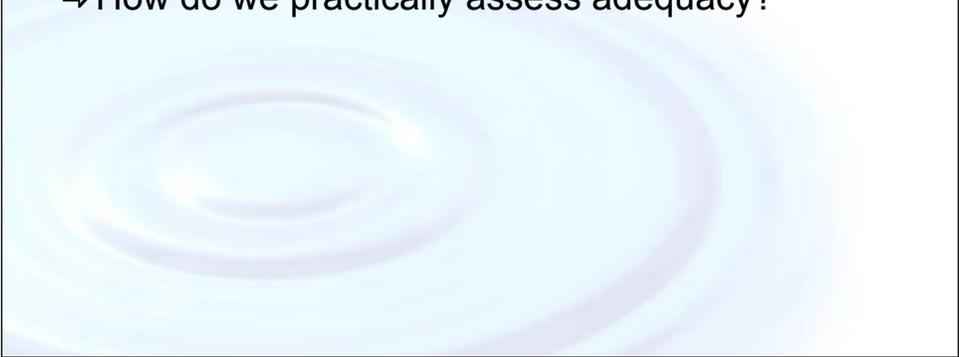# Peritoneal Dialysis Adequacy

Suzanne Watnick, MD
Associate Professor of Medicine
Training Program Director
Oregon Health & Science University

Outline of Talk

⇨ What is Adequacy (Definition)?

⇨ What do the current guidelines say?

⇨ What basic literature is important?

⇨ How do we practically assess adequacy?

Case to illustrate the issues…

- Mr H is a 37 yo caucasian gentleman, ESRD x 4 years due to T1 DM since age 2
  - He chose PD because he still works full time
  - Gastroparesis is his biggest complaint
    - He stopped his midday exchange x 1 mo
    - Insists he feels better: ⬇ nausea, better appetite
  - Regimen: 4 x 2.0L nighttime exchanges of 1.5% Dianeal; final fill and midday exchange 1.5L of 2.5% Dianeal

Case continues

- The renal fellow gets all the appropriate information, and tells Mr H that he should not have stopped his daytime exchange.
- Is the fellow correct?
- Is Mr H receiving adequate dialysis?
- **What is adequacy**?

What is Adequacy?

Active learning exercise:
- How would you define adequacy in terms of replacing renal function?

In nephrology, adequacy first used to describe an appropriate dose of hemodialysis (HD)*
- Adequacy for peritoneal dialysis adopted later
- Conceptual overall goal equivalent to HD, calculations not equivalent**

*Frank Gotch introduced the concept of adequacy of dialysis when he proposed the 'Urea Clearance' concept as a measure of dialysis efficacy. - personal communication, George Porter, MD

**In HD, Kt/V equation is used to account for the fall in efficiency as urea concentrations diminish during the HD session. Note the logarithmic (ln) term :
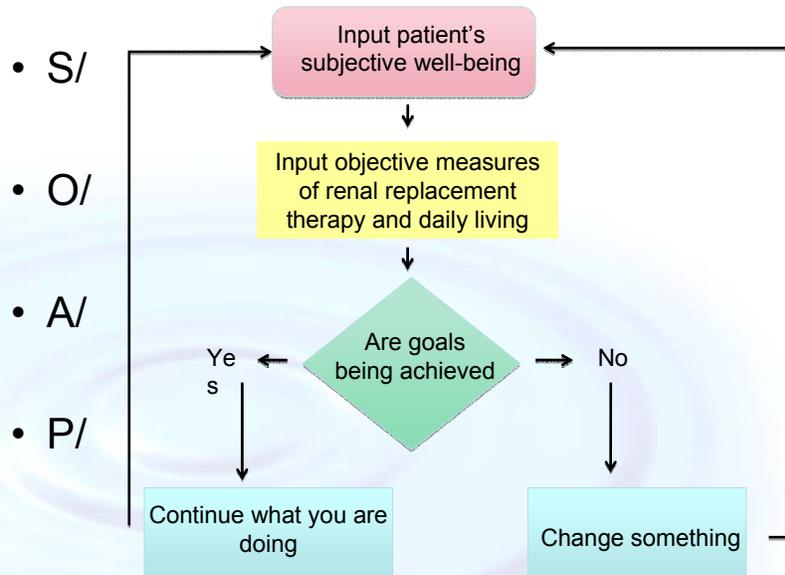
$$Kt/V\ (HD) = -\ln(R - .008 \times t) + (4 - 3.5 \times R) \times 0.55 UF/W$$

In CAPD, this fall in efficiency does not happen

- Kt/V relates to the actual mass of urea removed.

This means that Kt/V cannot be compared between HD and PD since they are different measures which happen to share the same name.

Adequacy Algorithm

- S/

- O/

- A/

- P/

Input patient's subjective well-being

Input objective measures of renal replacement therapy and daily living

Are goals being achieved

Yes

No

Continue what you are doing

Change something

Adequacy: the ability of a treatment plan (i.e., dialysis) to meet the needs and demands of the system (i.e., the body) at all times to maintain satisfactory (if not optimal) performance in the steady state (i.e., more than a minimal Kt/V).

What contributes to Adequacy?

Broad sense

Control of:

– Acid-base status
– BP and volume status
– Cardiovascular Risk
– Diet/nutrition
– Mineral/Bone disorders
– Small/middle molecules

Possibly most important:
How the patient feels!

Adequacy is a concept, not a number, and includes more than the issues listed above.

What contributes to Adequacy?

Narrow Sense:

- Appropriate small molecular weight solute clearance
- Specifically measured as urea clearance
  - In PD, you measure Kt/V_{total} = Renal Kt/V + Dialysate Kt/V
  - Renal ≠ Dialysate Kt/V but this is how it is practically calculated
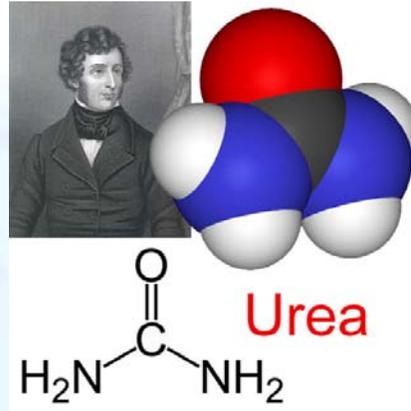
Urea

Fun fact: Urea was discovered by Hilaire Rouelle in 1773. It was the first organic compound to be artificially synthesized from inorganic starting materials, in 1828 by Friedrich Woehler.

Adequacy: Guidelines

KDOQI Guidelines

Minimal 'delivered' dose

- Total Kt/V$_{urea}$ AT LEAST 1.7 per week.
- sum of peritoneal and renal urea clearance
- Caveat: If urine output > 100cc/day, collection should be performed.

KDOQI = Kidney Disease Outcomes Quality Initiative, sponsored by the National Kidney Foundation (NKF)

Adequacy: Guidelines

ISPD Recommendations

– Adequacy should be interpreted clinically rather than via solute and fluid removal

– For small solute removal, total (renal + peritoneal) Kt/V_{urea} not less than 1.7 at any time

– If pt relies on residual renal function to achieve adequacy, monitor q1-2mo if able, but no less than q4-6 mo

1.7 is

Floor

Not

ISPD = International Society of Peritoneal Dialysis
Lo WK et al, Peritoneal Dialysis International 26:520, 2006
The Guidelines are much more extensive than what is listed here. Please refer to article for further information.

Show me the data

CANUSA Trial

- Led to prior guidelines of Kt/V_{urea} 2.0 target for CAPD, higher targets for CCPD and NIPD, without data, but from theoretic considerations
- Prospective observational cohort, 680 pts
- Looked at relationship of dialysis adequacy and nutritional status to mortality, morbidity, and technique failure
- Decr 0.1 of Kt/V_{urea} resulted in increased risk of death of 5%

CANUSA continued

- Findings based on assumption that
  - 1 unit of renal clearance = 1 unit of dialysis clearance
- Reanalysis showed survival related to:
  - residual renal function
    - Declined over time
  - Not dialysis clearance
    - Usually stable over time

Bargman et al, J AM Soc Nephrol 12:2158, 2001

Show me more data

- Prior Kt/V_{urea} goal (guidelines): 2.0
- Some patients looked clinically fine, but did not achieve goal
  - Resulted in conversion of some to HD
  - **Would lower Kt/V achieve clinically adequate clearances?**
  - 2 important Randomized Control Trials:
    - ADEMEX (Adequacy of PD in Mexico)
    - Hong Kong PD trial
    - Both showed a lower achieved Kt/V_{urea} did not lead to higher mortality rates.

ADEMEX 1

- 965 patients randomized to:
  - 4 daily 2L exchanges versus
  - Increase in dose to achieve peritoneal CrCl >60L/wk/1.73m2
- Achieved CrCl 46 v 57 L/wk/1.73m2
  - Kt/V 1.62 v 2.13
- No difference in overall survival
  - 68 v 69%, at least 2 year follow-up

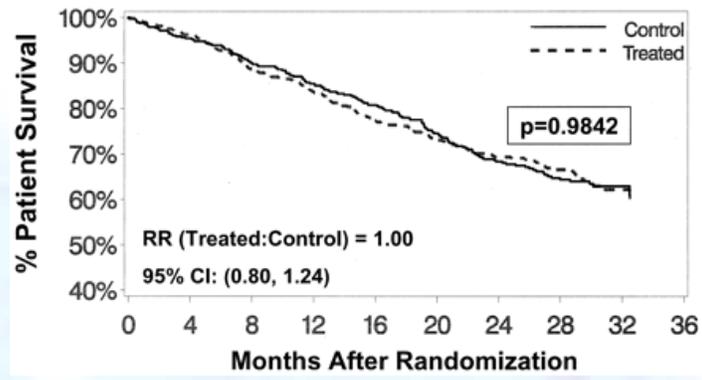Paniagua R et al. J AM Soc Nephrol 13: 1307, 2002
Note that clearance in peritoneal dialysis has typically been measured by either Kt/V or creatinine clearance (CrCl).
Note that both have a peritoneal and renal component.
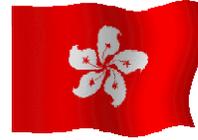A common discordance is to achieve Kt/V targets but not the creatinine clearance. Residual renal function can contribute a significant quantity to CrCl, so loss of residual renal function contributes disproportionately to in ability to achieve total target CrCl. Current guidelines emphasize CrCl less than prior, although current ISPD guidelines suggest a target of 45 L/wk/1.73m2 for Automated PD (APD), due to a more variable relationship between urea and creatinine clearances. (Evidence level C)

ADEMEX 2

% Patient Survival (y-axis): 100%, 90%, 80%, 70%, 60%, 50%, 40%

Control
Treated

p=0.9842

RR (Treated:Control) = 1.00

95% CI: (0.80, 1.24)

Months After Randomization (x-axis): 0, 4, 8, 12, 16, 20, 24, 28, 32, 36

No differences by age, diabetic status, or serum albumin

Hong Kong Trial 1

- 320 incident PD patients
- Target total Kt/V_{urea} (PD + RRF)
  - 1.5-1.7, 1.7-2.0, or > 2.0
- Good separation between groups
- Achieved appropriate total Kt/V_{urea}
  - Peritoneal Kt/V: differences from month 1
  - No difference in renal Kt/V
- Survival no different between groups

Lo WK et al. Kidney Int 64: 649, 2003

Hong Kong Trial 2

- No difference among groups in:
  - OVERALL MORTALITY
  - Overall nutritional status
  - Serum albumin
- Differences in:
  - ESA dose
  - Uremic symptoms
    - higher ESA doses and more symptoms in Kt/V group 1.5-1.7 only

Hong Kong 3

P = 0.99
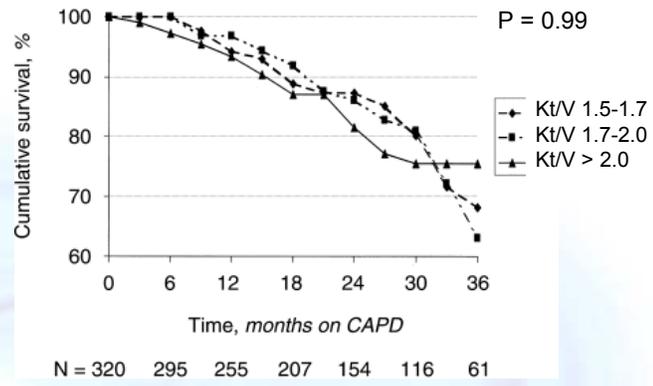
Effect of increasing Kt/V urea above 1.5 on mortality

Floor v Target Dialysis Dose

- Consensus:
  - Kt/V = 1.7 is a reasonable 'floor' dialysis dose, even though neither study showed a true minimum re: mortality benefit of dialysis dose
- Recall, many natural phenomena follow a normal distribution - If 1.7 is used as target Kt/V_{urea}, some will fall above and some will fall below.
- An important thought experiment for learners:
  - what is a reasonable target so to achieve an 'adequate' Kt/V of 1.7 in almost all patients?

There is no clear answer to this thought experiment in the literature. Some centers advocate for a target Kt/V of 2.0 (the prior KDOQI guideline) to achieve an 'adequate' dose of peritoneal dialysis, as defined by small solute clearance.

There are many factors that determine clearance for PD patients. Some of these include factors not changeable via prescription (body size, peritoneal transport characteristics, residual renal function) and those changeable via prescription (frequency of exchanges, dwell volume, tonicity of solutions, day versus night dwells).

Equations 1
Weekly Kt/V for PD

- Kt/V_{urea} – not necessarily the optimal measurement, but what we use
- K = Volume cleared/time (Liters/day)
- t in days
- $V_d$urea ~ TBW (in Liters)
- Kt/V in PD over 1 day x 7 = adequacy over 1 week

Kt/Vurea was adapted from the HD literature
Determinants of K here: Surface area and urea permeability of the peritoneal membrane, blood flow, dialysate flow.
(note the K in PD is relatively analogous to HD where determinants of K are surface area and urea permeability of the dialyzer, blood flow, and dialysate flow).

Equations 2

Calculate K_{urea}

Renal Clearance: $C_x = \dfrac{[U_x] \times \text{urine Volume}}{[P_x]}$

PD Clearance: $C_x = \dfrac{[D_x] \times \text{dialysate Volume}}{[P_x]}$

So, $K_{urea} = D/P_{urea} \times \text{dialysate V}$

Note that both clearance formulas illustrate clearances – U/P for renal (urinary) clearance is analagous to the D/P for the peritoneal (dialysate) clearance.

Equations 3
Weekly PD clearance

$$Kt/V = \frac{[D/Purea \times Dial\ Volume] \times 7days}{V_d urea}$$

What is Mr H's dialysate clearance?
He weighs 70kg. He brings in his solutions.
Samples show: dialysate urea = 36 mg/dl
Serum urea = 42 mg/dl
24 h dialysate Volume (see slide 3) = 11.6 L*
V_d urea (TBW) = 70kg x 0.6 = 42 L

The unitless answer is 1.67 for the week

* To the learner, ensure calculations for 24h dialysate volume are clear before proceeding further.
Mr H's 24 hour dialysate volume put into his peritoneal space = 9.5L (2.0L x 4 plus final fill of 1.5L), but he also ultrafiltered 2.1 L for a total 24hr volume of 11.6 L
Also, ensure you understand the calculation and answer for the weekly PD clearance.

Equations 4
Calculate renal Kt/V$_{urea}$

$$Kt/V = \frac{[U/P_{urea} \times Urine\ Volume] \times 7\ days}{V_d urea}$$

What is Mr H's residual renal clearance?
Urine urea = 437 mg/dl
Serum urea (as before) = 42 mg/dl
Urine Volume = 365 ml = 0.365 L
V$_d$urea (as before) = 42 Liters

Renal Kt/V = 0.62 for the week

Note this equation is identical to the one for Kt/V for peritoneal dialysis, except urine urea is substituted for dialysate urea, and Urine Volume is substituted for dialysate volume.
The learner should ensure that he or she arrives at the same answer as the slide for renal Kt/V.

What is clinical adequacy?

Now let's discuss Mr H's adequacy

Total Kt/V =

Peritoneal + renal Kt/V = 1.67 + 0.62 = 2.29

Note: He is achieving adequacy

1) by numbers

2) by subjective measures

he SAYS he feels better

3) by physical well-being

not previously described, but his volume status, BP, 'lytes, minerals, & anemia are on target

After reviewing the slide set, the renal fellow has to concede that Mr H is doing better even though he is doing less dialysis. This is not necessarily the typical case. However, it does emphasize the importance of recognizing a patient's concerns and considering that a non-traditional mechanism of achieving adequacy can both a happier provider and patient make. Return to slide 4 at this point, and ensure that you can answer the questions that were posed.

Adequacy is….

- A state of well-being, not specifically defined by one number
- A minimum total Kt/V_{urea} of 1.7 if you require a number
  - Sum of renal function and dialysate Kt/V_{urea}
  - RCT data exist! (rare in nephrology)
- Determined by both patient & provider
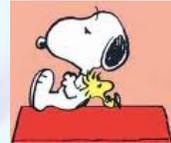
References

- Adequacy of dialysis and nutrition in continuous peritoneal dialysis: association with clinical outcomes. Canada-USA (CANUSA) Peritoneal Dialysis Study Group. J Am Soc Nephrol 1996; 7:198.
- Bargman, JM, Thorpe, KE, Churchill, DN. 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.
- Paniagua, R, Amato, D, Vonesh, E, 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.
- Lo, WK, Ho, YW, Li, CS, et al. Effect of Kt/V on survival and clinical outcome in CAPD patients in a randomized prospective study. Kidney Int 2003; 64:649.
- Lo, WK, Lui, SL, Chan, TM, et al. Minimal and optimal peritoneal Kt/V targets: results of an anuric peritoneal dialysis patient's survival analysis. Kidney Int 2005; 67:2032.
- Jansen, MA, Termorshuizen, F, Korevaar, JC, et al. Predictors of survival in anuric peritoneal dialysis patients. Kidney Int 2005; 68:1199.
- Lam, MF, Tang, C, Wong, AK, et al. ASPD: A prospective study of adequacy in Asian patients on long term, small volume, continuous ambulatory peritoneal dialysis. Perit Dial Int 2006; 26:466.
- K/DOQI Clinical Practice Guidelines for Peritoneal Dialysis Adequacy. Am J Kidney Dis 2006; 47(Suppl 4):S1.
- European Best Practice Guidelines for peritoneal dialysis. Nephrol Dial Transplant 2005; 20(Suppl 9):1.
- Lo, WK, Bargman, JM, Burkart, J, et al. Guideline on targets for solute and fluid removal in adult patients on chronic peritoneal dialysis. Perit Dial Int 2006; 26:520.
- Brimble, KS, Walker, M, Margetts, PJ, et al. Meta-analysis: Peritoneal membrane transport, mortality, and technique failure in peritoneal dialysis. J Am Soc Nephrol 2006; 17:2591.

Question #1

- A 52-year-old Caucasian gentleman on peritoneal dialysis for 2 years comes for his quarterly adequacy measurements. His CCPD prescription consists of five 2.8 L exchanges, with a final fill of 2 L in the morning, all of which are 2.5% Dianeal (total volume of 16 L per day). He says that he makes 3 cups of urine a day. It is time to perform his peritoneal dialysis adequacy measurements.

Question #1: Continued

- At minimum, you should request:
  - A. Aliquots of PD fluid at zero, 2, and 4 hours for urea, creatinine, and glucose measurements after an initial exchange of 2.0 L containing 2.5% Dianeal.
  - B. Aliquots of PD fluid collected at zero and 24 hours for urea and creatinine from the cycler's final morning drain and urine collected over the past day.
  - C. Creatinine clearances from PD effluent and urine collected over the past 2 days
  - D. Creatinine clearances from PD effluent and urine collected over the past day
  - E. Urea clearances from PD effluent and urine collected over the past day

Question #1: Correct answer is E

- Main Point: Describe how adequacy measurements are accomplished for peritoneal dialysis

- Although all clearances are not created equal, we do add renal and dialysate clearances to get total clearance. (Renal Kt/V urea + dialysate Kt/V urea = total Kt/V urea for each patient.) This sum gives the total dialysis 'adequacy', as measured by urea clearance. Although this is not necessarily an ideal measurement of adequacy, it is the current measurement from which regulatory bodies assess peritoneal dialysis clearances. Current KDOQI guidelines state that total Kt/V should not go below 1.7.

Question #1: Discussion Continued

- How is this done? Patients collect a 24-hour urine sample for urea clearance, from which the renal Kt/V urea can be calculated. The patients also record 24 hour volume removal (ultrafiltration) from their peritoneal dialysis effluent, and bring aliquots from the drain bags for that period. (It would be too cumbersome to bring more than 16 liters to the dialysis unit!) Creatinine clearances have been measured as part of peritoneal dialysis adequacy in the past, and can give information about clearance, but are not the current standards by which regulatory bodies and most dialysis units monitor adequacy. Thus, answers c and d, which do not have a urea component, are incorrect. The description of aliquots at zero, 2 and 4 hours describe a peritoneal equilibration test (PET) to decribe peritoneal membrane characteristics, thus 'a' is not correct. Aliquots collected only from the morning drain will not capture clearances from the daytime fill, so 'b' is incorrect.

Question #2

- A 67 yo African American woman has been on peritoneal dialysis for 3 years. She has had declining residual renal function. She used to have a Kt/V urea of > 2.2, but now her Kt/V urea is 1.81. The woman states that she feels great, and no different from how she felt a year ago when her Kt/V urea was 2.12. Her dialysis nurse is insistent that she increase the size and number of dwells, despite the reluctance of the patient.

Question #2: Continued

- The best evidence to back up the patient's claims would be which statement:
  - A. More than one RCT has shown no worse outcome with Kt/Vurea 1.7-2.0 versus >=2.0.
  - B. More than one observational trial has shown no worse outcome with Kt/Vurea 1.7-2.0 versus >= 2.0.
  - C. More than one RCT has shown African Americans have equivalent outcomes with Kt/Vurea 1.7-2.0 versus > 2.0
  - D. More than one observational trial has shown that Kt/Vurea is not the optimal measurement of PD adequacy.

Question #2: Correct answer is A

- Main Point – Describe the existing evidence base regarding peritoneal dialysis adequacy measurements and outcomes.

- It is helpful to be aware of two trials with reference to this question. The ADEMEX trial randomized patients to a dialysis dose of 4 x 2L exchanges per day or a targeted creatinine clearance of >= 60 L/week/1.73m2. (The average Kt/V urea for each group was 1.80 vs 2.27.) Mortality was not different between groups. A trial by Lo et al, from Hong Kong, targeted a total Kt/V urea of < 1.7, 1.7-2.0, or > 2.0 per week. Mortality was not different between groups, and the groups achieving Kt/V 1.7-2.0 and > 2.0 were remarkably similar in other ways as well. The group < 1.7 had a higher drop out rate and required more erythropoietin. RCTs, such as the ADEMEX trial and a trial by Lo et al from Hong Kong, have shown that outcomes such as mortality as a result of clearance targets in the 1.7-2.0 range are not worse than outcomes for a total Kt/Vurea >2.0. Even if observational trials did exist, 'a' would still be a better choice than 'b' because data from RCTs are superior to those from observational trials. The ADEMEX trial had primarily Mexican patients, and the trial from Hong Kong was racially homogeneous, too. No RCT has had substantial African American populations. Thus, 'c' is not the most correct answer. 'D' is incorrect because there have not been trials to show that other measurements of adequacy are more predictive of outcomes than Kt/Vurea.