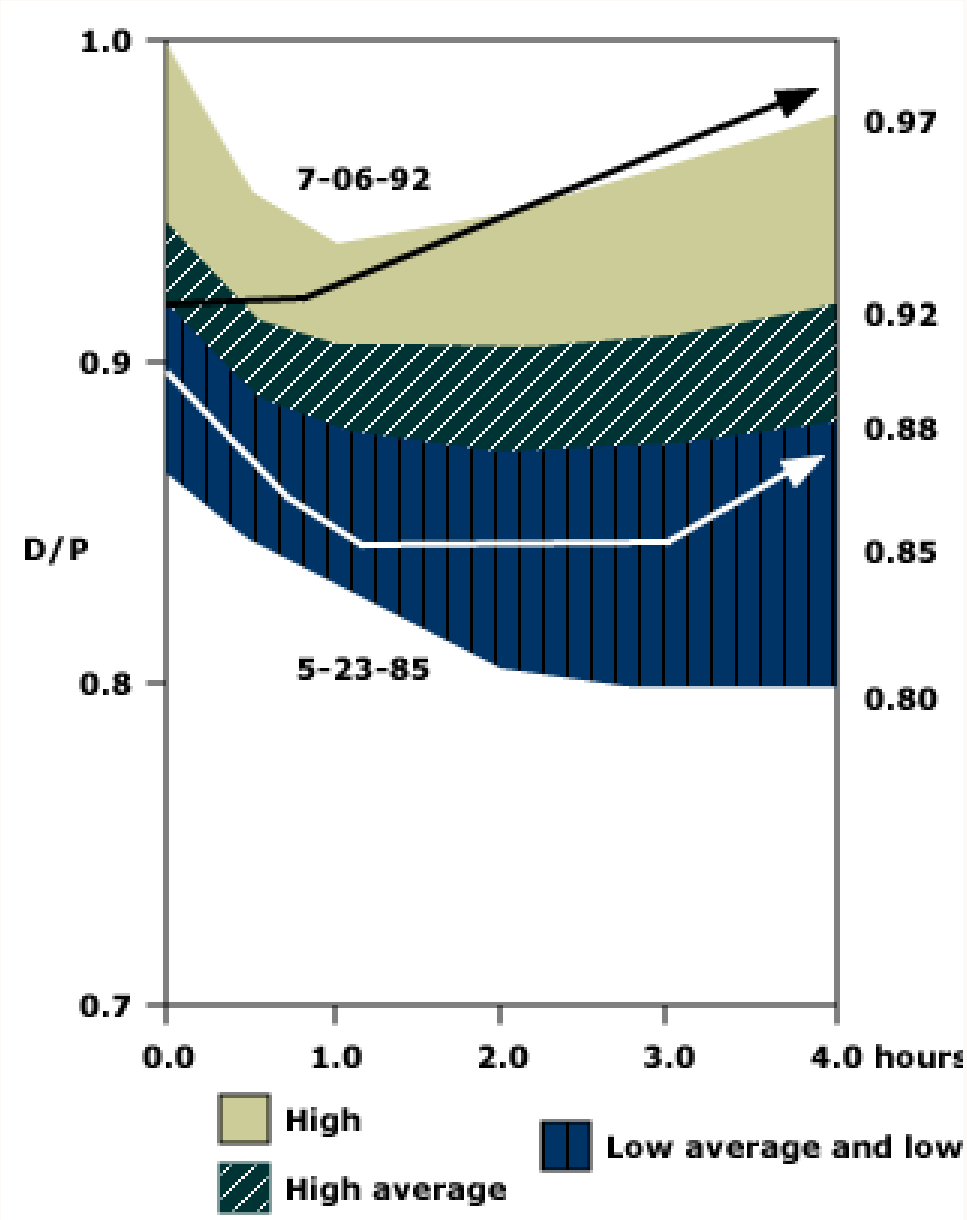
1. Patients with residual kidney function (RKF) (urine volume is >100 mL/day):
   - Minimal delivered total weekly Kt/Vurea (PD+RKF) ≥1.7
   - Total (PD+RKF) solute clearance must be measured after 1 month and every 4 months thereafter
   - 24-hour urine collection for volume and RKF every 2 months
2. Patients without RKF:
   - Minimal delivered weekly Kt/Vurea ≥1.7
   - Total solute clearance must be measured after 1 month and every 4 months thereafter

1. K/DOQI clinical practice guidelines for peritoneal dialysis adequacy. Am J Kidney Dis 2006; 47(Suppl 4):S1.

PD Complications

- Ultrafiltration Failure
- Biocompatibility: Glucose degradation product and icodextrin-related complications
- Encapsulating sclerosing peritonitis
- Peritonitis
- Mechanical and other

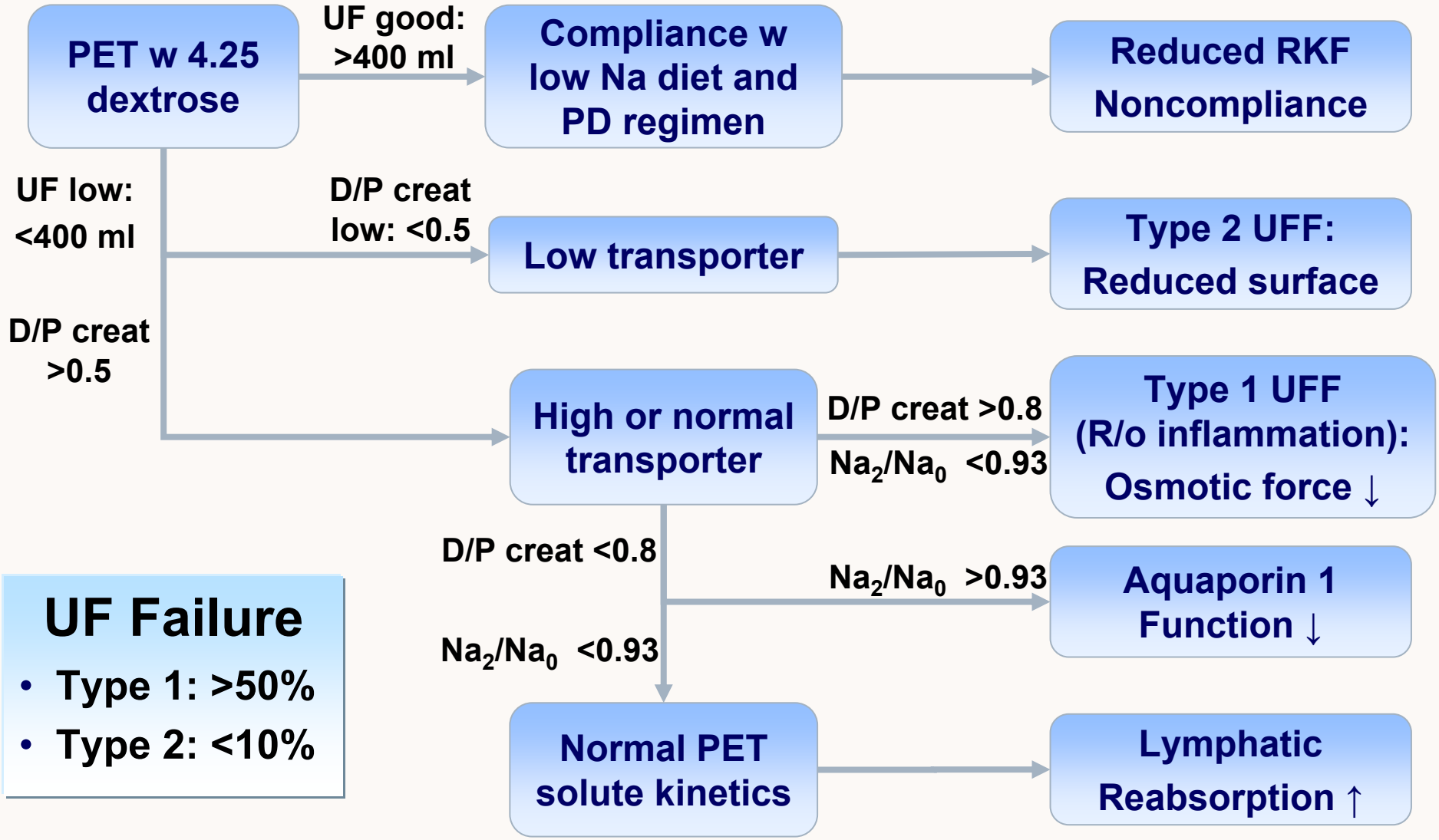
The PET used to assess Na-sieving



Sodium D/P (dialysate/plasma) ratios versus time as measured in 1985 (5/23/85, white curve) and 1992 (7/06/92, black curve) in a patient with progressive loss of ultrafiltration. Values are superimposed upon the standard curves. The initial curve is normal, displaying an initial drop of the ratio; the second curve is abnormal with no decrease at the beginning of dwell. The curve rises steadily after a one hour dwell.

1. ©UpToDate; Misra M and Khanna R: Mechanisms of solute clearance and ultrafiltration in peritoneal dialysis; accessed 08/04/2009

PET helps diagnose UF failure (UFF)



UF Failure

- Type 1: >50%
- Type 2: <10%

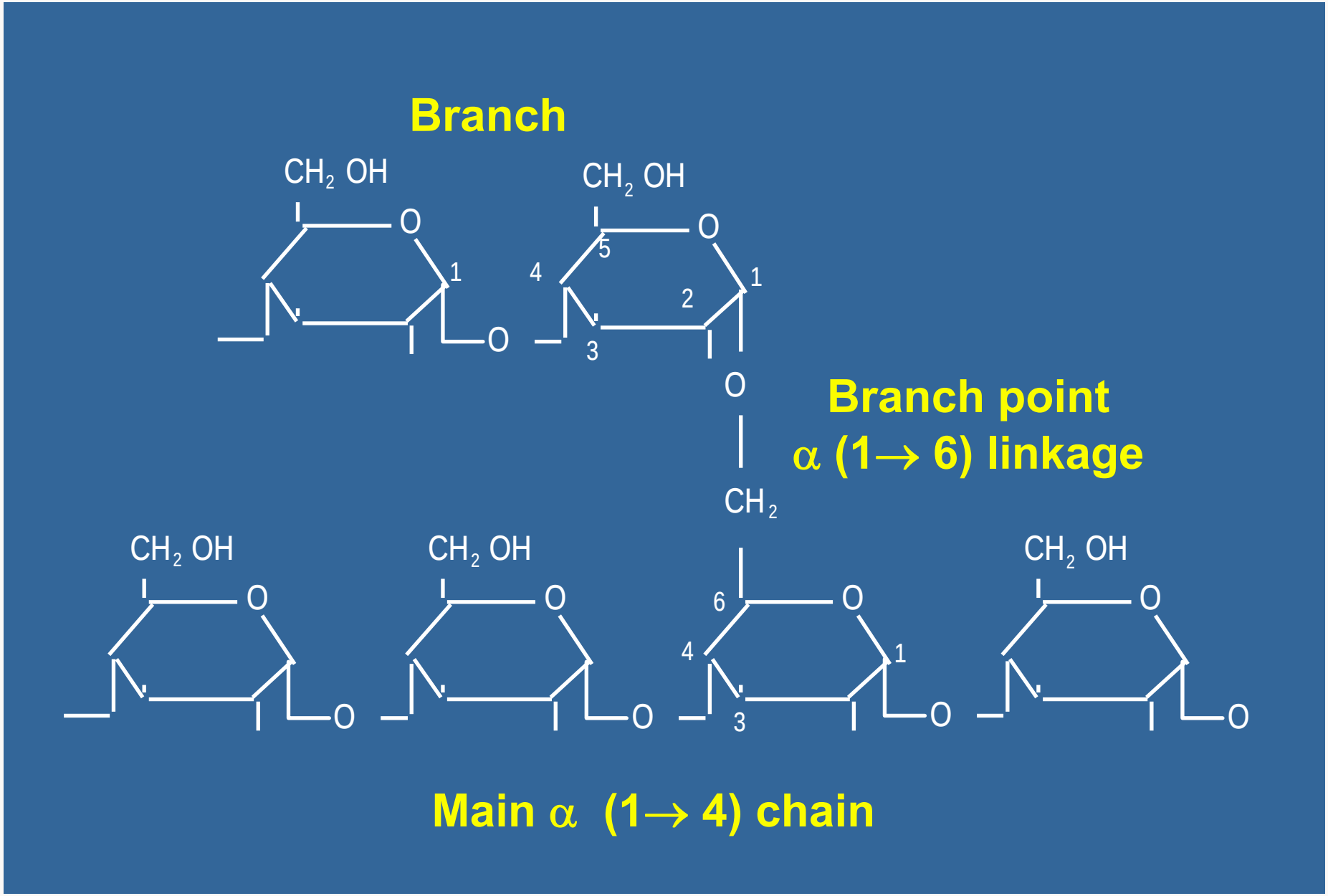
1. Smit et al: Analysis of the prevalence and causes of ultrafiltration failure PDI 2004; 24:562–70
2. Coester M: Peritoneal function in clinical practice… NDT Plus (2009) 2: 104–110
3. Gomes et al: Categorization of sodium sieving…NDT 2009; 0: gfp319v1-gfp319

Biocompatibility of PD fluids

1. Glucose-related problems[1]
   - Un-physiologic (very high) glucose content induces cellular and interstitial changes (TGF-β, VEGF signaling)
   - Toxic glucose degradation products are formed during heat sterilization of single compartment bags
2. Icodextrin (hexose oligo-polysaccharid) as colloid osmotic:
   - 10-15% absorbed and results in elevated plasma maltose levels: can cause pseudo hyperglycemia by cross-reacting with glucose on some portable glucometers[2]
   - Sterile peritonitis, particularly with some batches with toxic contaminants (bacterial peptido-glycans)[3]

1. Sitter, T, et al. Impact of glucose in peritoneal dialysis. Perit Dial Int 2005; 25:415.
2. Riley, SG et al. Spurious hyperglycaemia and icodextrin in peritoneal dialysis fluid. BMJ 2003; 327:608.
3. 14. Seow, YY. Icodextrin-associated peritonitis among CAPD patients. Nephrol Dial Transplant 2003; 18:1950.

Structure of Icodextrin



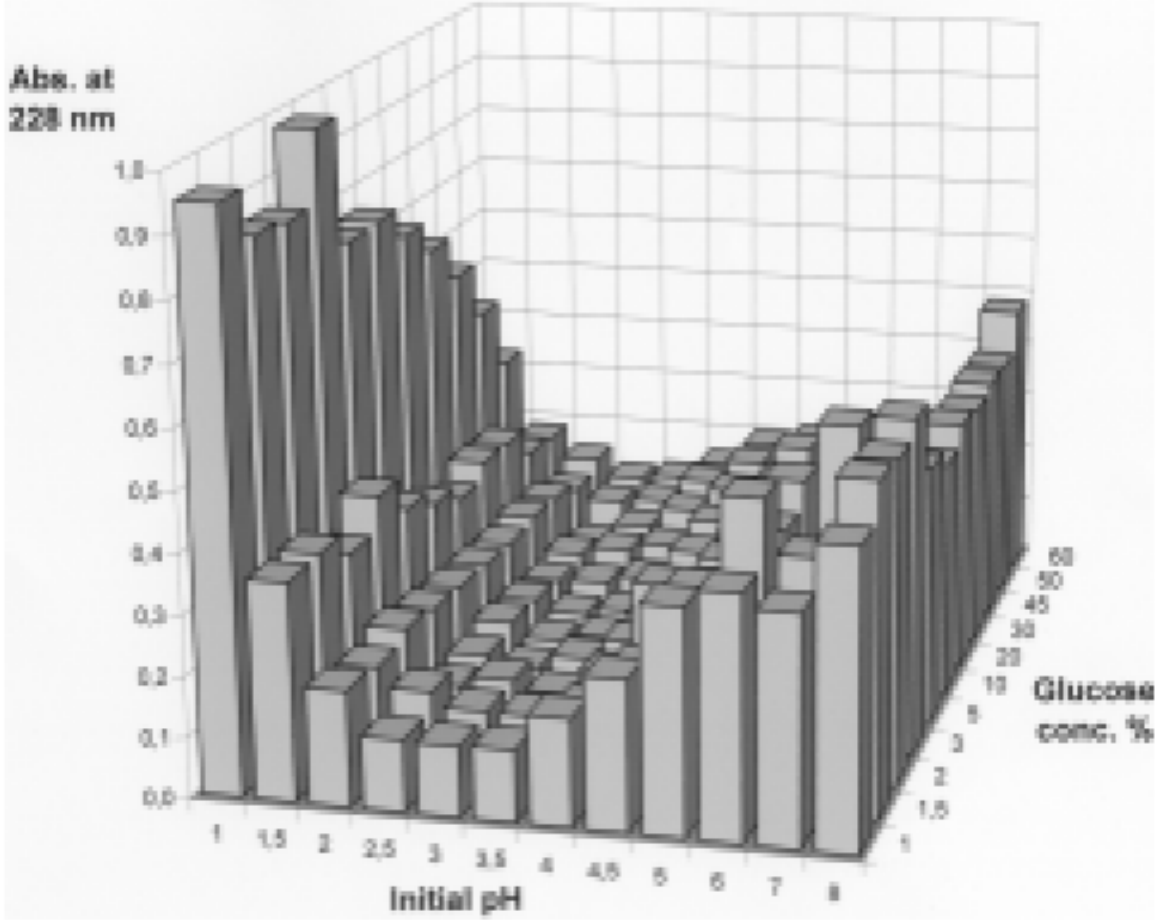
Icodextrin Sterile Peritonitis

1. Etiology and Incidence:
   - 2001 incidence estimated 10-30% per year
   - Manufacturer reports link to batches with peptidoglycan (PGN) concentration >10 ng/ml
2. Recurrent icodextrin sterile peritonitis
   - 7 patients (20%) exposed to recalled lots developed sterile peritonitis
   - 2/7 resolution despite continuing icodextrin; 2/7 undergo catheter removal
   - 3/7 clear when icodextrin stopped, recur with re-exposure to PGN free dialysate
   - Hypersensitivity to trace amounts PGN vs. novel antigen

1. Foggensteiner et al (letter): Perit Dial Int 22 (1): 89, 2002.
2. Seow, YY. Icodextrin-associated peritonitis among CAPD patients. NDT 2003; 18:1950.
3. Povlsen et al. (letter) PDI 23:509, 2003

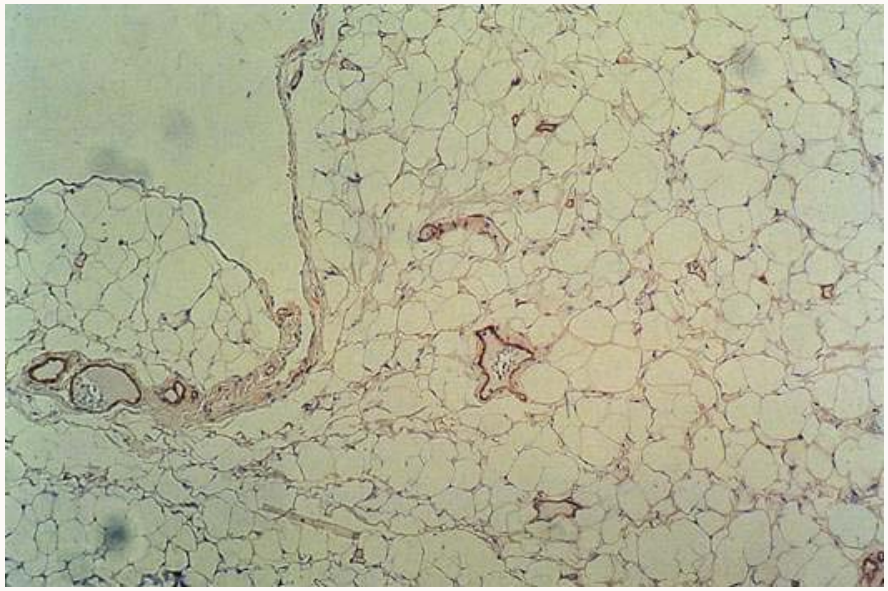
Toxic glucose degradation products (GDPs) in Peritoneal Dialysis Fluid

- Acetaldehyde
- Glyoxal
- Methylglyoxal
- 3-deoxyglucosone
- Formaldehyde
- 3,4-dideoxy-glucosone-3-ene (3,4-DGE)

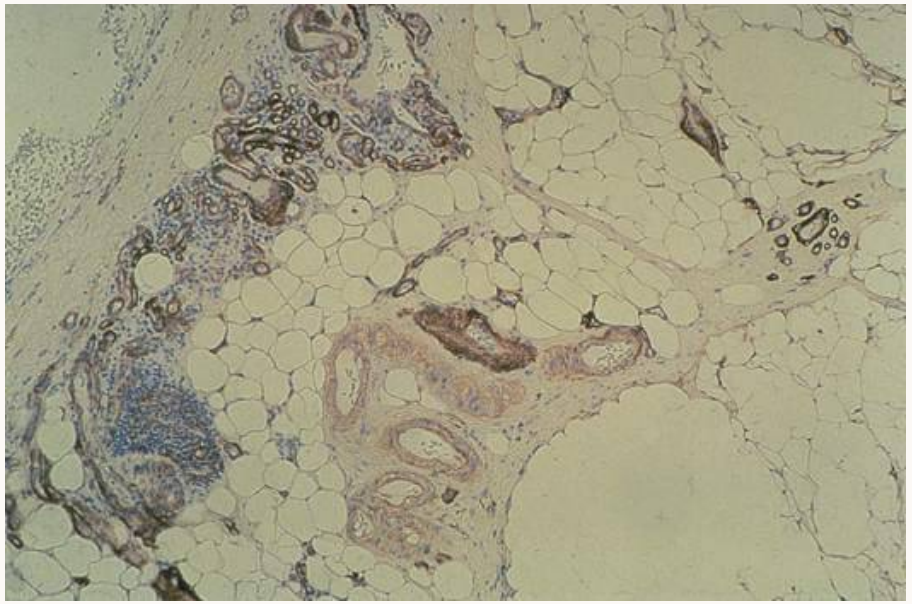


Kjellstrand P et al. PDI 21:338, 2001

Alterations of the peritoneum on PD: Effects of Chronic Glucose Dialysate



Initiation of CAPD



25 months CAPD

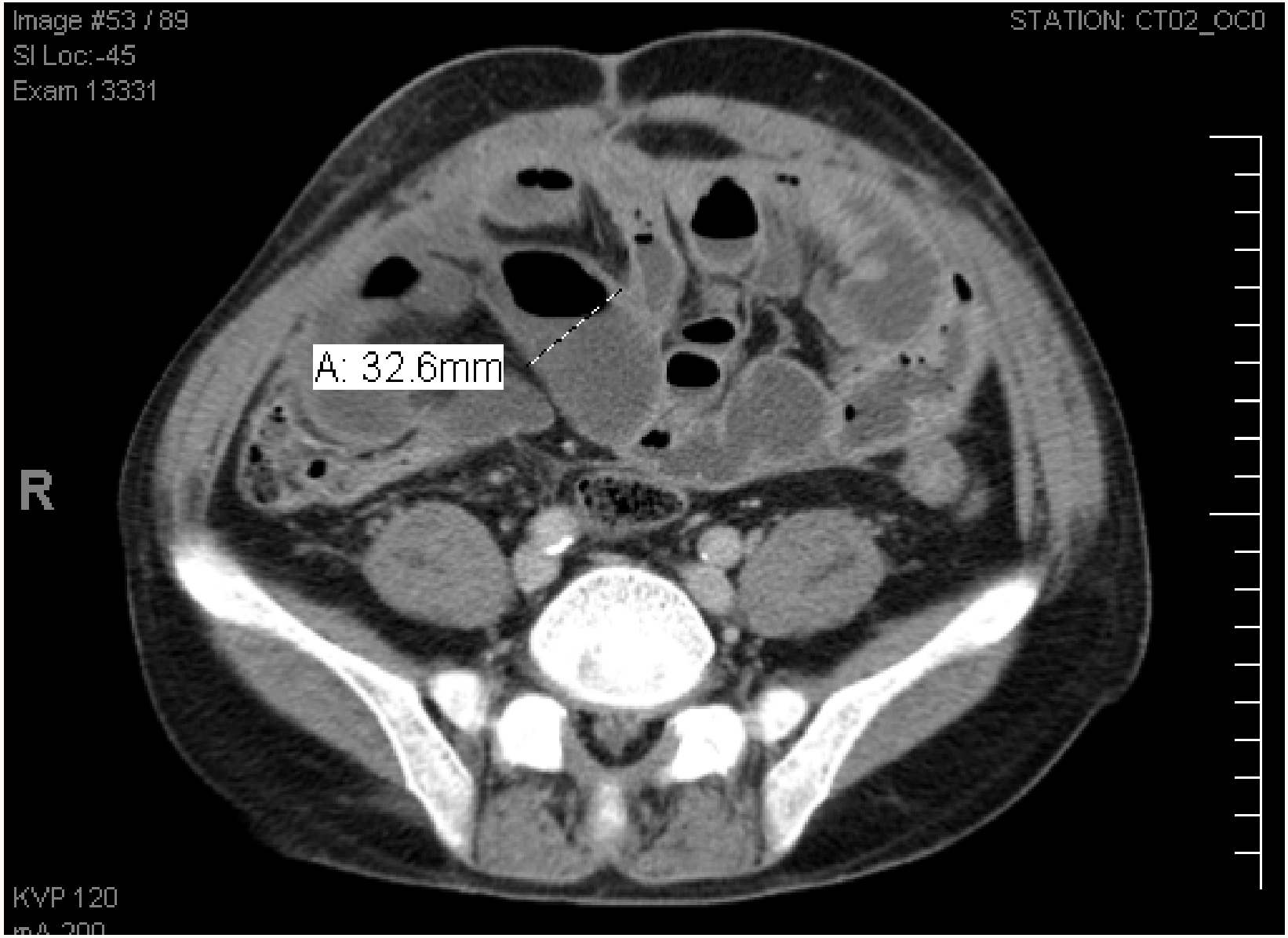
Mateijsen M. Perit Dial Int 19:517, 1999)

Sclerosing Encapsulating Peritonitis

1. Etiology and diagnosis (incidence 0.5-2.5% of PD patients):
   - Usually develops after years of PD
   - Associated with high glucose and acetate in PD fluid, prior peritonitis, beta-blockers
   - Diagnosis established with imaging findings (CT or MRI)
2. Treatment:
   - Adjust PD regimen for maximum biocompatibility (early EPS)
   - Transfer patient to HD temporarily or permanently
   - Corticosteroid treatment
   - Expert surgical adhesio-lysis
3. Prognosis:
   - Risk of death and PD technique failure with transfer to HD high

Kawanishi, H, et al. Encapsulating peritoneal sclerosis in Japan: a prospective, controlled, multicenter study. Am J Kidney Dis 2004; 44:729.

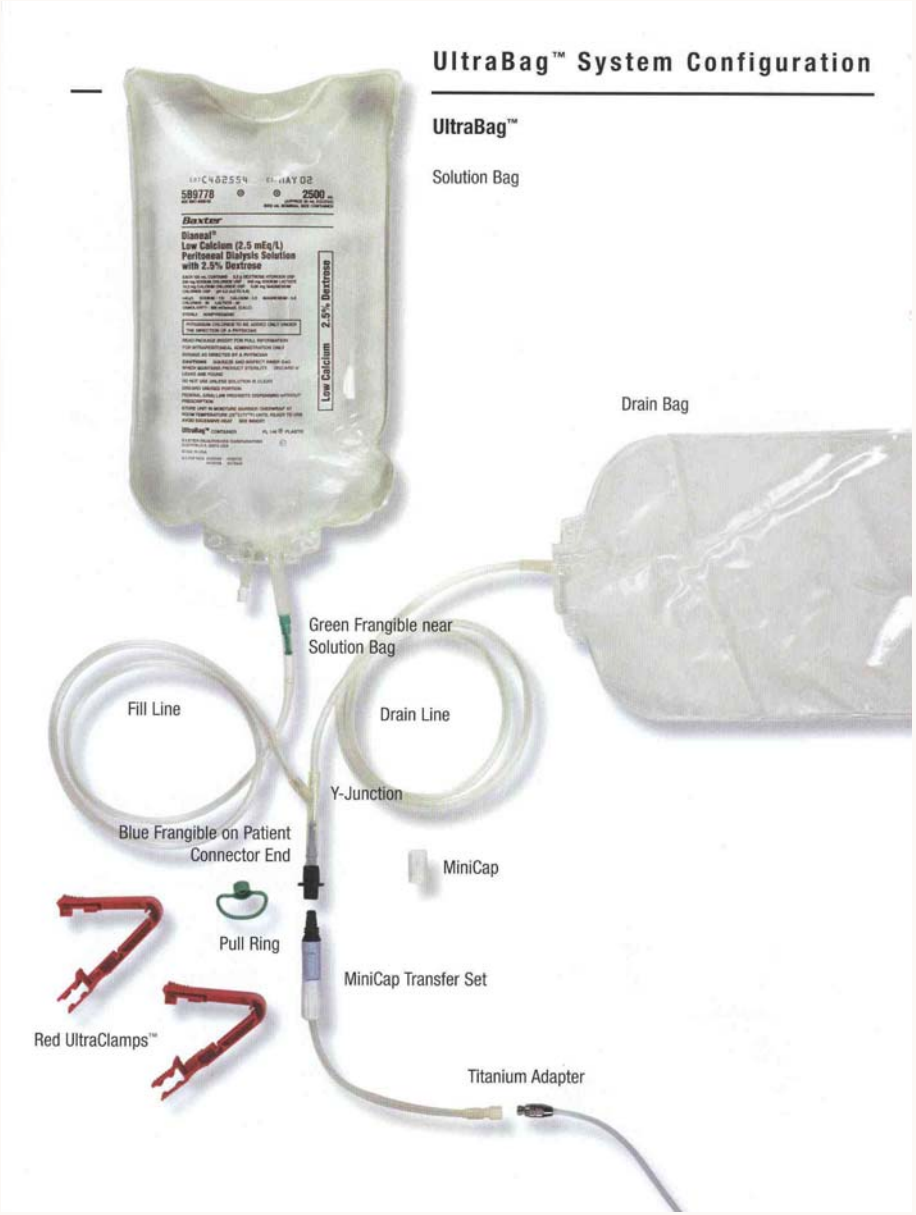
Sclerosing Encapsulating Peritonitis



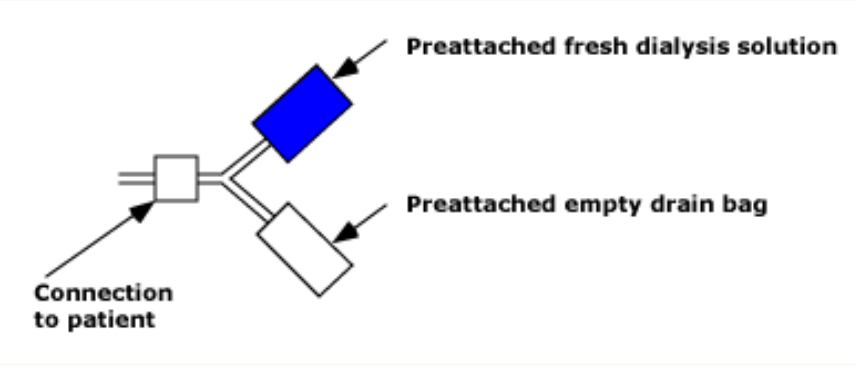
Peritonitis in the PD patient

1. Etiology and diagnosis:
   - Differentiate simple versus complicated (transluminal-touch contamination, peri-luminal, trans-visceral, hematogenous)
   - <1 % associated with bacteremia
   - Evaluate symptoms; fluid cloudiness, WBC count, cultures
2. Prevention is the most important intervention:
   - Proper training of the patient in exchange procedures
   - Use of Y-connect system possible with double bags; APD
   - Antibiotic prophylaxis before bacteremic procedures (e.g. dental, colonoscopy) and PD catheter insertion
3. Treatment (usually with intra-peritoneal antibiotics)
   - Consider severity and local antibiotic sensitivity profile
   - Use non-nephrotoxic drugs to preserve RKF

Y-connection with double bag for CAPD



- Fresh fluid: no need for manual spike
- Drain bag: pre-connected; sterile
- Minimizes risk of intra-luminal contamination



Daly, CD et al. Do the Y-set and double-bag systems reduce the incidence of CAPD peritonitis? A systematic review of randomized controlled trials. Nephrol Dial Transplant 2001; 16:341.

Other PD Complications

1. Mechanical complications:
   - Gastroesophageal-reflux and delayed gastric emptying: Reduce fill volume if feasible, use motility agents (metoclopramide, erythromycin)
   - Back and abdominal pain: reduce fill volumes if possible, CCPD, use more bio-compatible fluids
   - Pleural effusion due to pleuro-peritoneal leak: 1.6-10% of patients; reducing supine fill volumes and pleurodesis may help
2. Other complications
   - Hypokalemia: more liberal K diet and or supplements will usually correct the problem
   - Hypomagnesemia: theoretically a 0.5 mmol/L PD Mg level may be optimal; hypermagnesemia should be avoided as it may contribute to adynamic bone disease