II. NKF-K/DOQI CLINICAL PRACTICE GUIDELINES FOR PERITONEAL DIALYSIS ADEQUACY: UPDATE 2000

NOTE: The citation for these guidelines should read as follows: National Kidney Foundation. K/DOQI Clinical Practice Guidelines for Peritoneal Dialysis Adequacy, 2000. Am J Kidney Dis 37:S65-S136, 2001 (suppl 1)

Acronyms and Abbreviations

Abbreviation	Term
ACE	angiotensin-converting enzyme
BSA	body surface area
BUN	blood urea nitrogen concentration
CANUSA	Canada/USA Peritoneal Dialysis Study
CAPD	continuous ambulatory peritoneal dialysis
CCPD	continuous cycling peritoneal dialysis
C_{Cr}	creatinine clearance
$C_{r\,Cr}$	residual renal creatinine clearance
CKD	chronic kidney disease
DI	dialysis index
DPI	dietary protein intake
eC	effective clearance
ESRD	end-stage renal disease
GFR	glomerular filtration rate
HD	hemodialysis
$K_{p\,Cr}$	peritoneal creatinine clearance
K_pt/V_{urea}	the peritoneal component of Kt/V_{urea}
$K_{pr}t/V_{urea}$	the sum of peritoneal and renal Kt/V_{urea}. These terms are interchangeable in that Kt/V_{urea} is total unless otherwise noted.
Kt/V_{urea}	urea clearance × time normalized by total body water, the volume of distribution of urea
K_rt/V_{urea}	the renal component of Kt/V_{urea}
MTC	mass transfer coefficient
n	normalized
nBSA	normalized body surface area
NIPD	nocturnal intermittent peritoneal dialysis
nPCR	normalized protein catabolic rate
nPNA	normalized protein equivalent of total nitrogen appearance
nV	normalized volume
PCR	protein catabolic rate
PD	peritoneal dialysis
PET	peritoneal equilibration test
PNA	protein equivalent of nitrogen appearance
QOL	quality of life
RKF	residual kidney function
RRF	residual renal function
SGA	subjective global assessment
SHR	standardized hospitalization rates
SUN	serum urea nitrogen concentration
t	time
UKM	urea kinetic modeling
UNA	urea nitrogen appearance
URR	urea reduction ratio
USRDS	United States Renal Data System
V	volume of distribution. When referring to urea, this is total body water

Introduction

THIS WORK GROUP was charged with preparing practice guidelines for the "adequacy of peritoneal dialysis," a topic that could be defined broadly or narrowly. The Work Group elected to focus its guidelines on those areas of "adequacy" that needed the most urgent development, knowing that subsequent guidelines will be developed or that others were currently under development (eg, for management of peritonitis). In addition, the Work Group focused on topics for which guidelines would likely have the greatest impact on patient outcomes. However, the Work Group's focus should not be construed to mean that areas not covered are unimportant.

Some external reviewers criticized these guidelines as too complex, while others wrote that they were not thorough enough. Some wanted guidelines merged, and others thought the guidelines were too dense. The Work Group considered all these issues.

We advise the reader to first become familiar with the Table of Contents, which provides a listing of the Clinical Practice Guidelines for Peritoneal Dialysis Adequacy; detailed rationales are provided for each guideline. Redundancies are often intentional because it is anticipated that a reader might review only selected topics. However, the Work Group considers these guidelines as best viewed in their entirety, rather than in their component parts.

There is a paucity of data on children in the areas covered by these guidelines. Pediatricians were represented on the Work Group, and outside pediatric consultations were obtained. Because some recommendations for adults do not apply to children, additional recommendations are included when appropriate for pediatric patients. For the purpose of these guidelines, a child was considered to be a patient less than 19 years of age.

An "effective dose" is that which achieves its stated goal. That goal is some form of outcome measure(s), and could be determined by patient, provider, payer, regulator or a combination of these parties. At the lower extreme is the "minimal effective dose." In certain circumstances this may be interpreted as "adequate." At the other extreme is the "maximal effective dose," the dose above which there are no additional benefits. For hemodialysis and peritoneal dialysis the maximal effective dose is not known. Somewhere between these extremes is the "optimal dose," the dose above which the additional derived benefit does not justify the additional cost or burden. If one accepts this definition, the Work Group intended to more precisely define "optimal dose" targets in a clinically relevant and quantitative fashion. It was the intention of the Work Group to bring "adequate dose" to the level of "optimal dose" by raising the outcome goals or expectations. The present guidelines attempt to make recommendations based on available scientific/medical evidence, resorting to expert opinion only when necessary. It is clearly stated in each guideline title when recommendations were based on evidence, opinion, or both. Even when guidelines were based on opinion, that opinion is supported by direct or extrapolated evidence.

These guidelines are intended for use by health care professionals trained to understand variations in the practice of medicine and the necessity for such variation. These guidelines are not intended for punitive use by any oversight official who does not understand the reasons or the necessity for practice variations including variations in societies different from that of the United States.

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I. Initiation of Dialysis

BACKGROUND

Two clinical guidelines for when to initiate dialysis are provided because there appear to be two independent predictors of clinical outcome. The first guideline is based on the level of kidney function (as measured by K_rt/V_{urea} per week); the second is based on nutritional indices and is located in the K/DOQI Clinical Practice Guidelines in Chronic Renal Failure (Guideline 27).[2]

Although less than 1% of American dialysis patients begin dialysis with a serum creatinine concentration <8.0 mg/dL or a C_{Cr} >10 mL/min, approximately 60% suffer from nausea/vomiting at the time of dialysis initiation.[3] Thus, the likelihood of malnutrition in this population is high. Evidence from the Modification of Diet in Renal Disease (MDRD) study[4] and a recent large Australian study[5] clearly show that when the glomerular filtration rate (GFR) decreases to 25 to 50 mL/min, patients adapt by reducing their protein intake. Protein intake continues to decline as kidney disease progresses to kidney failure, administratively termed end-stage renal disease (ESRD). These observations have been corroborated in a prospective study.[6] As kidney function deteriorates, protein and energy intake decreases, leading to changes in body weight, fat mass, serum albumin, and transferrin concentrations. Earlier initiation of dialysis may prevent or perhaps even reverse this deterioration in nutritional status. Increased serum albumin concentration has been shown to parallel the increase in Kt/V_{urea} for HD patients.[7] In addition, an editorial review of cited data[8] suggests that albumin level at initiation of dialysis is predictive of survival.[9]

Adverse clinical and economic consequences of failure to properly manage patients with progressive chronic kidney disease as they approach ESRD and become dialysis dependent were first described in Britain.[10] These observations have now been corroborated in other regions of Britain, the United States, and France.[11-14] Specifically, costs, hospitalization, and morbidities decrease if attention is paid to nutrition, acid-base status, hypocalcemia, hyperphosphatemia, anemia, hypertension, volume status, and dialysis access (vascular or peritoneal). Hence, it is likely that delays in referral for initiation of dialysis result in unnecessary morbidity and potentially higher costs as well. While seeing a nephrologist does not guarantee that patients will be adequately prepared and referred for dialysis, it dramatically increases the likelihood that this will occur.[13]

The initiation of dialysis guidelines as described in this section are based on adult data. No such data exist yet in children.

GUIDELINE 1

When to Initiate Dialysis—Kt/V_{urea} Criterion (Opinion)

Unless certain conditions are met, patients should be advised to initiate some form of dialysis when the weekly renal Kt/V_{urea} (K_rt/V_{urea}) falls below 2.0. The conditions that may indicate dialysis is not yet necessary even though the weekly K_rt/V_{urea} is less than 2.0 are:

1. Stable or increased edema-free body weight. Supportive objective parameters for adequate nutrition include a lean body mass >63%, subjective global assessment score indicative of adequate nutrition (see Guideline 12: Nutritional Status Assessment, and Appendix B: Detailed Rationale for Guideline 2) and a serum albumin concentration in excess of the lower limit for the lab, and stable or rising; and

2. Nutritional indications for the initiation of renal replacement therapy are detailed in Guideline 27 of the NKF-K/DOQI Clinical Practice Guidelines on Nutrition, part of which is reproduced as Guideline 2 of the PD Adequacy Guidelines.

3. Complete absence of clinical signs or symptoms attributable to uremia.

A weekly K_rt/V_{urea} of 2.0 approximates a kidney urea clearance of 7 mL/min and a kidney creatinine clearance that varies between 9 to 14 mL/min/1.73 m^2. Urea clearance should be normalized to total body water (V) and creatinine clearance should be expressed per 1.73 m^2 of body surface area. The GFR, which is estimated by the arithmetic mean of the urea and creatinine clearances, will be approximately 10.5 mL/min/1.73 m^2 when the K_rt/V_{urea} is about 2.0.

Rationale A detailed rationale is described in Appendix A. The following is a summary.

It is paradoxical that nephrologists have fo-

cused on optimizing urea clearance once patients are started on dialysis, but have accepted much lower levels of kidney urea clearance during the pre-dialysis phase of patient management. For example, a weekly total (residual renal plus peritoneal dialysis) Kt/V_{urea} ($K_{pr}t/V_{urea}$) of 2.0 or higher is associated with improved outcomes in patients on PD (see Guideline 15: Weekly Dose of CAPD), yet dialysis is usually not initiated until weekly K_rt/V_{urea} falls to the range of 0.71 to 1.3. There is no definitive direct proof for the belief that a given level of urea clearance by the kidney is associated with better control of uremia than PD with this same urea clearance. In fact, recent studies suggest that the relationship between protein intake and weekly Kt/V_{urea} is nearly identical in patients with chronic renal failure not yet on dialysis and in patients on PD. Thus, until proven otherwise, residual kidney and peritoneal clearances of small solutes should be considered equivalent.

Once K_rt/V_{urea} falls below 2.0 per week, patients should be considered at increased risk for malnutrition and uremic complications. With further decreases in K_rt/V_{urea} in the absence of renal replacement therapy, the risk increases. Dialysis, or some form of renal replacement therapy, should be strongly considered when K_rt/V_{urea} falls below 2.0 (or C_{Cr} falls in the range of 9 to 14 mL/min/1.73 m^2) and definitely implemented if:

1. Despite vigorous attempts to optimize protein and energy intake, any of the following nutritional indicators show evidence of deterioration: (a) more than a 6% involuntary reduction in edema-free usual body weight (%UBW) or to less than 90% of standard body weight (NHANES II) in less than 6 months; (b) a reduction in serum albumin by greater than or equal to 0.3 g/dL and to less than 4.0 g/dL (see Nutrition Guideline 3), in the absence of acute infection or inflammation, confirmed by repeat laboratory testing; or (c) a deterioration in SGA by one category (ie, normal, mild moderate, severe; see Nutrition Guideline 9 and Nutrition Appendix VI).

If PD is initiated, the K_pt/V_{urea} could be increased incrementally so the combined weekly value of $K_rt/V_{urea} + K_pt/V_{urea}$ ($K_{pr}t/V_{urea}$ or total Kt/V_{urea}) does not fall below the target level of 2.0. With the incremental initiation approach frequent measurement of residual kidney function (RKF) will be necessary to assure that total delivered solute removal does not drop below targets (see Guidelines 3: Frequency of Delivered PD Dose and Total Solute Clearance Measurement Within Six Months of Initiation, and Guideline 5: Frequency of Measurement of Kt/V_{urea}, Total C_{Cr}, PNA, and Total Creatinine Appearance). Alternatively, the initiation of a "full dose" of PD may be offered (equivalent of four 2-L exchanges per day, which may yield a weekly K_pt/V_{urea} of 1.5 to 2.0, depending on transport characteristics, ultrafiltration, and body size). With initiation of "full dose" PD, frequency of measurement of RRF can be less intense.

The Work Group strongly supports the opinion that the PD outcome data for a weekly Kt/V_{urea} of $\geq$2.0 are so compelling that using the same figure for initiation of dialysis justifies the small risks of performing peritoneal dialysis. Those risks include infections and the possibility that increasing the length of time on PD contributes to eventual patient "burn-out." If a patient is suspected to be at high risk for these complications, PD may not be the best choice for renal replacement therapy. The Work Group acknowledges that the risks of early initiation of PD are not clearly known, but that the risks of late initiation are known and are unacceptable. Furthermore, not knowing which initiation strategy (incremental versus full therapy initiation) is better, the Work Group recommends that either approach be used to reach or exceed targets.

Compared to CAPD, it is more complex to calculate the incremental dose of hemodialysis (HD) that would be needed such that the total continuous delivered weekly Kt/V_{urea} would be greater than 2.0. However, it can be estimated using the fundamental assumption underlying CAPD, that at the same protein catabolic rate, continuous renal replacement therapy must keep the steady state BUN equal to the average pre-hemodialysis BUN. (See Appendix G for further discussion of this assumption.) If weekly K_rt/V_{urea} is 1.6 , for example, a one time per week HD treatment must deliver an equilibrated (double-pool) Kt/V_{urea} of 2.0 to achieve a total continuous weekly Kt/V_{urea} equivalent to 2.0. This is quite difficult to achieve, so two HD treatments per week may be more realistic for this level of RRF. If weekly K_rt/V_{urea} is 0.5, two

HD treatments must each deliver an equilibrated (double-pool) Kt/V_{urea} of 2.0 to achieve a total continuous weekly Kt/V_{urea} equivalent to 2.0. This is also quite difficult to achieve, so three HD treatments per week may be more realistic for this level of RKF. More technical details about intermittent HD are described in Appendix A, including the role of biocompatible membranes to help preserve RKF.

It is a general consensus that patients with diabetes should initiate dialysis at levels of RKF higher than in patients with causes of ESRD other than diabetes. That practice is not altered by this guideline.

The Work Group also recognizes that for many clinicians, initiating dialysis based on Kt/V_{urea} is a new concept. Therefore, we have attempted to equate this to the traditional measure of urea clearance, C_{Cr}, and GFR (estimated by the arithmetic mean of urea and creatinine clearance).

The Work Group recognizes that the patient will play a major role in accepting the initiation of dialysis based on a certain "laboratory value." It is the responsibility of the care providers to make clear to the patient the rationale for initiating dialysis when the above conditions become applicable. In particular, the nephrologist must explain to the patient the risk of malnutrition with delayed initiation of dialysis and the strong inferential evidence that survival might be improved with an earlier start of dialysis. Thus, appropriate patient education regarding an informed decision about dialysis is necessary. Medical conditions that may explain why dialysis is not being initiated when weekly K_rt/V_{urea} is less than 2.0 need to be documented. These conditions are described above.

Some individuals have expressed concern that this guideline will run afoul of the Health Care Financing Administration (HCFA) regulations regarding the initiation of dialysis (eg, form 2728, ESRD Medicare Medical Evidence Report). The leadership of the NKF-K/DOQI is working with HCFA to ensure that this will not be the case.

GUIDELINE 2

Indications for Renal Replacement Therapy

In patients with chronic kidney failure (eg, GFR $<$ 15 to 20 mL/min) who are not undergoing maintenance dialysis, if protein-energy malnutrition (PEM) develops or persists despite vigorous attempts to optimize protein and energy intake and there is no apparent cause for malnutrition other than low nutrient intake, initiation of maintenance dialysis or a renal transplant is recommended. (Opinion)

Note: This is Guideline 27 of the K/DOQI Nutrition Guidelines, reproduced here without the specific reference citations included. See the Nutrition Guidelines[2] for these details. This Guideline was written by members of both the PD Adequacy and Nutrition Work Groups.

Rationale It is well documented that mortality and morbidity are increased in individuals with ESRD who begin dialysis therapy with overt evidence of PEM. Accumulating evidence also indicates that initiation of dialysis more in line with current NKF-K/DOQI practice guidelines (ie, GFR $\sim$10.5 mL/min) results in improved patient outcomes compared with when dialysis is delayed until the GFR is $<$5 mL/min and symptomatic uremia and associated medical complications are present. Furthermore, there is evidence that initiating maintenance dialysis under these circumstances, and when there has been nutritional deterioration, results in an improvement in nutritional indices. There is no evidence that earlier initiation of dialysis leads to improved nutritional status among patients without overt uremia. Moreover, it has not been established that improved nutritional status at the initiation of dialysis directly leads to improved survival or fewer dialysis-related complications. Despite the lack of evidence from controlled clinical trials, interventions that maintain or improve nutritional status before the requirement for renal replacement therapy are likely to result in improved long-term survival.

There is ample evidence that the survival of patients with ESRD is closely associated with their nutritional status (Guidelines 3 through 6, 8, 18, and 23). These findings have been demonstrated not only in large, diverse populations of prevalent maintenance dialysis (MD) patients, but also in patients commencing MD therapy. Hypertension, pre-existing cardiac disease, and low serum albumin concentrations were independently associated with diminished long-term survival in 683 ESRD patients who started dialysis

during 1970 through 1989. In 1,982 hemodialysis (HD) patients, a low serum albumin concentration at the initiation of dialysis was associated with a significant increase in the relative risk of death. A direct relation between serum albumin and survival and an independent association between modified SGA and survival was observed in 680 incident CPD patients. In contrast, in one study no significant associations were found between serum albumin, creatinine, and urea concentrations and survival in incident HD patients. The sample size in the latter study was relatively small (n = 139), and 94% of the study sample were black (83%) or Hispanic (11%). No studies have specifically examined the relations among other nutritional indicators (eg, %SBW, PNA, and DEXA) and survival in incident HD or peritoneal dialysis patients.

Low-protein (eg, 0.60 g protein/kg/d), high energy (35 kcal/kg/d) diets may retard the rate of progression of chronic kidney disease (CKD) and should maintain patients with chronic renal disease in good nutritional status (Guidelines 24 and 25). However, it is recognized that such low-protein diets may not maintain adequate nutritional status in all patients, particularly if an adequate energy intake is not maintained (Guideline 25). Furthermore, there is evidence that the spontaneous intake of protein and energy, and other indicators of nutritional status, tend to diminish in patients with progressive CKD who are consuming unregulated diets. Therefore, patients with CKD need to undergo nutritional assessment at frequent intervals so that any deterioration in nutritional status can be detected early (Guidelines 23 and 26 and Appendix IV). The plan of care and nutritional interventions outlined in Guideline 18 for the nutritional management of the dialysis patient is also appropriate for patients with progressive CRI.

Because of the association between PEM and poor outcome, it is recommended that MD be initiated or kidney transplantation performed in patients with advanced CKD (ie, GFR $<$20 mL/min) if there is evidence of deteriorating nutritional status or frank PEM, no other apparent cause for the malnutrition, and efforts to correct the nutritional deterioration or PEM are unsuccessful, despite the absence of other traditional indications for dialysis (eg, pericarditis or hyperkalemia). Although the following criteria are not considered rigid or definitive, initiation of renal replacement therapy should be considered if, despite vigorous attempts to optimize protein and energy intake, any of the following nutritional indicators show evidence of deterioration: (1) more than a 6% involuntary reduction in edema-free usual body weight (%UBW) or to less than 90% of standard body weight (NHANES II) in less than 6 months; (2) a reduction in serum albumin by greater than or equal to 0.3 g/dL and to less than 4.0 g/dL (Guideline 3), in the absence of acute infection or inflammation, confirmed by repeat laboratory testing; or (3) a deterioration in SGA by one category (ie, normal, mild, moderate, or severe; Guideline 9 and Appendix VI).

RECOMMENDATIONS FOR RESEARCH

1. Studies to assess the optimal timing and indications for commencing renal replacement therapy are needed.

2. Serial evaluations of nutritional status in the course of these studies will help to determine whether initiation of dialysis indeed improves nutritional status.

3. Studies should be conducted to determine whether any GFR level can be used to indicate when maintenance dialysis should be initiated.

4. Whether earlier initiation of renal replacement therapy can prevent the development or worsening of PEM and its attendant complications needs to be evaluated in a controlled study.

II. Measures of Peritoneal Dialysis Dose

GUIDELINE 3

Frequency of Delivered PD Dose and Total Solute Clearance Measurement Within Six Months of Initiation (Opinion)

The total solute clearance (delivered PD dose plus residual kidney function) should be measured at least twice and possibly three times within the first 6 months after initiation of PD. For patients initiating dialysis for the first time and/or patients with substantial residual kidney function, the first measurement should be performed approximately 2 to 4 weeks after initiation of PD. For patients transferring from another renal replacement therapy to PD and/or for patients who do not have substantial residual kidney function, the first measurement of delivered dose of PD should be made by 2 weeks after initiation of PD. To establish a baseline, at least one and possibly two additional measurements will need to be performed in the subsequent 5 months. The frequency of measurement of residual kidney function depends on the PD prescription of incremental versus full dose (see Table II-1).

Rationale Adequate total solute clearance (delivered dose of PD plus residual kidney function) will improve patient outcomes (see Guideline 15: Weekly Dose of CAPD). To assure delivery of adequate solute clearance, measurements for solute clearance are required. In dialysis, as in other human endeavors, continuous education and repetition of a process diminish the frequency of errors, or at least increase the likelihood of recognition of such errors and compensation for them. Furthermore, physiological variations occur which must be taken into account.[17] These lines of reasoning apply to measurement of the dose of PD. Thus, measurement of delivered PD dose should be repeated periodically. The recommendation to measure C_{Cr} and Kt/V_{urea} three times within the first 6 months relates to items discussed in Guideline 7: PD Dose Troubleshooting, specifically, establishing a baseline creatinine excretion and following residual kidney function. The rationale for three measurements in the first 6 months is to establish a more accurate baseline excretion of creatinine.

Table II-1. Peritoneal Dialysis Dose and Total Solute Clearance Measurement Schedule: Initial 6 Months

	PD Fluid		PET	Urine*	
Month	K_pt/V_{urea}	$C_{Cr\,p}$		K_rt/V_{urea}	$C_{Cr\,r}$
1†	X	X	X	X	X
2‡				Y	Y
3‡				Y	Y
4‡	X	X		X	X
5‡				Y	Y
6‡	X	X		X	X

NOTE. X, measurement; Y, additional measurement if "incremental" PD utilized.

* For patients who void infrequently (<3 times in 24 hours), collect urine over a 48-hour period.

† If possible, at the end of month 1, but at the end of training if that is more convenient.

‡ The measurement interval in months 2 to 6 is flexible. At least one additional measurement after the first month's measurement is necessary. If the results of the second measurement are similar to those of the first measurement, an adequate baseline is established, obviating the third measurement. If the result of the second measurement is discrepant, a third measurement is necessary to establish a more reliable baseline.

Two measurements within the first 6 months are probably sufficient if the results are similar. Based on our collective personal experience, the Work Group believes that patient compliance with a prescribed PD regimen is highest soon after initiation of PD, eg, within the first 6 months; hence, this period is used to establish a baseline.

Delivered peritoneal dialysis dose depends on many factors, including the transport properties of the peritoneal membrane, assessed by the peritoneal equilibration test (PET).[18,19] There is evidence that the PET performed within the first week after initiation of PD may yield higher transport results than a PET performed a few weeks later.[20] This difference is statistically significant, but may not be clinically relevant. It may be more convenient to perform the first PET at the end of training, rather than at the end of the first month, and the Work Group thinks this is acceptable. However, the results after a month of PD may more accurately reflect peritoneal transport properties for the subsequent period.

In patients initiating ESRD therapy for the first time who have some RKF, delaying the PET and the first measurement of delivered dose for a month is safe and appropriate. However, for patients initiating PD because of transfer from

HD and/or for patients who do not have substantial RKF, the first measurement of delivered dose of PD should be performed earlier. In the absence of substantial RKF, waiting 1 month to measure delivered dose may result in inadequate dialysis for 1 month. Thus, the Work Group recommends that these patients undergo measurement of delivered dose of PD at 2 weeks postinitiation, assuming maintenance exchange volumes have been achieved. Patient care technicians may be able to perform these measurements.

If "incremental" PD is initiated instead of "full dose" (see Guideline 1: When to Initiate Dialysis—Kt/V_{urea} Criterion, and Appendix A, Detailed Rationale for Guideline 1), RKF must be followed carefully and frequently such that PD dose can be increased as RKF deteriorates. While urine production rate is presumed to be a clue to deteriorating RKF, that is not always the case.[21] Thus, for patients initiating PD with "incremental" PD, the Work Group recommends measuring RKF every 2 months. For patients on "full dose" PD, the Work Group recommends measuring RKF with total solute removal measurements every 4 months. If urine production rate is decreasing, measure RKF every 2 months or as often as needed and considered helpful, but at least every 4 months. Once weekly K_rt/V falls to less than 0.1, RKF can be considered negligible and its routine measurement can be stopped. Guideline 11: Dialysate and Urine Collections, addresses this subject again.

GUIDELINE 4

Measures of PD Dose and Total Solute Clearance (Opinion)

Both total weekly creatinine clearance normalized to 1.73 m^2 body surface area (BSA) and total weekly Kt/V_{urea} should be used to measure delivered PD doses.

Rationale A valid and reproducible measure of PD dose is essential to assess the quantity of dialysis delivered to an individual patient. The quantity of dialysis is an important component of the quality of dialysis. Of the few available measures of PD dose, total weekly Kt/V_{urea} and total creatinine clearance normalized to 1.73 m^2 BSA are the best, because they are most strongly associated with mortality and morbidity (see Guideline 15: Weekly Dose of CAPD). Additionally, when properly performed, these measures are reproducible enough to be useful in routine clinical practice.

The urea-based measure, Kt/V_{urea}, measures removal of the direct product of protein catabolism. The creatinine clearance (C_{Cr}) measures removal of a product of muscle metabolism, which provides insight into lean (ie, fat-free, edema-free) body mass and possibly into compliance (see Guideline 7: PD Dose Troubleshooting). In Guideline 1: When to Initiate Dialysis—Kt/V Criterion, and Guideline 15: Weekly Dose of CAPD, there is a discussion of the comparison of these two different measures. See Guideline 6: Assessing Residual Kidney Function, for a definition of total weekly C_{Cr}.

These two recommended measures have both been used to measure delivered dialysis dose. Since each measure provides slightly different information, the Work Group recommends that both measures be used. Both creatinine and urea concentration can be obtained on the same sample of urine, blood, and dialysate. No additional samples need to be collected to perform both, rather than one, of these measures. Most laboratories perform both measures simultaneously (eg, 6/60, Chem 6, etc) on automated equipment and the cost is the same for one or both measures.

GUIDELINE 5

Frequency of Measurement of Kt/V_{urea}, Total C_{Cr}, PNA, and Total Creatinine Appearance (Opinion)

After 6 months, total Kt/V_{urea} , total C_{Cr} , and PNA (with all its components) should be measured every 4 months, unless the prescription has been changed or there has been a significant change in clinical status (see Table II-2).

Rationale Despite the establishment in 1993 of ESRD Network/Health Care Finance Administration guidelines that measurements of delivered PD dose and total solute clearance be performed twice yearly, a Network Core Indicator review of 1,208 patient charts in 1995 revealed that data sufficient to calculate such measures were available for only one third of the patients. The preliminary 1996 results reveal that 69% of the patient charts have such data (Diane Frankenfield, a member of the HCFA/HSQB ESRD Core Indicators PD Subcommittee, written communication, December 4,

Table II-2. Peritoneal Dialysis Dose and Total Solute Clearance Measurement Schedule After 6 Months

	PD Fluid		Urine*	
Month	K_pt/V_{urea}	$C_{Cr\,p}$	K_rt/V_{urea}	$C_{Cr\,r}$
7				
8			X†	X†
9				
10	X	X	X	X
11				
12			X†	X†
13				
14	X	X	X	X

NOTE. X, measurement.

* If incremental PD is still being utilized at this point, the frequency of RKF testing applies as described in Table 1 of Guideline 3: Frequency of Delivered PD Dose and Total Solute Clearance Measurement Within Six Months of Initiation. For patients who void infrequently (<3 times in 24 hours), collect urine over a 48-hour period. Urine testing can cease when the residual kidney function component is a weekly $K_rt/V_{urea} < 0.1$.

† For young children who have greater difficulty with accurate urine collection than adults, this may be deferred until full urine and dialysate collections occur every 4 months (see Guideline 11: Dialysate and Urine Collection).

1996; also available on the Internet at http://www.hcfa.gov/medicare/hsqb/hsqb1.htm).

Measurements of delivered PD dose and total solute clearance are easy to perform, but require attention to detail and precision in technique for patients and dialysis staff. A variety of clinical and psychosocial events can interrupt and invalidate these measurements. It is imperative that these measurements become a routine for the patients and facility staff. Setting a goal of performing measurements every 4 months builds flexibility and leeway into a complex care plan, while assuring that a lengthy interval of possibly inadequate PD does not occur. The 4-month interval between complete measurements of total Kt/V_{urea}, total C_{Cr}, and PNA is recommended because it strikes a balance: every 4 months is often enough to be clinically helpful, but not so often as to be intrusive into a patient's lifestyle or to create a burden for the dialysis facility. Awareness of loss of RKF must be paramount. If "incremental" PD is initiated instead of "full dose" (see Guideline 1: When to Initiate Dialysis—Kt/V Criterion, and Appendix A: Detailed Rationale for Guideline 1), RKF must be followed carefully and frequently such that PD dose can be increased as RKF deteriorates. While urine production rate is presumed to be a clue to deteriorating RKF, that is not always the case.[21] Thus, for patients initiating PD with "incremental" PD, the Work Group recommends measuring RKF every 2 months (see Table II-2). For patients on "full dose" PD, the Work Group recommends measuring RKF with total solute removal measurements every 4 months. If urine production rate is decreasing, measure RKF every 2 months, or as often as needed and considered helpful, but at least every 4 months. Once weekly K_rt/V falls to less than 0.1, RKF can be considered negligible and its routine measurement can be stopped. Guideline 11: Dialysate and Urine Collections, addresses this subject again.

The impact of a change in prescription should be assessed within 2 to 4 weeks in order to determine if the recommended change has actually been executed and if it has accomplished its goal. The promptness of the assessment is important because clinical events could occur in the interval which could postpone the measurement or confound the results (see Guideline 10: Timing of Measurement).

Some clinical events may impair the quality of delivered PD. A change in clinical condition which warrants measurement of delivered PD dose is defined as any serious problem which affects nutritional status, the ability of the patient to perform PD mechanically or technically (such as stroke or arthritis, loss of surface area from surgery, decreased exchange volumes due to hernias, etc), or permanently affects the transport properties of the peritoneum (eg, protracted peritonitis).[22] Many conditions that lead to hospitalization fall into one of these categories. Any suggestion of exacerbation of uremia should prompt a measurement of delivered dose of PD.

The Work Group recognizes that technical problems in urine collections in some children may justifiably decrease the frequency of urine collections in selected cases.

GUIDELINE 6

Assessing Residual Kidney Function (Evidence)

Residual kidney function (RKF), which can provide a significant component of total solute and water removal, should be assessed by measuring the renal component of Kt/V_{urea} (K_rt/V_{urea})

and estimating the patient's glomerular filtration rate (GFR) by calculating the mean of urea and creatinine clearances.

Rationale A detailed rationale is presented in Appendix C. The following is a summary.

During the first few years of dialysis therapy, residual kidney function (RKF) contributes significantly to total solute and water removal. Preservation of RKF may be particularly important to the effectiveness of long-term PD. For solute removal targets to be met (see Guideline 15: Weekly Dose of CAPD, and Guideline 16: Weekly Dose of NIPD and CCPD) in many patients without a possibly unacceptable dialytic burden, there must be a substantial contribution from RKF.

As GFR declines over time, the contribution of secreted creatinine to total creatinine clearance (C_{Cr}) rises disproportionately and C_{Cr} becomes an inaccurate marker of GFR. Since the peritoneal membrane does not secrete solute, the GFR measure that corrects for creatinine secretion is the preferred measure to add to peritoneal clearance. In the case of a low GFR, the measurement of GFR with endogenous solutes is best done by defining GFR as the arithmetic mean of urea and creatinine clearance. This arithmetic mean essentially corrects for secretion of creatinine. This GFR measure is added to peritoneal C_{Cr}, normalized to 1.73 m^2 of body surface area and is totaled for a week. This is the "total weekly creatinine clearance."

$$\text{GFR(mL/min)} = \frac{\text{kidney urea clearance(mL/min)} + \text{kidney creatinine clearance(mL/min)}}{2}$$

$$\text{Total weekly } C_{Cr} = \text{GFR} + \text{Peritoneal } C_{Cr}$$

normalized to 1.73 m^2 of Body Surface Area

The MDRD study derived two equations which may approximate GFR,[23] which are noted in Appendix C.

An alternative measure of RKF is residual renal urea clearance, normalized to total body water, K_rt/V_{urea}. This measure can be directly added to the peritoneal urea clearance component, K_pt/V_{urea}, to create the total urea clearance normalized to total body water, $K_{pr}t/V_{urea}$ (shortened to Kt/V_{urea}).

Creatinine clearance corrected for renal secretion and Kt/V_{urea} are both valuable measures in the management of PD patients. Each measure offers different information. Since the dialysate and urine collections are being performed for either measure, the Work Group recommends that both measures be determined.

GUIDELINE 7

PD Dose Troubleshooting (Opinion)

In adult patients, a daily creatinine excretion in urine and dialysate that differs from the baseline rate (as determined during the first 6 months in Guideline 3, Table II-1) by >15% should prompt an investigation for noncompliance, improper collection of drained dialysate and/or urine, or altered peritoneal transport function. Compliance should not be assessed by comparing measured to predicted creatinine excretion.

Rationale Twenty percent of PD patients report some noncompliance with their dialysis prescription.[3] Preliminary data suggest that total daily creatinine excretion or appearance can be used as an indicator of compliance in CAPD. The premise for such use is that, in noncompliant patients who perform the proper number of exchanges only during the day of the clearance measurement,[24] the amount of creatinine excreted in 24 hours (equal to the daily amount of creatinine in the spent dialysate and urine plus an estimated amount of creatinine lost through other routes, primarily the gastrointestinal tract) will exceed the amount of creatinine produced daily. Essentially, noncompliance creates an unsteady state of recently accumulated creatinine. Thus, an increase in the daily excretion of creatinine in dialysate plus urine may indicate noncompliance just prior to the collection.[25] Other potential causes of variation in the measured amount of creatinine excreted include changes in muscle mass (see Guideline 13: Determining Fat-Free, Edema-Free Body Mass), improper collection of dialysate or urine due to timing errors, and inaccurate urine or dialysate creatinine measurement by the laboratory.[25] Finally, another potential cause of change in total creatinine excretion may be peritoneal membrane transport dysfunction. Quantitatively, a very large transport defect must occur to result in 15% variation in the daily creatinine excretion. However, if this is sus-

pected, a peritoneal equilibration test (PET) or its alternative should be performed.

A similar approach should be considered in children, although only a small number of pediatric patients have been studied in this manner.[26] Furthermore, in growing children with increasing muscle mass, there will be an increase in total creatinine excretion over time.

The Work Group's decision to use a variance of >15% in creatinine appearance over the established baseline was based on convincing but indirect evidence in adult patients. There are no data to support a similar approach in children. In PD patients who appear to be stable, creatinine appearance may vary by up to 15%, depending on a variety of factors.[27] This variance of >15% is simply a suggestion or warning to the clinician that the creatinine excretion data are not consistent with prior evaluations and suggests a need for further investigation. The intensity of the investigation that the variance triggers is a clinical decision that requires taking many issues into consideration.

The Work Group does not recommend assessing compliance by comparing measured creatinine excretion to predicted creatinine excretion. Our reasoning is as follows: The estimated amount of creatinine lost in the gut is equal to 0.036 × serum creatinine concentration in mg/dL × body weight.[28] The predicted creatinine production, in mg/day, is calculated by the Cockroft-Gault formulae[29] as follows:

$$\text{For men: } [28 - (0.20 \times \text{Age})] \times \text{Weight}$$

$$\text{For women: } [24 - (0.17 \times \text{Age})] \times \text{Weight}$$

where age is in years and weight is in kilograms.[24,30,31] These formulae were derived in a nondialysis population. The discrepancy between measured and predicted creatinine generation is expressed as the ratio of measured/predicted creatinine generation.[24]

The use of a cut-off value of measured/predicted creatinine generation to identify noncompliance is not warranted because the measured/predicted creatinine generation in compliant CAPD patients appears to vary widely.[24,32,33] In addition, the increase in the amount of creatinine excreted during the clearance day in noncompliant patients is very small in most cases.[34-36] Measured/predicted creatinine generation is better used sequentially in a patient after establishing baseline values during a period of close observation (see Table II-1).[32,36] At least for short periods of time (days or weeks), the steady-state excretion of creatinine is constant in CAPD patients,[33,37] although a variation of 15% may be essentially physiologic.[27] However, since absolute creatinine excretion is being measured and compared to a previously established reliable baseline measurement, the Work Group considers the use of predicted creatinine production to be unnecessary.

In summary, the Work Group recommends establishing a baseline creatinine excretion on the basis of 2 to 3 measurements in the first 6 months of PD (see Guideline 3: Frequency of Delivered PD Dose and Total Solute Clearance Measurement Within Six Months of Initiation). The Work Group feels that following these measures longitudinally will be more helpful than comparing measured to predicted creatinine appearance. Causes for any subsequent deviation from the baseline total creatinine excretion over time should be sought, recognizing that noncompliance is only one of several possible explanations.

RECOMMENDATIONS FOR RESEARCH

Since preservation of RKF is important for solute removal and contributes to total renal replacement therapy, there is a need to identify contributors to loss of RKF. For example, do antibiotics play a role? Hypotension? Other factors? Does aggressive solute removal and/or highly efficient dialysis remove stimulatory factors favoring remnant kidney hyperfiltration?

Why does GFR vary so much on a day-to-day basis and how does one account for this in adequacy studies? Is this a collection artifact or true physiologic variation? What factors alter the daily production and excretion of creatinine? Is it a function of creatinine production or simply excretion? If the latter, is it variation in renal secretion, filtration, or both? Urine output also varies dramatically on a day-to-day basis. Is this simply a volume phenomenon or is it a reflection of true clearance changes? Why does creatinine appearance vary even in compliant patients? In

children who are growing, how often should total creatinine excretion be measured and is it useful as an assessment of compliance with dialysis prescription?

The recommendation that >15% variance in creatinine appearance be considered as indicative of a status change or noncompliance should be validated.

An accurate, reproducible, and easy-to-perform method of measuring RKF should be developed.

III. Measurement of Peritoneal Dialysis Dose

GUIDELINE 8

Reproducibility of Measurement (Opinion)

Accurate measurement of total Kt/V_{urea} and total creatinine clearance (C_{Cr}) requires collection and analysis of urine, dialysate, and serum in a way that yields reproducible and valid results. Dialysate creatinine concentration must be corrected for the presence of glucose in some assays. Peritonitis precludes reliable measurement of delivered PD dose for up to a month. Compliance with complete collections is mandatory. For patients who void ≥3 times per day, a 24-hour urine collection is sufficient. For patients who void less frequently, a 48-hour collection is recommended. For CAPD patients, the serum sample can be obtained at any convenient time. For NIPD patients, the serum sample should be obtained at the midpoint of the daytime empty period. For CCPD patients, the serum sample should be obtained at the midpoint of the daytime dwell.

Rationale A detailed rationale is presented in Appendix D. The following is a summary.

Measurement of PD dose must be performed in a valid and reproducible fashion. The measure of creatinine concentration in effluent dialysate must be corrected for the presence of glucose with some creatinine assays. Each facility must determine whether this is necessary by specifically inquiring of its laboratory whether the creatinine assay used by that lab is altered by high glucose concentrations. PD dose measures should not be made until a month after peritonitis resolves, because peritonitis causes residual effects on membrane transport. Either total dialysate collections or aliquots (ie, samples of dialysate) can be used with proper patient training and compliance. For CAPD patients, the timing of the blood sample is not important. For patients on NIPD or CCPD, the blood sample must reflect the overall average for the entire 24 hours. For NIPD patients, the serum sample should be obtained at the midpoint of the daytime empty period. For CCPD patients, the serum sample should be obtained at the midpoint of the daytime dwell. For most NIPD and CCPD patients, these time points occur in the early afternoon.

GUIDELINE 9

Estimating Total Body Water and Body Surface Area (Opinion)

V (total body water) should be estimated by either the Watson[38] or Hume[39] method in adults using actual body weight and by the Mellits-Cheek method[38] in children using actual body weight.

Watson method[38]:

For Men: V (liters) = 2.447 + 0.3362*Wt (kg) + 0.1074*Ht (cm) − 0.09516*Age (years)

For Women: V = −2.097 + 0.2466*Wt + 0.1069*Ht

Hume method[39]:

For Men: V = −14.012934 + 0.296785*Wt + 0.192786*Ht

For Women: V = −35.270121 + 0.183809*Wt + 0.344547*Ht

Mellits-Cheek method for children[40]:

For Boys: V (liters) = −1.927 + 0.465*Wt (kg) + 0.045*Ht (cm), when Ht ≤132.7 cm

V = −21.993 + 0.406*Wt + 0.209*Ht, when height is ≥132.7 cm

For Girls: V = 0.076 + 0.507*Wt + 0.013*Ht, when height is ≤110.8 cm

V = −10.313 + 0.252*Wt + 0.154*Ht, when height is ≥110.8 cm

Body surface area, BSA, should be estimated by either the DuBois and DuBois method,[41] the Gehan and George method,[42] or the Haycock method[43] using actual body weight.

For all formulae, Wt is in kg and Ht is in cm:

DuBois and DuBois method: $BSA\ (m^2) = 0.007184*Wt^{0.425}*Ht^{0.725}$

Gehan and George method: $BSA\ (m^2) = 0.0235*Wt^{0.51456}*Ht^{0.42246}$

Haycock method: $BSA\ (m^2) = 0.024265*Wt^{0.5378}*Ht^{0.3964}$

Rationale A detailed rationale is presented in Appendix E. The following is a summary.

The Watson and Hume formulae were derived by comparing total body water measurements to simple anthropometric measurements (weight, height, age) in subjects without edema, volume deficit, or end-stage renal disease. In peritoneal dialysis patients, the Watson and Hume formulae provide reasonable approximations of isotopic body water measurements. Volume abnormalities (edema) are apparently

the major cause of discrepancy. The Mellits-Cheek formulae were derived from subjects aged 1 month to 34 years for males and 1 month to 31 years for females. In each case, the measurement of total body water was performed in normal subjects by the use of deuterium oxide distribution, with simultaneous measurement of weight and height.

The Work Group recommends the use of the Watson or Hume formulae in adults and the Mellits-Cheek formula in children as methods for estimating V. Attention should be paid to the presence of edema at the time of the clearance study. A special case is the underweight patient. (See Table II-1, Appendix E for a definition.) Successful efforts to restore weight to a normal level in such a patient will result in a rising V and consequently in a proportionally declining $K_{pr}t/V_{urea}$. This does not alter the methodology of estimating total body water using actual weight. It does affect target doses of dialysis, however. This issue is discussed again in Guideline 15: Weekly Dose of CAPD.

Like the formulae given above for total body water, the formulae for BSA were determined in a normal population. Many of the disclaimers described for calculating V are less of an issue in calculating BSA, because the relationship to the defining simple anthropometric measurements is less influenced by clinical conditions accompanying ESRD. Historically, many nephrologists have utilized the method of DuBois and DuBois, and much of our data are from its application. Only 9 subjects were used to define this formula.[41] More than 400 subjects, including many children, were used to define the formula of Gehan and George,[42] and in an independent comparison, the Gehan and George method was preferred.[44] The Haycock formula is based on measurements of 81 subjects ranging from premature infants to adults.[43]

Amputation alters the relationship between body height and weight. This causes a mathematical distortion of the calculation of both anthropometric V and BSA, because the calculation of each takes this relationship into account.[45,46] Modification of V and BSA in patients with amputations are described in detail in Appendix E.

GUIDELINE 10

Timing of Measurement (Opinion)

Routine measurements of total Kt/V_{urea} and total creatinine clearance should be performed when the patient is clinically stable (eg, stable weight, stable BUN and creatinine concentrations) and at least 4 weeks after resolution of peritonitis.

Following a change in prescription or a major change in clinical status (eg, hospitalization, weight loss), but in the absence of recent peritonitis, measurements of delivered weekly Kt/V_{urea} and total weekly C_{Cr} should be performed within the next 4 weeks and then at 4-month intervals.

Rationale The effect of body weight on the calculation of V is discussed in the rationale for Guideline 9: Estimating Total Body Water and Body Surface Area, and in Appendix E: Detailed Rationale for Guideline 9. Variations in serum urea and creatinine concentration can potentially increase the error in the clearance calculations and indicate that the patient is not in a steady state.

Peritonitis may, in some instances, affect peritoneal solute transport for long periods. The rationale for waiting 4 weeks after resolution of peritonitis to repeat the clearance studies is presented in Appendix D: Detailed Rationale for Guideline 8.

The Work Group recommends frequent assessment of delivered dose of PD and total solute clearance, specifically every 4 months after the first 6 months of PD (see Guideline 11: Dialysate and Urine Collections). Major changes in clinical status (eg, patient compliance, weight gain, weight loss, technical/mechanical complications, some causes of hospitalization) may alter PD dose requirements. For example, pneumonia may contribute to loss of residual kidney function, which would be undetected unless measured. Therefore, in the absence of peritonitis, a major change in clinical status should prompt a re-evaluation of weekly Kt/V_{urea} and total weekly C_{Cr}, and this should occur within 1 month following the change in clinical status. Within 1 month following a PD prescription change, weekly Kt/V_{urea} and total weekly C_{Cr} should be measured to demonstrate that the goals of the prescription change have been achieved. If the patient is not stable, all attention should be directed to deter-

mining the cause of the instability and to correcting it. This may or may not include measuring the delivered dose of PD. There will be circumstances in which the change in clinical status might only alter RKF (eg, exposure to nephrotoxins), not delivered dose of PD. While one must be cautious in assuming that persistent urine flow rate implies stable RKF,[21] a clinical clue that deterioration has occurred may be a decrease in what previously had been a stable daily urine volume.[47] In those settings, only measurement of RKF is indicated.

GUIDELINE 11

Dialysate and Urine Collections (Opinion)

Two to three total solute removal measurements are required during the first 6 months of PD (see Guideline 3: Frequency of Delivered PD Dose and Total Solute Clearance Measurement Within Six Months of Initiation). After 6 months, if the dialysis prescription is unchanged:

1. Perform both complete dialysate and urine collections every 4 months; and
2. Perform urine collections every 2 months until the renal weekly K_rt/V_{urea} is <0.1.

Thereafter, urine collections are no longer necessary, as the RKF contribution to total Kt/V_{urea} becomes negligible. In young children, urine collections are recommended only with complete dialysate collections (see Table II-2 reproduced from Guideline 5).

Rationale Loss of residual kidney function is the major cause of decreasing clearance in PD subjects followed longitudinally.[48,49] The CANUSA study demonstrated substantial loss of kidney function at 6-month intervals.[49] The Work Group concludes that measurements of urinary clearances should be performed at 2-month intervals to prevent long periods of underdialysis. For young children in whom urine collections are difficult (requiring special collection apparatus, etc), urine collections can be deferred until the next total solute removal measurement (see Guideline 3: Frequency of Delivered PD Dose and Total Solute Clearance Measurement within Six Months of Initiation, and Guideline 5: Frequency of Measurement of Kt/V_{urea}, Total C_{Cr}, PNA, and Total Creatinine Appearance).

RECOMMENDATIONS FOR RESEARCH

The optimal timing of blood sampling for subjects on asymmetric PD (NIPD, CCPD) should be determined. The recommendations we have made are based on pharmacokinetic theory.

Comparison of the "batch" and "aliquot" methods of dialysate sampling should be studied.

Development of a clinically applicable method of assessing TBW in children undergoing PD is recommended.

Methodology to calculate renal urea and creatinine clearance and PNA from random urine samples should be developed.

IV. Assessment of Nutritional Status Specifically as It Relates to Peritoneal Dialysis

GUIDELINE 12

Assessment of Nutritional Status (Opinion)

Nutritional status of adult PD patients should be assessed on an ongoing basis in association with Kt/V_{urea} and C_{cr} measurements using the Protein equivalent of Nitrogen Appearance (PNA) and Subjective Global Assessment (SGA). For pediatric PD patients, nutritional status should be assessed using the PNA and other standard nutritional assessments (see Guideline 14 of the Clinical Practice Guidelines for Peritoneal Dialysis Adequacy and the K/DOQI Clinical Practice Guidelines for Nutrition in Chronic Renal Failure).

Rationale A detailed rationale is presented in Appendix F. The following is a summary.

There is strong indirect evidence linking survival on dialysis with nutritional status both at initiation of dialysis (see Section I: Initiation of Dialysis) and during longitudinal follow-up. Better survival has been reported in PD patients with high normalized protein equivalent of nitrogen appearance (nPNA)[50] (see Guideline 28: Measurement of Normalized PNA in PD Patients). Positive correlations between nPNA and clearance of urea or creatinine have been reported repeatedly in PD subjects.[51-54] The correlation between nPNA and Kt/V_{urea} may indicate increased appetite and dietary protein intake as Kt/V_{urea} increases, but also may simply reflect the fact that nPNA and Kt/V_{urea} are mathematically linked.[55] This mathematical linkage makes the correlation between nPNA and Kt/V_{urea} in cross-sectional studies of questionable clinical significance. However, nPNA tends to increase in the same subjects when Kt/V_{urea} and creatinine clearance (C_{Cr}) are increased by increasing the dose of PD,[53] especially if the increase in the dose of PD was prescribed because of inadequate clearances.[56] In the latter instance, the association between Kt/V_{urea} and nPNA is not the result of a mathematical coupling. In addition, there is strong evidence suggesting that quality and quantity of dialysis influences nutrition.[57,58] While the precise relationship between kidney function (or dialysis therapy) and nutrition is not yet adequately understood, it is the Work Group's opinion that adequate renal replacement therapy is necessary for normal appetite and metabolism. Thus, nutritional problems may reflect inadequate dialysis which, if corrected, may lead to subsequent improved outcomes.

Although nutritional status is influenced by many nondialysis-related factors, appetite suppression, nausea, and vomiting are major clinical features of uremia and inadequate dialysis. Therefore, nutritional status is also an important measure of PD adequacy. Of the available measures of nutrition, PNA is recommended because it provides an estimate of protein intake and protein losses. The SGA is recommended because it is a valid clinical assessment of nutritional status and is strongly associated with patient survival.

Protein equivalent of total nitrogen appearance (PNA) Nitrogen intake is almost entirely from protein. The final product of protein catabolism is urea. Therefore, if steady-state nitrogen balance conditions exist, one can work backward from urea excretion to determine what the protein intake was. Yet, other protein losses (urinary, peritoneal dialysate, diarrhea) also reflect the body's turnover of protein. Studies in dialysis patients show that predictable mathematical relationships exist between urea excretion, protein catabolism, and dietary protein intake. If peritoneal protein losses are greater than 15 g/day, PNA should be calculated as protein catabolic rate + protein losses. If dialysate protein losses are less than 15 g/day, the formula:

$$PNA(g/d) = 10.76*(0.69*UNA + 1.46)$$

can be used to calculate PNA where UNA is total urea nitrogen appearance in grams per day.[58a] PNA is an indirect method for estimating dietary protein intake, a key measure of nutritional status in dialysis patients. There are alternative Bergstrom formulae to obtain the PNA surrogate for dietary protein intake:

$$PNA(g/24\ hours) = 15.1 + (6.95 \times \text{urea nitrogen appearance in g/24h}) + \text{dialystate and urine protein in g/24 hours}$$[59]

In the absence of direct measurement of urinary and dialystate protein losses, this less accurate formula may be used:

PNA(g/24 hours) = 20.1

+ (7.50 × urea nitrogen appearance in g/24 h)

When protein losses are high, this second formula should not be used. Both formulae will require normalization to body mass in kg.

Subjective global assessment (SGA) The SGA is a simple assessment that uses the clinician's experience to subjectively rate a patient's nutritional status based on the medical history and physical exam. The SGA was modified for use in PD patients as described in Appendix F: Detailed Rationale for Guideline 12. This assessment is valuable because it does not focus on a single variable; rather, it forces the clinician to view the patient more broadly. SGA addresses four items (recent weight change, anorexia, subcutaneous tissue, and muscle mass) scored on a 7-point Likert scale (see Appendix B: Detailed Rationale for Guideline 2). It can be performed by physicians, nurses, or registered dietitians during routine clinic visits. Several studies have validated that the SGA accurately reflects nutritional status in dialysis patients and, in the CANUSA study, a higher SGA was associated with a lower risk of death.

The SGA is easy to perform and can be performed within minutes during a routine clinic visit. There are no data to dictate how often to perform the SGA, so the Work Group bases its opinion on the following: the SGA should be done often enough to detect changes and to intervene in a timely manner. It should be performed in association with measurement of Kt/V_{urea} and C_{Cr}, every 4 months after the initial 6 months (see Guideline 5: Frequency of Measurement of Kt/V_{urea}, Total C_{Cr}, PNA, and Total Creatinine Appearance).

The SGA has not been validated as a means of nutritional assessment in the pediatric PD population.

GUIDELINE 13

Determining Fat-Free, Edema-Free Body Mass (Opinion)

Total creatinine appearance should be used to determine fat-free, edema-free body mass.

Rationale Fat-free, edema-free body mass is probably a more accurate term for what had previously been called lean body mass. It is an important index of overall nutritional status. Total daily creatinine production, measured as the sum of creatinine excreted in dialysate and urine plus the estimated creatinine lost in the gut,[28] can be used to calculate fat-free, edema-free body mass. Fat-free, edema-free body mass reflects somatic protein stores in the same way that serum albumin reflects visceral protein stores.[60] In adults, fat-free, edema-free body mass in kilograms is computed by the equation[60,61]:

Fat-free, edema-free body mass = 0.029

× total creatinine production in mg/day + 7.38.

Norms vary by patient gender and size. A steady-state of creatinine excretion should exist for the equation result to be valid. Factors other than muscle mass can affect the fat-free, edema-free body mass calculation by creatinine kinetics. These factors include errors in the collection or measurement of creatinine in urine or dialysate and large variations in the dietary intake of creatine plus creatinine (meat). Fat-free, edema-free body mass estimates by creatinine kinetics may be a better index of nutritional status in PD patients, because they reflect dry fat-free, edema-free body mass and changes in muscle mass better than dual-energy x-ray absorptiometry or bioimpedance.[62] The day-to-day variability of total creatinine excretion is only 2% to 4% over a short time interval,[33,37] but is up to 15% over much longer intervals.[27]

Serum creatinine concentration is not, by itself, an index of adequacy of peritoneal dialysis because of the large variations in creatinine production between individuals. However, a change in serum creatinine concentration may indicate changes in creatinine and urea removal to a much larger extent than a change in serum urea concentration.[63,64] A rising serum creatinine concentration is usually caused by a decrease in total creatinine clearance, often secondary to a loss of residual kidney function, and much less frequently by an increase in muscle mass. A decreasing serum creatinine concentration is caused more often by progressive loss in muscle mass and less often by an increase in total clearance. In other words, increases in peritoneal solute transport or

recovery of kidney function do not occur very often.

GUIDELINE 14

Use of the Modified Borah Equation to Assess Nutritional Status of Pediatric PD Patients (Opinion)

Nutritional status of pediatric PD patients should be assessed at least every 6 months by standard clinical nutritional evaluations and by the modified Borah equation[65]:

$$PNA(g/d) = [6.49*UNA] + [0.294*V] + \text{protein losses(g/day)}$$

Rationale The equation described in Guideline 12, Assessment of Nutritional Status, from the glossary[65] is a further modification of the original Borah equation.[66] Since this modification has not been validated in children, the Work Group recommends using the modification above from Kopple et al[65] and Keshaviah et al.[67]

Although not validated in children, this modified Borah equation contains a factor, V, that controls for patient size, and has been employed in pediatric studies. Furthermore, dialysate protein losses must be measured directly in the dialysis effluent and not estimated when using the modified Borah equation in children. The use of equations in which dialysate protein losses are estimated has been studied in very few pediatric PD patients.[68]

The dialysate protein measurement is the only additional laboratory determination from standard total solute removal measurements, as described in Guideline 4: Measures of PD Dose and Total Solute Clearance. Thus, this nutritional assessment could be easily merged to accompany total solute removal measurements.

RECOMMENDATIONS FOR RESEARCH

The precise relationships among PNA, dialysis dose, and outcome are unclear. Although these relationships are currently being studied in hemodialysis patients, they should also be examined in PD patients. There are probably limits, for example, to the role of increasing delivered dialysis dose in order to improve appetite and nutritional parameters. Other questions of interest include: How does improved dialysis affect nutrition, and above what delivered dose does that effect dissipate, if at all? What interventions act synergistically with improved dialysis to improve nutritional parameters? What complications interfere with nutrition, in what manner, and can the interference be overridden by another type of intervention?

A standardized nutritional assessment tool for children analogous to the SGA should be developed.

V. Adequate Dose of Peritoneal Dialysis

GUIDELINE 15

Weekly Dose of CAPD (Evidence)

For CAPD, the delivered PD dose should be a total Kt/V_{urea} of at least 2.0 per week and a total creatinine clearance (C_{Cr}) of at least 60 L/wk/1.73 m^2 for high and high-average transporters, and 50 L/wk/1.73 m^2 in low and low-average transporters.

Rationale A detailed rationale is presented in Appendix G. The following is a summary.

Theoretical constructs predict that a weekly peritoneal Kt/V_{urea} between 2.0 and 2.25 will provide adequate dialysis. These constructs assume no residual renal function, full equilibration of plasma and dialysate urea, a target serum urea nitrogen concentration between 60 and 80 mg/dL, and nPCR between 1.0 and 1.2 g/kg/day.

Clinical studies addressing the validity of these predictions can be divided into those using univariate and those using multivariate statistical analyses. The former are methodologically weaker. Four studies which used univariate analysis suggest that total (renal and peritoneal) weekly Kt/V_{urea} values greater than 1.5, 1.89, 2.0, and 2.0, respectively, are associated with better patient survival than lower values.

Three studies from France, Italy, and North America (CANUSA) have used multivariate statistical analysis. The French study found better survival among patients with an initial weekly Kt/V_{urea} >1.7 but did not evaluate changes in Kt/V_{urea} associated with loss of residual kidney function. The Italian study evaluated prevalent CAPD patients with minimal residual kidney function. Improved patient survival was observed with a weekly Kt/V_{urea} >1.96. Values higher than 1.96 were not associated with increased survival but the statistical power to detect this association was low. The CANUSA study of 680 incident continuous peritoneal dialysis patients reported a 5% decrease in patient survival in association with every 0.1 decrease in total weekly Kt/V_{urea}, for Kt/V_{urea} between 1.5 and 2.3. There was no association between Kt/V_{urea} and technique failure or hospitalization. The predicted 2-year survival associated with a constant total Kt/V_{urea} of 2.1 was 78%. These predictions assume that renal and peritoneal Kt/V_{urea} are equivalent.

Clinical experience suggests that a total weekly creatinine clearance >50 L/1.73 m^2 is required for adequate dialysis. Among patients with minimal residual function in the Italian study, a weekly Kt/V_{urea} of 1.96 correlated with a weekly creatinine clearance (C_{Cr}) of 58 L. The CANUSA study reported a 7% decrease in patient survival in association with a 5 L/1.73 m^2/wk decrease in C_{Cr}. Unlike the situation for Kt/V_{urea}, both technique failure and hospitalization were worse with decreased weekly creatinine clearance. The predicted 2-year survival of 78% was associated with a weekly Kt/V_{urea} of 2.1 or a weekly C_{Cr} of 70 L.

There are insufficient data to address the issue of *adequate* compared to *optimal* dialysis (see Introduction). The latter is in part defined as the dialysis dose above which the incremental clinical benefit does not justify the patient burden or financial costs. Nor are there sufficient data to evaluate the relative importance of renal and peritoneal clearances. The recommendations assume equivalence but this requires further study. The correlation between Kt/V_{urea} and C_{Cr} will vary with residual renal function (see Fig II-2, Appendix A). The higher C_{Cr} observed in the CANUSA study compared to the Italian study was due to the greater residual renal function in the former.

Based on the available evidence, the minimum delivered dialysis dose target Kt/V_{urea} should be 2.0 per week; the minimum weekly target C_{Cr} should be 60 L/1.73 m^2. If there is discordance in achieving these targets, the Kt/V_{urea} should be the immediate determinant of adequacy because it directly reflects protein metabolism and is less affected by extreme variations in residual renal function (see Appendix A and Fig II-2). However, a cause for the discrepancy should be sought and the patient followed closely for signs of underdialysis.

A special case is the underweight patient, defined in Appendix E: Detailed Rationale for Guideline 9. Successful efforts to restore weight to a normal level in such a patient will result in a rising V, and consequently in a proportionally declining $K_{pr}t/V_{urea}$. To achieve a weekly

$K_{pr}t/V_{urea}$ of 2.0 at the increased weight, the weekly target $K_{pr}t/V_{urea}$ provided during the malnourished state must be greater than 2.0. The Work Group recommends that the target $K_{pr}t/V_{urea}$ should be raised in a malnourished CAPD patient to the level that would provide a weekly $K_{pr}t/V_{urea}$ of 2.0 for that patient if he or she were at the desired weight. That level is calculated by multiplying the target of 2.0 for CAPD times the ratio of $V_{desired}/V_{actual}$. This is described in detail in Appendix E: Detailed Rationale for Guideline 9, and discussed in Guideline 17: PD Dose in Subpopulations. The same upward target adjustment should be made in creatinine clearance. The target creatinine clearance should be adjusted upward by multiplying the target for that therapy (CAPD or APD) by the ratio of $BSA_{desired}/BSA_{actual}$.

Even after controlling for delivered dose, low and low-average transporters have better patient and technique survival than do high and high-average transporters.[69] In the absence of adequate residual kidney function, low and low-average transporters may not be able to achieve a C_{Cr} of 60 L/wk/1.73 m^2 on any reasonable dialysis prescription. However, because urea clearance is less affected than creatinine clearance by transport status, low and low-average transporters can achieve a weekly Kt/V of 2.0. Therefore, it seems reasonable to lower the C_{Cr} target in low and low-average transporters without fear of jeopardizing patient outcome. These patients must be observed closely for evidence of inadequate dialysis.

Clinical judgment suggests that the target doses of PD for children should meet or exceed the adult standards. However, there are currently no definitive outcome data in pediatric patients to suggest that any measure of dialysis adequacy is predictive of well-being, morbidity, or mortality.[69a] There also are minimal data regarding the real protein needs of children, especially young children, on dialysis.[69b] It is the opinion of the Work Group that the nutritional requirements per kilogram of body weight are higher in children than in adults. Therefore, PD doses in children, and especially small infants who have very high protein requirements, may have to be higher than PD doses in adults.

GUIDELINE 16

Weekly Dose of NIPD and CCPD (Opinion)

For NIPD, the weekly delivered PD dose should be a total Kt/V_{urea} of at least 2.2 and a weekly total creatinine clearance of at least 66 L/1.73 m^2.

For CCPD, the weekly delivered PD dose should be a total Kt/V_{urea} of at least 2.1 and a weekly total creatinine clearance of at least 63 L/1.73 m^2.

Rationale In the absence of data that relate delivered dose of automated PD (APD) to patient outcomes, targets for NIPD and CCPD are based on opinion.

Theoretically, there is an 8% difference in clearance between CAPD and NIPD. This difference is based on calculations which describe a 200% increase in the intermittent HD clearance required to achieve the same solute removal as in continuous dialysis (Kt/V_{urea} of 4.0 in HD and 2.0 in CAPD), holding protein intake constant.[70,71] The Work Group assumed that the delivered dose of NIPD would need to be 8% higher than the CAPD dose (108% of 2.0 = 2.16, rounded up to 2.2). The Work Group assumed that the requisite delivered dose of CCPD would be intermediate between those for CAPD and NIPD. Some variations of CCPD with diurnal exchanges of less duration than the nocturnal exchange of CAPD may be considered equal to CAPD. However, in order to simplify recommendations, the target weekly total dose for CCPD is 2.1. The recommendations for creatinine clearance are percentage adjustments corresponding to the changes in Kt/V_{urea} targets for these groups.

Clinical judgment suggests that the target doses of PD for children should meet or exceed the adult target doses. There are no definitive outcome data in pediatrics to suggest that any measure of dialysis adequacy is predictive of well-being, morbidity, or mortality.

GUIDELINE 17

PD Dose in Subpopulations (Opinion)

There is no adequate basis for recommending any change in the target doses of dialysis discussed in Guidelines 15: Weekly Dose of CAPD,

and Guideline 16: Weekly Dose of NIPD and CCPD, for various patient subpopulations (eg, patients with diabetes or who are elderly), with the exception of the malnourished patient, whose target dose is increased by the ratio of the $V_{desired}/V_{actual}$ for Kt/V_{urea}. For creatinine clearance, the target dose in a malnourished patient is increased by the ratio $BSA_{desired}/BSA_{actual}$. Transport status is not considered a subpopulation in the context of this guideline.

Rationale There are no data available in the literature on which to base a recommendation for different adequacy targets for patients with diabetes or for the elderly. However, it must be remembered that malnourished patients may appear to have an adequate Kt/V_{urea} due to calculation of V from the actual or malnourished body weight. If V were calculated from an estimate of desired body weight, the target would reflect that target body weight. This is discussed in Guidelines 9: Estimating Total Body Water and Body Surface Area, and Guideline 15: Weekly Dose of CAPD, and in detail in Appendix E: Detailed Rationale for Guideline 9.

The fact that historically the size indicator to normalize C_{Cr} is BSA and for Kt_{urea} has been total body water (V) contributes to the discrepancy between these clearance measures and confounds population comparisons (male versus female, obese versus lean, edematous versus nonedematous).

In the absence of data in these subpopulations, if no other cause of malnutrition is discovered, the target delivered dose of dialysis should be increased by multiplying the target Kt/V_{urea} for a normally nourished patient by the ratio of the $V_{desired}/V_{actual}$, and the target creatinine clearance should be increased by the ratio of $BSA_{desired}/BSA_{actual}$. These modifications are described in Guideline 15: Weekly Dose of CAPD, and Appendices E and G.

GUIDELINE 18

Use of Empiric and Computer Modeling of PD Dose (Evidence)

Both empiric and computer modeling methods can be used to estimate adequate doses of PD. Specific prescriptions are described below.

Rationale The Work Group has elected to describe these two empiric and computer modeling approaches in detail. They are by no means mutually exclusive.

EMPIRIC APPROACH FOR DETERMINATION OF DOSE OF PERITONEAL DIALYSIS

A. General Evaluation of the Patient With Kidney Failure

1. Explain all options (transplant, HD, and PD) to patients/parents/caregivers in a nonbiased manner.
2. Review medical condition/comorbidities to determine if contraindications, relative or absolute, exist for any modality (see Section VIII: Suitable Patients for PD).
3. If no medical contraindications exist and the patient is a candidate for self therapy, allow patient to choose a modality.
4. Place the chronic dialysis access (PD or HD). The Vascular Access Work group recommends that vascular accesses be placed in patients on PD. The PD Adequacy Work Group feels that this decision should be made on an individual patient basis, but our position does not necessarily disagree with the recommendations of the Vascular Access Work Group.
5. If dialysis is needed at the time of presentation, place the temporary HD access, or after placing the PD catheter, initiate therapy as suggested under point B.2, below.

B. Initiation of Peritoneal Dialysis

1. If possible, wait 10 days to 2 weeks after catheter placement to start PD.
2. If PD must be started in less than 10 days following catheter placement, do low-volume, supine dialysis.
3. Obtain baseline 24-hour urine collection for urea and creatinine clearance (see Guideline 6: Assessing Residual Kidney Function). These collections are for solute clearance calculations, assessment of creatinine generation, and PNA determinations.
4. Note patient's weight and the presence or absence of edema.
5. At initiation of dialysis, explain to patient/parents/caregivers that the patient's prescription will be individualized. Specifically, state that their instilled volume almost certainly will need to increase over time. For patients who choose

Automated Peritoneal Dialysis (APD), one or more daytime dwells will be needed in approximately 85% of patients. Patients should know from the start of PD that their total solute clearance will be monitored and that, if their residual kidney function or peritoneal transport changes over time, their prescription may need to change as well.

C. Initial Dialysis Prescription for Adults

Initial dialysis can be prescribed empirically based on patient's weight, amount of residual kidney function, and lifestyle constraints. These empiric recommendations should be implemented prior to peritoneal equilibration testing.

PD may be initiated incrementally, or as full therapy, depending on RKF at the time of initiation (see Guideline 1: When to Initiate Dialysis—Kt/V_{urea} Criterion). For example, if K_rt/V_{urea} is 1.8 per week, only 0.2 K_pt/V_{urea} is needed per week. Assuming complete urea equilibration (serum to dialysate) at 6 hours, a single 2-L overnight exchange would contribute 14 L per week. If V is 40 L, this contributes a K_pt/V_{urea} of 14/40 or 0.35 per week. Any ultrafiltrate would add further to total solute removal. That, plus the K_rt/V_{urea} of 1.8, brings the $K_{pr}t/V_{urea}$ to at least 2.15, satisfying the target requirement. This approach uses basic principles of dialysis prescription development. Thus, the dose of K_pt/V_{urea} depends on the K_rt/V_{urea} as the Work Group has emphasized throughout these guidelines. Keeping in mind that the weekly $K_{pr}t/V_{urea}$ goal is at least 2.0, the following more intense empiric approach is reasonable:

1. Patients with an estimated underlying GFR >2 mL/min
   a. If patient's lifestyle choice is CAPD:
      BSA $<1.7\ m^2 \rightarrow 4 \times 2.0$ L exchanges/day
      BSA 1.7 to 2.0 $m^2 \rightarrow 4 \times 2.5$ L exchanges/day
      BSA $>2.0\ m^2 \rightarrow 4 \times 3.0$ L exchanges/day
   b. If patient's lifestyle choice is CCPD:
      BSA $<1.7\ m^2 \rightarrow 4 \times 2.0$ L (9 hours/night) + 2.0 L/day
      BSA 1.7 to 2.0 $m^2 \rightarrow 4 \times 2.5$ L (9 hours/night) + 2.0 L/day
      BSA $>2.0\ m^2 \rightarrow 4 \times 3.0$ L (9 hours/night) + 3.0 L/day
   c. If patient's lifestyle choice is NIPD:
      Specific attention to certain details will be required. Nightly intermittent peritoneal dialysis (NIPD) is not a therapy that is typically used at the initiation of dialysis. It has been reserved for high or rapid transporters. However, in patients with significant RKF (and ability to diurese), they may initially do well on nightly exchanges only (dry day) because of the supplemental clearance provided by the patient's RKF. See further comments on NIPD under point 2.c, below.
2. Patients with an estimated underlying GFR ≤2 mL/min
   a. If patient's lifestyle choice is CAPD:
      BSA $<1.7\ m^2 \rightarrow 4 \times 2.5$ L/day
      BSA 1.7 to 2.0 $m^2 \rightarrow 4 \times 3.0$ L/day
      BSA $>2.0\ m^2 \rightarrow 4 \times 3.0$ L/day (Consider use of a simplified nocturnal exchange device to achieve optimal dwell times and to augment clearance.)
   b. If patient's lifestyle choice is CCPD:
      BSA $<1.7\ m^2 \rightarrow 4 \times 2.5$ L (9 hours/night) + 2.0 L/day
      BSA 1.7 to 2.0 $m^2 \rightarrow 4 \times 3.0$ L (9 hours/night) + 2.5 L/day
      BSA $>2.0\ m^2 \rightarrow 4 \times 3.0$ L (10 hours/night) + 2×3.0 L/day (Consider combined HD/PD or transfer to HD if clinical situation suggests need.)
   c. If patient's lifestyle choice is NIPD:

Many of the issues discussed above for patients with an estimated underlying GFR >2 mL/min still apply to urine volume. Namely, if RKF provides enough diuresis, NIPD may provide enough solute removal for a while. This should be tested early on. If during training, it is noted that a patient has very low drain volumes with no apparent mechanical problem or leak, a PET should be done to determine if the patient is a rapid transporter. If so, NIPD can be prescribed using kinetic modeling.

D. Initial Dialysis Prescription for Children

In view of the close, age-independent relationship between peritoneal surface area and body surface area (BSA), the use of BSA as a normalization factor for the prescribed exchange volume in children is preferred. An instilled volume

of at least 1,100 mL/m^2 is recommended for most pediatric patients, although individual tolerance must be considered.[72]

It should be emphasized that the preceding prescriptive guidelines are general empiric guidelines for patients initiating PD, generally as first renal replacement therapy. For patients transferring from HD with minimal RKF, prompt adequacy testing is required. The above empiric recommendations must be individualized and guided by documentation that the delivered dose equals the prescribed dose. Furthermore, the instilled volumes are ones that theoretically will result in a weekly target Kt/V_{urea} of greater than 1.9 for the average patient. Low transporters may be below creatinine targets if RKF is low. Finally, although most patients tolerate instilled volumes of greater than 2.0 L, this needs to be evaluated for each patient.

E. Observations Needed During Training

1. Determine 4-hour drain volumes during training. This is to note if drain volumes are as expected for typical 4-hour dwells with 1.5%, 2.5%, or 4.25% dextrose exchanges. This is not a formal peritoneal equilibration test (see below), but is done to determine if the patient's peritoneal membrane transport characteristics are markedly different from the mean.
2. Monitor for evidence of leakage in the vicinity of the catheter.
3. Complete laboratory studies.
   a. Delay baseline peritoneal equilibration test (PET) until after training (see F below).
   b. Perform serum chemistries and complete blood count.
   c. If a computer-assisted kinetic modeling system is available, enter preliminary data to predict if the current prescription will be adequate.

F. Early Follow-Up

1. Perform 24-hour dialysate and urine collection for Kt/V_{urea}, creatinine clearance, PNA calculation, creatinine generation, and $D/P_{Creatinine}$ and D/P_{Urea} values. These should be done 2 to 4 weeks following initiation (see Table II-1 and Guideline 3: Frequency of Delivered PD Dose and Total Solute Clearance Measurement Within Six Months of Initiation).

2. Perform peritoneal equilibration testing (PET) approximately 1 month following initiation of PD, an appropriate time physiologically. This baseline PET could be performed at the end of a prolonged ($>$1 week) training period (see Guideline 3: Frequency of Delivered PD Dose and Total Solute Clearance Measurement Within Six Months of Initiation). This PET (1 month) is used as the baseline measure of peritoneal membrane transport characteristics, not to determine total solute clearance. This PET is done to rule out unsuspected problems or deviation from mean transport characteristics. Low transporters will probably require high-dose CAPD or CCPD. High transporters will eventually have ultrafiltration problems (when RKF diuresis fails) and will need short-dwell therapy such as NIPD. Average transporters will have the most flexibility (ie, all options will be feasible).

3. Perform serum chemistries and complete blood count.

4. If a computer-assisted modeling program is available, enter baseline data. Actual data from 24-hour collection can be compared.

5. If clearances are at or above target, continue routine monitoring on a regular basis. Look for changes in 24-hour urine studies and PET data. Kinetic modeling can be used to guide future therapy.

6. If clearance is below target at 1 month, a change in prescription may be needed. Compliance issues and collection procedures should be evaluated for abnormalities.

G. Adjusting Dialysis Prescription

If kinetic modeling is not available, unless PET has changed, dialysis dose is most effectively increased by increasing the instilled volume, therefore maximizing mass transfer and dwell time. Another option would be to increase the number of exchanges/day while maintaining maximum dwell time, ie, by using a single nighttime exchange to increase to 5 equal dwells/day. To this end, simplified mechanical exchange systems have been developed to perform a nocturnal exchange.

If kinetic modeling is available, use these programs to tailor a new prescription to meet

adequacy target goals and patient lifestyle issues. This is discussed in the next section.

COMPUTER-ASSISTED KINETIC MODELING APPROACH TO ACHIEVING TARGET DOSES OF PERITONEAL DIALYSIS

As mentioned above, the availability of computer-assisted kinetic modeling to tailor PD prescriptions to transport type, body size, lifestyle, etc. may have distinct advantages. Much of what is described in the preceding discussion of the empirical approach has a mathematical basis. Computer-assisted kinetic modeling is a logical extension of the empirical approach in that it uses computer calculations to speed and assist the physician in PD prescription development. PD solution manufacturers, such as Baxter and Fresenius, provide urea kinetic modeling (UKM) models without charge.

The major advantage of this approach is the flexibility and speed of the calculations of solute clearance. Recent studies have shown that certain models very accurately predict dialysis delivery.[73-76] Kinetic modeling is especially important for APD therapies because the dwell times are so variable and may not approach the optimal for many patients. Since the models accurately and reliably predict the delivered dose, the patients and caregivers can discuss options in a timely manner. The trial and error empirical approach discussed above moves at a much slower rate. Even with computer-assisted UKM, actual measurements are still necessary to confirm adequate dose delivery. But with computer-assisted UKM, the process is accelerated. The only theoretical disadvantage of a computer kinetic modeling approach is that there might be a tendency for the caregivers not to learn the principles behind the modeling program which form the basis for the prescription strategies.

The use of computer-based modeling to achieve target PD doses has been applied successfully to a small number of children.[77,78]

The dose of PD is defined as the sum of the total daily or weekly kidney + peritoneal urea clearance normalized to the total body water, the $K_{pr}t/V_{urea}$, which is a dimensionless parameter expressed as either the total daily or weekly fractional clearance of body water for urea.[79,80] It is substantially more difficult to compute the appropriate prescribed dialysis dose in PD than in HD. In HD, Kt/V_{urea} is delivered in a single dialysis session and can be precisely calculated from the dialyzer mass transfer coefficient (MTC), constant blood and dialysate flows, ultrafiltration rate, and treatment time.[70,81] The delivered Kt/V_{urea} and PCR (or PNA) can both be calculated from the predialysis and postdialysis BUNs from a single dialysis.[70,81]

In PD, however, the total daily peritoneal clearance, K_pt, is comprised of the sum of the clearances provided by several discrete exchanges. This therapy consists of several batch exchanges during which clearance and ultrafiltration are not constant (unlike the situation in HD) but fall exponentially to zero over the course of each exchange. The peritoneal mass transfer coefficient (MTC), which controls the rate of solute transport between blood and dialysate (and hence clearance), is an individual patient characteristic[71,82] which must be determined and which can clearly vary as a function of exchange volume and body position.[83,84] In HD, ultrafiltration contributes minimally to urea clearance, while in PD it contributes up to 25% or more of total clearance and must be included in calculation of the dose. The net ultrafiltration can be precisely controlled in HD, while in PD it is a complex function of glucose absorption, membrane water permeability and lymphatic flow. The PD prescription variables include MTC, which is dependent on patient, body position, and exchange volume; distribution of exchanges between ambulatory and supine cycler exchanges; exchange volume(s); exchange times; and the osmotic gradient or percent dextrose in each exchange. Additionally, residual kidney urea clearance must be measured and included in the prescription and body water or V estimated from age, gender, and surface area.[39,85]

In current clinical practice, the peritoneal dialysis prescription is usually based on transport categorization using the peritoneal equilibration test (PET) and subsequently more finely tuned through empirical prescription changes guided by clinical experience, as described in the preceding section of this guideline.

With computerized UKM many possible PD regimens with variable exchange schedules and volumes can be tailored to be compatible with individual patient lifestyle preferences and to

minimize total dialysate volume relative to required $K_{pr}t/V_{urea}$. A PD prescription can be quickly and rigorously evaluated mathematically using programs written for the personal computer.[73-75,86] These programs all require baseline transport characterization using either the PET or peritoneal function test data.

The most common method to monitor delivered $K_{pr}t/V_{urea}$ is measurement of total daily peritoneal and kidney urea clearance by analysis of blood, total drained dialysate, and 24-hour urine for urea nitrogen. Although highly reliable for determination of $K_{pr}t/V_{urea}$ and PCR/PNA, batch analyses do not provide data to distinguish between noncompliance and/or possible changes in MTC when the delivered $K_{pr}t/V_{urea}$ deviates from that expected with the current prescription. There is further discussion of this subject in Guideline 7: PD Dose Troubleshooting, and Guideline 8: Reproducibility of Measurement.

An alternative technique is measurement of BUN, urine volume, and urea nitrogen in aliquots of each exchange[87] combined with the patient's report of the exchange time and volume for each exchange. A further discussion of aliquot methodology is in Guideline 8: Reproducibility of Measurement. Although this technique, based on the peritoneal function test approach, requires substantially more dialysate urea nitrogen measurements in addition to measurement of $K_{pr}t/V_{urea}$ and PCR (or PNA), it permits calculation of a MTC for each exchange. If there are important deviations from the reported exchange schedule, the deviant exchanges will be identified by markedly deviant MTCs.

There are advantages and disadvantages of both the PET and PFT measurements. The wide range of exchange times, including nearly complete equilibration in long exchanges and the assumption of constant BUN, will result in some variability in the MTCs measured with the PFT which do not reflect true differences. On the other hand, the MTC calculated with a single 2-L exchange under carefully controlled conditions will not always accurately reflect the MTC under clinical exchange conditions with variable exchange volumes and body position.

A simple kinetic technique for routine monitoring of delivered $K_{pr}t/V_{urea}$ and PCR/PNA in established patients for whom the MTCs for urea and creatinine and 24-hour dialysate creatinine have been previously established is measurement of BUN and serum creatinine and dialysate urea and creatinine from an aliquot of one exchange. This data combined with the number of exchanges, exchange times, and exchange volumes reported by the patient permits calculation of $K_{pr}t/V_{urea}$, PCR/PNA, and expected total dialysate creatinine content.[81] The validity of the data can be assessed by comparison of the calculated dialysate creatinine content to the measured historical value for the patient (see Guideline 7: PD Dose Troubleshooting). In this way, both $K_{pr}t/V_{urea}$ and PCR/PNA can be estimated from measurements of urea nitrogen and creatinine in a blood sample and a small aliquot of one exchange using computerized UKM. When there is deviation of more than 10% in the expected creatinine excretion, more complete dialysate collections would be indicated for analysis of therapy.

RECOMMENDATIONS FOR RESEARCH

The amount of dialysis required for malnourished patients is not known. While there probably is consensus that such patients need extra dialysis, the requisite increase is unclear and should be studied. Other malnutrition-related questions of interest include: Can aggressive dialysis delivery reverse malnutrition? What V is to be used in malnourished patients?

Can increasing dialysis dose improve outcomes in a linear manner, or is there a dose above which no benefit is noted, or complications or costs outweigh the benefits?

A multicentered study of pediatric patients to evaluate clinical outcome as a function of delivered PD dose should be initiated. Urea kinetic modeling computer programs specifically designed for children should be developed and validated in a prospective trial.

Although there is a database documenting the validity of UKM to describe transport in PD,[71,73-75,88,89] UKM has not been widely used to prescribe and control the delivered dose. Since the risk of mortality may be highly nonlinear with increased dose of delivered dialysis,[90,91] it is reasonable to assume that the coefficient of variation on mean $K_{pr}t/V_{urea}$ should not exceed 10% to 15% for

individual patients. A multicenter clinical trial to study clinical outcome as a function of $K_{pr}t/V_{urea}$, using UKM to control $K_{pr}t/V_{urea}$ prospectively in individual randomized patients is recommended.

Do patients with diabetes need higher targets for delivered dose of PD? Should PD delivered dose be increased in hospitalized patients during acute illness or stress?

VI. Strategies for Increasing the Likelihood of Achieving the Prescribed Dose of Peritoneal Dialysis

GUIDELINE 19

Identify and Correct Patient-Related Failure to Achieve Prescribed PD Dose (Opinion)

Potential patient-related causes of failure to achieve prescribed peritoneal dialysis dose should be investigated and corrected. These include:

- Failure to comply with the prescription.
- Lack of understanding of the importance of adherence to the full prescription.
- Sampling and collection errors.

Rationale A detailed rationale is presented in Appendix H. The following is a summary.

Preliminary data from the USRDS DMMS Wave II project show that 487 CAPD patients self-report full compliance with 82.8% of their exchanges.[3] One exchange/week is missed by 11.5% of patients and 2 to 3 exchanges/week are missed by 4.5% of patients, all self-reported. The American Association of Kidney Patients completed a patient self-reported survey about the impact of these DOQI guidelines and came up with a very similar number for frequency of missed exchanges.

Conditions causing noncompliance in PD patients have not been adequately analyzed. From studies on compliance with chronic drug regimens, it is known that patients are more compliant when they are convinced about the appropriateness and beneficial effects of the prescribed treatment and that frequent reinforcement of the importance of the treatment is associated with better compliance. Therefore, it is the opinion of the Work Group that, in addition to giving careful consideration to the selection of medically appropriate candidates for PD, as detailed in Section VIII: Suitable Patients for Peritoneal Dialysis, special emphasis should be placed on education of PD patients about the importance and technique of the PD prescription. Instructions should be repeated at least every 6 months, and patients should be monitored for signs of change in compliance. Monitoring the output of creatinine in the dialysate plus urine, as detailed in Guideline 7: PD Dose Troubleshooting, is recommended by the Work Group as a method for measuring compliance.

GUIDELINE 20

Identify and Correct Staff-Related Failure to Achieve Prescribed PD Dose (Opinion)

Potential staff-related causes of failure to achieve prescribed peritoneal dialysis dose should be investigated and corrected. These include:

- Errors in prescription.
- Inadequate monitoring of delivered dose.
- Inadequate patient education.

Rationale To increase the likelihood of achieving a prescribed dose of PD, it is necessary to elucidate the staff-related causes of failure to achieve a prescribed dose of peritoneal dialysis. The Work Group found no reports addressing this issue in PD; the following discussion represents the opinion of the Work Group members.

Inadequate understanding of the physiology and kinetic principles of PD by the physicians and nursing staff may result in:

- Errors in patient selection.
- Errors in the prescription of the PD dose.
- Errors in monitoring whether the prescribed dose is delivered.
- Errors in PD dose modification to achieve the prescribed goal.
- Inability to test for and recognize patient noncompliance.
- Inadequate patient education.

The impact of patient education on patient compliance with the PD prescription was discussed in Guideline 19: Identify and Correct Patient-Related Failure to Achieve Prescribed PD Dose. The chance of inappropriate prescription of the PD dose is enhanced when the prescribing physician has a sketchy knowledge of the principles of clearance studies in PD. It has recently been recognized that nephrology fellowship curricula lack emphasis on training in dialysis.[92] To prescribe and deliver the proper dose of PD, nephrologists must ensure adequate education and training in PD.

The use of computer modeling in PD may help achieve the prescribed dose by suggesting various options to alter the PD dose. This approach may assist in avoiding unrealistic PD dose schedules for certain patients (see Guideline 18: Use of Empiric and Computer Modeling of PD Dose).

The use of total creatinine appearance/output data in detecting noncompliance is important, as discussed in Section II: Measures of Peritoneal Dialysis Dose.

Inadequate education may be a key factor in the patient nonadherence to the prescribed dose of therapy resulting in the above-mentioned shortcuts. The American Association of Kidney Patients reports that PD patients are willing to increase the frequency and/or volumes of exchanges, if necessary, and that explanations (education) and participation in decision making are good incentives. Inadequate education may stem from both poor educator understanding of the principles of clearance and lack of proper teaching technique. Staff responsible for patient education should be trained and competent in both the principles of clearance and the technique of patient instruction.

RECOMMENDATIONS FOR RESEARCH

Validate methods of assessing compliance.

Evaluate the association between patient understanding of PD techniques and compliance. Specifically, what is the role of inadequate patient knowledge in noncompliance?

Evaluate effect of staff's knowledge of clearance principles and teaching techniques and repetition frequency of patient instruction on proper delivery of PD dose.

Is there a psychological profile which is predictive of noncompliance? If so, what is the best method to characterize this profile?

VII. Clinical Outcome Goals for Adequate Peritoneal Dialysis

BACKGROUND

Throughout these Guidelines, the Work Group has focused on patient outcomes. Improving patient outcomes is the primary objective of the K/DOQI (Kidney Disease Outcomes Quality Initiative). The Work Group realizes that definitions of goals regarding patient outcomes are needed. As stated in the Introduction to these guidelines, the goals are integral to the definitions of adequate, optimal, and effective dialysis.

GUIDELINE 21

Measurement of PD Patient Survival (Opinion)

Survival of PD patients should be quantitated serially as an outcome measure.

Rationale Patient survival is an objective outcome that is dependent upon many variables, some controllable and some uncontrollable. Suboptimal doses of delivered dialysis will adversely affect patient survival in adults (data unavailable in children), as discussed in detail in Guideline 15: Weekly Dose of CAPD. A primary goal of ESRD therapy is to prolong life while minimizing uremic symptoms. United States Renal Data Systems (USRDS) data from hemodialysis patients have demonstrated an association between low Kt/V and increased incidence of death from coronary artery disease, other cardiac disease, cerebrovascular accidents, and other conditions.[93,94] There is also evidence that underdialysis adversely affects mortality in PD patients with ischemic cardiac disease or left ventricular dysfunction.[16,95] Thus, patient survival is a measure of renal replacement program effectiveness. Case mix must be factored into survival analysis, however. The USRDS case mix analysis is an excellent starting point, addressing age, race, primary renal disease, and presence or absence of diabetes. The USRDS is attempting to refine case mix further by addressing other underlying comorbidities. At dialysis centers with a small number of patients, survival may need to be evaluated over many years to obtain a reliable estimate.

GUIDELINE 22

Measurement of PD Technique Survival (Opinion)

PD technique survival, both dependent and independent of peritonitis, should be quantitated serially in PD patients as an outcome measure.

Rationale It is common for ESRD patients to change renal replacement therapy modalities during the course of their treatment. Reasons for transfer include: complications of the therapy, inability to perform the therapy (lack of suitable access, no partner to do self care, medical contraindication), and patient request/lifestyle issues. Patient case mix, geographical location, and experience with PD in complicated cases are factors affecting transfer. For some patients, for optimal outcome, it may be medically appropriate to transfer from PD to HD; this does not imply failure of the therapy or the dialysis facility.

Peritonitis remains the primary cause of transfer from PD. It is acknowledged that at times peritonitis is the "precipitating" event for transfer, while the real underlying reason is patient burnout, noncompliance, inadequate dialysis, a request based on lifestyle, or an underlying exit site infection. Overall peritonitis rates can be influenced by the center. An association between malnutrition and frequency of peritonitis has been reported.[96] Inadequate dialysis may lead to inadequate dietary protein intake and malnutrition as described in detail in Section IV: Assessment of Nutritional Status as it Relates to Peritoneal Dialysis. The relationship between solute clearance and frequency or severity of peritonitis has not been adequately studied. For example, it is not clear if inadequate dialysis or malnutrition directly predispose the patient to peritonitis. However, peritonitis is an important outcome and its frequency and severity is an index of the overall suitability of PD. It is, therefore, the opinion of the Work Group that peritonitis should be monitored.

Inadequate dialysis is directly responsible for at least 10% of transfer to HD.[93] There is an association between PD technique failure and total solute clearance,[16,97] and one possible reason for poor technique survival rates may be underlying inadequate dialysis. While the CA-

NUSA study found a relationship between creatinine clearance and PD technique survival, the investigators suspected this was more related to RKF than delivered dose of PD. In the CANUSA study, technique survival was approximately 75% at 2 years in North America.[16] However, peritonitis was not analyzed as a variable in the multivariate analysis. No difference was found in technique survival between patients from Canada and the United States. Average Kt/V_{urea} started at 2.38 and decreased to 1.99 over 2 years. The risk of technique failure increased by 5% for every 5-L/week decrease in creatinine clearance. These findings corroborated data from Tattersall et al,[97] who found that patients with a lower Kt/V_{urea} had a lower rate of technique survival. The lower rate of technique survival was related to underdialysis, not to peritonitis or hernia development. The nutritional parameter of nPCR has been shown to be predictive of CAPD technique failure in a multivariable analysis.[98]

It is a common perception that patients transferring from any renal replacement therapy are at increased risk for death in the immediate post-transfer period. However, indirect evidence from the USRDS does not support that perception.[99] Early demise following transfer may be due to a variety of reasons, including the underlying cause of transfer, inadequate dialysis on PD, and malnutrition. Therefore, the Work Group recommends that technique survival be measured at each PD facility. Admittedly, there may be center-specific differences for rates of transfer and that at centers where there are small numbers of PD patients, these rates may need to be evaluated over many years. It is recommended that these rates be evaluated both dependent and independent of peritonitis, although, in one study (CANUSA), there was no significant difference between the two evaluations.[16]

PD technique survival is dependent upon many factors including infections, patient motivation, ultrafiltration (transport characteristics), and total solute clearance. Thus, PD technique survival is not a simple outcome measure for the adequacy of PD. Nonetheless, centers should strive to achieve the goal of a 75% 2-year technique survival rate (the rate noted in CANUSA). Case mix must be factored into survival statistics.

GUIDELINE 23

Measurement of Hospitalizations (Opinion)

ESRD-related and ESRD-unrelated hospitalizations (admissions/year, hospitalized days/year) in PD patients should be quantitated as an outcome measure.

Rationale Hospitalization is an indicator of the overall effectiveness of treatment of chronic conditions and therefore constitutes an important outcome for dialysis patients. The number of admissions per year and total number of hospital days per year are two separate, but related, serial measures of outcome. Hospitalizations of PD patients can be related or unrelated to ESRD. An association between low creatinine clearance and increased overall hospitalization rate has been reported.[16] Based on this evidence, the Work Group recommends that cause, frequency, and length of hospitalizations of PD patients be monitored. Categorizing hospitalizations according to whether they are related to ESRD or not offers certain advantages for analysis and, therefore, it is the opinion of the Work Group that this type of stratified analysis should be performed.

According to the USRDS, PD patients are hospitalized an average of 1.8 times per year.[100] The CANUSA study found, by multifactorial analysis, an association between prolonged hospitalization and low creatinine clearance.[16] Some admissions are specific to PD, ie, not seen with other dialysis therapy, such as elective abdominal wall herniography. As larger instilled volumes are administered to maintain target doses of dialysis, there is an increased risk of leaks and hernia formation, both of which can lead to hospitalization. Admissions unrelated to ESRD are important indicators of morbidity (cardiac disease, infections, etc) in PD patients. Since hospitalization data are important outcome parameters for all dialysis patients and can reflect solute clearance, the Work Group recommends that they should be monitored.

Although it is uncertain whether inadequate dialysis is directly related to an increased risk of peritonitis and catheter infections, inadequate dialysis is related to uremic symptoms such as nausea, vomiting, and gastrointestinal bleeding. It is acknowledged that some centers may treat all episodes of peritonitis in the hospital, while others only admit those with severe or refractory

peritonitis. Therefore, in addition to tracking hospitalization rates, centers should also monitor reasons for hospitalization (related versus unrelated to ESRD, and specific reason for admission). The use of ICD-9 (International Classification of Diseases, 9th revision) or similar codes may be valuable in this process. The USRDS is attempting to categorize causes of hospitalizations as infectious, cardiovascular, dialysis access-related, and all other.

Hospitalizations from causes unrelated to ESRD may be related to inadequacy of PD. As discussed in Guideline 25: Measurement of PD Patient Survival, disease-specific (particularly cardiac) mortality is related to the dialysis dose for both HD and PD. Therefore, although studies of disease-specific hospitalizations and their relation to the dose of PD have not been reported, it is reasonable to monitor this relationship. Each outcome measure should be adjusted as well as possible for case mix. The USRDS is attempting to do so with Standardized Hospitalization Rates (SHRs).

GUIDELINE 24

Measurement of Patient-Based Assessment of Quality of Life (Opinion)

Patient-based assessment of quality of life (QOL) in PD patients should be evaluated serially as an outcome measure.

A patient-based quality of life instrument should have both generic and disease/treatment-specific measures of health-related quality of life and should be shown to be valid, reliable, and responsive prior to use. Once such an instrument is available, it should be administered at initiation of dialysis and at intervals determined to be appropriate by its validation studies.

Rationale Quality of life (QOL) can be assessed with generic or disease-specific measures. Many quality of life measures have been used in dialysis patients. However, fewer measures have been used for peritoneal dialysis than for hemodialysis patients.[101] Measures used in peritoneal dialysis patients and reported in the literature include[101]:

- Medical Outcomes Study Short Form 36 (SF-36).
- Sickness Impact Profile (SIP).
- Index of Well Being, Index of Overall Life Satisfaction.
- Index of Psychological Affect.
- General Health Questionnaire.
- Simmons Self Esteem Scale.
- Profile of Mood States.
- Multidimensional Health Locus of Control.
- Modality Specific Stresses Scale.
- General Treatment Stress Scale.
- Global Illness Stress on Self and Others, Global Adjustment to Illness Scale.
- Quality of Life (QL 100 mm) Analogue Scale.
- Dialysis Relationship Quality Scale.
- Social Leisure Activities Index, Social Support Satisfaction Scale.
- General Well Being Index.
- Index of General Affect, Overall Life Satisfaction.
- Katz Activities of Daily Living.
- Time Tradeoff Measures.

Unfortunately, many of these instruments do not have published data indicating that reliability (test-retest, inter-rater), validity (content, construct, internal consistency), and responsiveness-to-change have been rigorously tested.[100] For this reason, no particular instrument can be strongly recommended over another. Furthermore, many instruments developed for research purposes may be burdensome for patients or facilities, eg, require interviewer assistance or have complicated scoring algorithms. Nevertheless, generic and disease-specific measures hold promise as useful clinical tools.[102]

A popular generic measure used in peritoneal dialysis patients is the Medical Outcomes Study Short Form-36 (SF-36). Promising self-administered instruments used in peritoneal dialysis patients include the CHOICE Health Experience Questionnaire[103,104] and the Kidney Disease Quality of Life (KDQOL).[105]

The Work Group recommends that each facility keep abreast of future developments regarding these instruments. As experience increases and one or more instruments are clearly established as useful in PD patients, standardized QOL measurement should be integrated into the routine care and evaluation of patients, programs, and facilities.

GUIDELINE 25

Measurement of School Attendance, Growth, and Developmental Progress in Pediatric PD Patients (Opinion)

School attendance (in the absence of other comorbidities precluding school attendance), growth, and developmental progress should be measured serially in pediatric PD patients.

Rationale The ability of pediatric PD patients to attend school is an important measure of the success of PD.

Underdialysis may affect the cognitive development and statural growth of children. However, the exact relationship between dialysis dose and normal growth and development in children is not clear. Nonetheless, the Work Group believes that cognitive development and statural growth should be monitored serially in children and charted in relation to patient age.

GUIDELINE 26

Measurement of Albumin Concentration in PD Patients (Opinion)

A stable or rising serum albumin concentration that is greater than or equal to the lower limit of normal for each laboratory should be used as an outcome goal.

Rationale In PD patients, as with HD patients, there is strong evidence to suggest that a low serum albumin level is associated with an increased risk of technique failure and death.[16,50,106,107] Patients with the highest serum albumin levels have the lowest risk of death. In the CANUSA study, a difference of 0.1 g/dL serum albumin concentration was associated with a 5% change in the risk of technique failure, a 5% change in days hospitalized, and a 6% change in the risk of death.[16] Therefore, the Work Group recommends monitoring serum albumin concentration in PD patients because of its association with important outcomes.

Although the significance of serum albumin as a predictor of outcomes in adults is undisputed, its relationship to overall nutrition and, to a larger extent, to the levels of urea or creatinine clearance is unclear. That albumin synthesis depends on dietary protein intake is well known. However, catabolic illness can reduce albumin synthesis, and probably increase albumin degradation, even when dietary protein intake is not low. Observations in PD patients have provided indirect support for this effect of catabolic illness. Although serum albumin concentration is an important predictor of outcome,[50,106] it was not found to be significant in another study when comorbid conditions were entered as covariates in their model.[107] In this last study, the presence of comorbid conditions was associated with low serum albumin.[107] Several cross-sectional studies have identified a positive correlation between serum albumin concentration and solute clearance.[51,108,109] However, urea and creatinine clearance were not identified as predictors of serum albumin by multivariate analysis.[56,110] Age, comorbid factors (diabetes), and peritoneal solute transport were the major predictors of serum albumin in these multifactorial analyses.

Normal serum albumin concentrations vary by laboratory methodology; hence local standards should be used. If the serum albumin level is below normal for the laboratory, but is increasing, this suggests that the patient is anabolic and is increasing protein stores. Conversely, a low albumin or decreasing albumin level is likely to be associated with malnutrition or decreasing protein stores. Although there are no published data specifically addressing this point, it is the Work Group's opinion that a patient whose serum albumin has decreased 0.1 g/dL/month from a baseline of 4.0 g/dL to 3.7 g/dL may be at higher risk than a patient with a stable serum albumin concentration of 3.7 g/dL.

Taken together, the data discussed above suggest to the Work Group that:

- Serum albumin concentration should be monitored on a regular basis and a stable or rising value is desirable. It should be measured at least every 4 months.
- Serum albumin levels should be evaluated in the context of the patient's overall clinical status including comorbid diseases, peritoneal transport type, delivered dose of PD, and quality-of-life issues.
- The highest albumin level possible should be the goal for each patient.

It is the Work Group's opinion that an optimal serum albumin level can be obtained by adequate nutrition monitored frequently by the renal dietitian, prevention and treatment of catabolic illness, and maintenance of Kt/V_{urea} and creatinine

clearance at or above the levels recommended in Section V: Adequate Dose of Peritoneal Dialysis.

In summary, low serum albumin is a strong predictor of mortality and morbidity in PD patients. Therefore, serum albumin is an important outcome measure in PD patients and should be monitored, although an association between serum albumin and urea or creatinine clearance has not been convincingly shown. Efforts to maintain serum albumin in the normal range should include adequate nutrition, adequate clearances, and prevention and treatment of catabolic illness.

GUIDELINE 27

Measurement of Hemoglobin/Hematocrit in PD Patients

Providers should strive to achieve a hemoglobin level of 11 to 12 g/dL or a hematocrit of 33% to 36% in 75% of PD patients.

Rationale See NKF-K/DOQI's Clinical Practice Guidelines for the Treatment of Anemia of Chronic Renal Failure.

GUIDELINE 28

Measurement of Normalized PNA in PD Patients (Opinion)

Providers should strive to achieve a normalized PNA (nPNA) of greater than or equal to 0.9 g/kg/day in PD patients.

See Guideline 16 of the NKF/K/DOQI Clinical Practice Guidelines for Nutrition, which recommends a dietary protein intake of 1.2 to 1.3 g/kg body weight/day in clinically stable chronic peritoneal dialysis patients. Such a diet should lead to an nPNA equal to or greater than 0.9 g/kg/day.

Rationale The role of PNA is discussed in Guideline 12: Assessment of Nutritional Status.

Maintenance of positive nitrogen balance and the prevention of underlying malnutrition is important because of the documented detrimental impact of hypoalbuminemia and low SGA scores on patient survival.[16,80,106,110] From nitrogen balance studies, Blumenkrantz et al[111] estimated that PD patients need to ingest at least 1.2 g/kg/d of protein to maintain positive nitrogen balance.[109] This is higher than the recommended daily protein intake for healthy individuals, but not surprising due to the significant amount of protein known to be lost in dialysate. Despite these recommendations from balance studies, Bergstrom et al[53] and Nolph et al[51] have reported that many patients are in positive nitrogen balance with protein intakes of 0.9 to 1.0 g/kg/d. Cross-sectional studies would suggest that in the absence of significant comorbid diseases, patients with PD doses in the range of Kt/V_{urea} of 2.0 spontaneously ingest at least 0.9 g/kg/d of protein.[52,112,113] Total solute clearance and nPCR* are strongly correlated in cross-sectional studies.[57,114] However, it has been suggested that this is due in part to mathematical coupling of data.[55,115] Three studies have investigated the effect of an increased Kt/V_{urea} on nutritional status (nPCR and serum albumin concentration) in a limited number of subjects.[56,58,116] While nPCR increased as Kt/V_{urea} increased, an increase in serum albumin concentration did not occur. A reasonable conclusion from these data would be that in the absence of significant comorbidity, an increase in delivered dialysis dose should result in a corresponding increase in nPNA. In patients who show signs of malnutrition, their dialysis prescription should be closely evaluated with consideration to increasing their dose of dialysis if significantly below target. This is discussed in Guideline 15: Weekly Dose of CAPD.

No study of PD patients has demonstrated that nPNA is an independent predictor of outcome when a multiple regression model is used. Correlation coefficients relating DPI to nPCR are on the order of 0.6. However, PD patients who are neither anabolic nor catabolic tend to demonstrate higher correlation coefficients between nPNA and DPI.[53] Also, there are little data to show a significant relationship between nPCR and serum albumin levels.[56,110] Age, peritoneal transport type, presence of diabetes, and other comorbid diseases have a greater effect on albumin than does nPCR.

Despite these concerns, the Work Group recommends that PNA should be monitored. Low nPNA values in nonanabolic PD patients indicate a low DPI regardless of the values of other

*Studies that used the term PCR are cited in this rationale. Since the original study authors used the term PCR, this rationale will use the term PCR when specifically describing results from studies which used that term. However, the Work Group favors the term PNA.

nutritional indices.[54] One should strive to achieve an nPNA of at least 0.9 g/kg/day in adult PD patients. PNA values at this level or higher are likely to be associated with neutral or positive nitrogen balance in the absence of significant comorbidity or dialysate protein losses.

While the recommended dietary allowance for normal children is known, there are no definitive data regarding the real protein needs of children, especially young children on dialysis.[69b] However, clinical practice suggests that the protein needs of children on PD are greater than the recommended dietary allowance, in part related to dialysate protein losses. Current recommended protein intakes for children receiving PD, referenced for age are as follows[117]:

Age (Years)	*Protein Intake* for PD*
0-0.5	2.9-3.0
0.6-1.0	2.3-2.4
1-3	1.9-2.0
4-6	1.9-2.0
7-10	1.7-1.8
11-14	1.7-1.8
15-18	1.4-1.5†
19-21	1.3†

*Values are expressed in grams of protein/kg/day.
†Based on growth potential.

Because dialysate protein losses may vary widely in children, individualized recommendations for dietary protein intake may benefit from measurement of dialysate protein losses. An equivalent amount of protein to replace dialytic losses must be added to the recommended daily allowance for normal children.[118]

RECOMMENDATIONS FOR RESEARCH

The relationship between solute clearance and the frequency and/or severity of peritonitis has not been adequately studied. Specifically, does inadequate PD dose contribute to peritonitis?

Studies to assess whether an increase in nPNA is associated with an increase in serum albumin levels, nutritional status, or improved survival would be valuable.

Studies to further define the relationship between nPCR and outcome are needed. For example, the longitudinal follow-up of nutritional status (determined by a variety of methods) will be more influential in improving understanding of nutritional outcomes. Longitudinal studies should be emphasized over cross-sectional studies.

The relationship between PD dose and outcome parameters in children needs definition. Studies of nutritional interventions are lacking and are encouraged.

VIII. Suitable Patients for Peritoneal Dialysis

GUIDELINE 29
Indications for PD (Opinion)

Indications for PD include:

- Patients who prefer PD or will not do hemodialysis (HD).
- Patients who cannot tolerate HD (eg, some patients with congestive or ischemic heart disease, extensive vascular disease, or in whom vascular access is problematic, including the majority of young children).
- Patients who prefer home dialysis but have no assistant for HD, or whose assistant cannot be trained for home HD.
- ***Rationale*** There is a rapid change in solute transport as well as rapid shifting of volume within compartments during HD. Some patients with severe cardiac disease may be better managed on PD since these acute changes are avoided.[119-123] PD has been proposed as a method of managing refractory heart failure even in patients without renal failure.[124]

Advantages of PD in patients with cardiovascular disease include: better hemodynamic control, less acute hypokalemia (or electrolyte shifts) which could result in arrhythmia, and better control of anemia (important in patients with coronary artery disease). Although a comparison of PD to HD for patients with severe heart failure has not been published, there are several reports of successful PD performance in subjects with severe heart failure.[125-130] Tolerance of the procedure (PD), fluid management, prevention of arrhythmias, and patient survival were satisfactory in these reports.

Extensive peripheral or central venous occlusive disease prohibits surgical placement of some types of hemodialysis access. Manifestations of severe ischemia, even gangrene, of the hands follow placement of vascular access in the same wrist or forearm in a few patients with severe peripheral vascular disease, particularly diabetics.[131] Marginal vascular beds are at risk for ischemia or reduced perfusion during hypotension, which is frequent in some HD patients. These patients benefit from increased vascular stability, which can be achieved with PD.

Over a period of time, vascular accesses fail and revisions are no longer able to restore adequate blood flow. As a result, the patient receives inadequate hemodialysis and should be evaluated for PD.[119,122,132]

Home hemodialysis requires an assistant. For patients who prefer dialysis at home, the lack of a hemodialysis assistant may mandate PD. In addition, patients who have transportation problems to a hemodialysis center or live a great distance from a center may prefer home PD.[133]

The decision to initiate PD rather than HD in children is influenced by a variety of factors. Because of the difficulties in maintaining vascular access in infants and small children, PD is usually the modality of choice when weight is $<$20 kg. Regular school attendance by children of all ages can best be achieved with a home dialysis procedure. PD is typically preferred over HD. Finally, renal replacement therapy can also best be provided by PD when the child lives a long distance from a pediatric ESRD center.

GUIDELINE 30

Absolute Contraindications for PD (Opinion)

Absolute contraindications for PD include:

- Documented loss of peritoneal function or extensive abdominal adhesions that limit dialysate flow.
- In the absence of a suitable assistant, a patient who is physically or mentally incapable of performing PD.
- Uncorrectable mechanical defects that prevent effective PD or increase the risk of infection (eg, surgically irreparable hernia, omphalocele, gastroschisis, diaphragmatic hernia, and bladder extrophy).

Rationale *Documented Loss of Peritoneal Function.* PD efficiency relies on effective peritoneal blood flow, dialysate flow, sufficient peritoneal surface area, and permeability to allow adequate solute and fluid removal. Any compromise in these functions may result in inadequate peritoneal dialysis and thus the failure of PD.[120,134]

It should not be assumed that children who have previously undergone extensive abdominal surgery will not achieve successful PD. A trial of PD is warranted in such children and adequate dose delivery must be documented.

Psycho-Neurological Problems. The optimal performance of PD requires certain physical

and intellectual capabilities of the patient or caregiver. With major loss of mechanical function or eye-hand coordination, PD becomes difficult to perform. Patients or caregivers are responsible for problem identification and problem solving during PD. If the patient is deemed psychologically incompetent, these tasks and decisions may not be reliably or safely executed.[122,133]

Abdominal Mechanical Problems. The dialysate in the abdomen must be accessible to the vascular bed of the peritoneal membrane. Any mechanical problem that prevents this (eg, hernia sack, subcutaneous leak) will impair the efficiency of PD. Intra-abdominal pressure increases with dialysate infusion and during the ultrafiltration process, thereby exacerbating any structural defect such as hernia. Some of these abdominal defects are not surgically correctable.[122,123]

GUIDELINE 31

Relative Contraindications for PD (Opinion)

Relative contraindications for PD include:

- Fresh intra-abdominal foreign bodies (eg, 4-month wait after abdominal vascular prostheses, recent ventricular-peritoneal shunt).
- Peritoneal leaks.
- Body size limitations.
- Intolerance to PD volumes necessary to achieve adequate PD dose.
- Inflammatory or ischemic bowel disease.
- Abdominal wall or skin infection.
- Morbid obesity (in short individuals).
- Severe malnutrition.
- Frequent episodes of diverticulitis.

Rationale Fresh Intra-Abdominal Foreign Bodies. Newly implanted abdominal prostheses must be allowed sufficient time for healing to avoid leakage or possible dialysis-related peritonitis with potential spread to the prosthetic device or material. The time required for healing may vary from 6 to 16 weeks.[135-137] The bacterial seeding of any vascular prosthesis during hemodialysis is also a risk. The best type of dialysis in this setting is unclear.

Peritoneal Leaks. Peritoneal leakage into subcutaneous tissues, pleural space, or genitalia can be painful and cause local problems. Leaking into the vagina or rectum increases the risk of contamination. Unsatisfactory drainage and clearance, as well as medical complications, such as respiratory compromise in the case of diaphragmatic leak, can occur as a result of such leakage.[122,123,133]

Body Size Limitations. Body size can be a relative contraindication to PD when the patient is either too small to tolerate the prescribed dialysate volume or too large to achieve adequate dialysis. For patients with little or negligible RRF, there are definite size limitations for adults on CAPD with 4 daily exchanges.[138] However, even larger individuals can achieve acceptable clearances if they are treated with a combination of daily CAPD and nocturnal automated PD.[139] In large individuals, increase in the exchange volume is more efficient than increase in the number of daily exchanges. However, the patient with the increased exchange volume may experience abdominal pain or discomfort, shortness of breath, or loss of appetite as a result of abdominal pressure.[140]

Intolerance to PD Volumes Necessary to Achieve Adequate PD Dose. Intolerance to a PD volume is generally not known until it is attempted. Frequent exchanges with small volumes, as observed during automated PD, may not be able to provide an adequate delivered dose of PD. Raising volumes to the limit of tolerance may be problematic in patients with advanced lung disease or patients with recurrent hydrothorax. Infrequently, this may be applicable to some patients with polycystic kidney disease or severe lumbo-sacral disk disease.

Inflammatory or Ischemic Bowel Disease. Inflammatory or ischemic bowel disease or frequent episodes of diverticulitis are relative contraindications to peritoneal dialysis. It is reasonable to assume that there may be increased risk for transmural contamination by enteric organisms in these circumstances.[133]

Abdominal Wall or Skin Infection. Abdominal wall or skin infection can lead to contamination of the catheter exit site, tunnel, and peritoneal cavity through touch and cross contamination.[122] The decision to use PD in patients with a colostomy or ileostomy must be individualized, since successful application of PD has been described in such patients.

Morbid Obesity. Morbid obesity can pose special dilemmas in peritoneal catheter placement, the healing process, and in providing adequate dialysis. The possibility that increased caloric absorption from the dialysate could lead to further weight gain should also be considered.

Severe Malnutrition. Wound healing is compromised in severely malnourished patients. Self-dialysis such as PD may not be suitable for many severely malnourished patients because of inability to comply with the dialysis regime. Furthermore, peritoneal protein losses may not be tolerated.

Frequent Episodes of Diverticulitis. Diverticulitis during peritoneal dialysis often results in peritonitis. Peritoneal dialysis in patients with frequent episodes of diverticulitis places these patients at higher risk for peritonitis.

GUIDELINE 32

Indications for Switching from PD to HD (Opinion)

The decision to transfer a PD patient to HD should be based on clinical assessment, the patient's ability to reach HD dose target levels, and the patient's wishes. In particular, these patients should have vascular access addressed as advised by the NKF-K/DOQI Vascular Access Work Group.

Indications for switching from PD to HD include:

- Consistent failure to achieve target Kt/V_{urea} and C_{Cr} when there are no medical, technical, or psycho-social contraindications to HD.
- Inadequate solute transport or fluid removal. High transporters may have poor ultrafiltration and/or excessive protein losses (relative contraindication, obviously discovered after initiation and the first PET).
- Unmanageably severe hypertriglyceridemia.
- Unacceptably frequent peritonitis or other PD-related complications.
- Development of technical/mechanical problems.
- Severe malnutrition resistant to aggressive management (relative).

Patients should be informed of the risks of staying on PD at a level of adequacy below that recommended by their physician.

Rationale The above recommended indications for switching a patient from PD to HD are based on the following considerations:

Consistent Failure to Achieve Target Kt/V_{urea} and C_{Cr}. Consistent failure to achieve the target total solute removal with proper PD prescription management should lead to evaluation of compliance issues and deterrents to appropriate performance of peritoneal dialysis exchanges. After all avenues have been explored, if social or physical issues cannot be overcome, transfer to HD may be necessary as long as the same issues do not deter appropriate therapy (eg, adequate ultrafiltration, single pool delivered Kt/V_{urea} of 1.2 thrice weekly, etc) on this modality.[134,141]

Inadequate Solute Transport or Fluid Removal. Peritoneal solute transport determined by PET affects both solute and fluid removal by PD. Obviously, peritoneal transport type is discovered after initiation of PD by the first PET. High transporters may have poor ultrafiltration and/or excessive protein losses (relative contraindication). Excessive protein losses are those that exceed the patient's ability to compensate by an increase in dietary protein consumption. However, peritoneal urea and creatinine clearances tend to be adequate in high transporters. Many high transporters with poor ultrafiltration can be effectively dialyzed with short dwell periods and daytime exchanges, but such a regimen may become too burdensome for the patient's lifestyle.[120,134,141] Low transporters usually have adequate ultrafiltration, but, when they are relatively large, may have inadequate peritoneal clearance of creatinine, but not necessarily a decreased clearance of urea.[63]

Excessive protein losses can occur if the patient's underlying disease includes active nephrosis, if the patient is a high transporter, or if frequent peritonitis occurs. The resulting malnutrition will increase the patient's mortality and morbidity. In some children who are actively nephrotic, protein losses may be successfully replaced by supplemental (eg, nasogastric, gastrostomy) tube feedings.

There are medical complications that may develop or have been present prior to initiation of

dialysis, but these may become apparent only after peritoneal equilibration testing and adequacy studies.

Inadequate solute transport documented by measures of Kt/V_{urea} and creatinine clearance must be evaluated. If the maximum PD prescription has been reached (increases in volumes and frequency of exchanges including use of nocturnal cycling) or the procedure is no longer achievable due to lifestyle complications, hemodialysis as an alternative should be explored.[120]

These guidelines have defined adequate solute transport with regard to urea and creatinine. However, the failure to adequately remove other solutes such as potassium may require switching to another form of renal replacement therapy.

Inadequate ultrafiltration is usually secondary to high transport characteristics or a mechanical defect hampering catheter patency or drainage.[142] In rare instances, inadequate ultrafiltration is associated with low peritoneal transport characteristics, probably due to a significant reduction in the area of the peritoneal membrane, or secondary to increased peritoneal lymphatic flow.[143]

Unacceptably Frequent Peritonitis. The definition of unacceptably frequent peritonitis has to be individually determined for each patient. Such considerations as the availability of hemodialysis facilities will inevitably play a role.

Unmanageably Severe Hypertriglyceridemia. Unmanageably severe hypertriglyceridemia, resulting from, or exacerbated by, the dextrose load intrinsic to the dialysate, may increase the risk for cardiovascular disease.

Development of Technical/Mechanical Problems. Irreparable technical or mechanical defects, such as catheter malposition, resulting in access failure.

Severe Malnutrition Resistant to Aggressive Management (Relative). Due to the continuous protein loss associated with PD, malnourished patients must be aggressively evaluated and treated. If treatment of malnutrition is not successful, transfer to HD is indicated.

RECOMMENDATIONS FOR RESEARCH

The topic of suitability of patients for PD or HD has not been thoroughly investigated. Prospective comparisons of PD and HD for specific ESRD patient categories (eg, those with severe heart failure, those with advanced malnutrition, those with large body size, etc) are needed to define the subsets of ESRD patients which are most suitable or unsuitable for PD.

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X. Appendices

Appendix A: Detailed Rationale for Guideline 1

GUIDELINE 1

When to Initiate Dialysis—Kt/V_{urea} Criterion (Opinion)

Unless certain conditions are met, patients should be advised to initiate some form of dialysis when the weekly renal Kt/V_{urea} (K_rt/V_{urea}) falls below 2.0. The conditions that may indicate dialysis is not yet necessary even though the weekly K_rt/V_{urea} is less than 2.0 are:

1. Stable or increased edema-free body weight. Supportive objective parameters for adequate nutrition include a lean body mass >63%, subjective global assessment score indicative of adequate nutrition (see Guideline 12: Nutritional Status Assessment, and Appendix B: Detailed Rationale for Guideline 2) and a serum albumin concentration in excess of the lower limit for the lab, and stable or rising; and

2. Nutritional indications for the initiation of renal replacement therapy are detailed in Guideline 27 of the NKF-K/DOQI Clinical Practice Guidelines on Nutrition, part of which are reproduced as Guideline 2 of the PD Adequacy Guidelines.

3. Complete absence of clinical signs or symptoms attributable to uremia.

A weekly K_rt/V_{urea} of 2.0 approximates a renal urea clearance of 7 mL/min and a renal creatinine clearance that varies between 9 to 14 mL/min/1.73 m^2. Urea clearance should be normalized to total body water (V) and creatinine clearance should be expressed per 1.73 m^2 of body surface area. The GFR, which is estimated by the arithmetic mean of the urea and creatinine clearances, will be approximately 10.5 mL/min/1.73 m^2 when the K_rt/V_{urea} is about 2.0.

Rationale In patients with chronic kidney disease, progression of kidney failure should be monitored by following total weekly renal urea nitrogen clearance (K_rt_{urea}) normalized to urea volume of distribution (V), ie, K_rt/V_{urea}.[1,2] This does not imply that a weekly collection of urine is necessary. A daily collection multiplied by seven yields a reasonable approximation of weekly clearance. The knowledge of K_rt/V_{urea} is especially important when glomerular filtration rate (GFR) falls below 25 to 50 mL/min, at which time spontaneous decrease in dietary protein intake is commonly observed.[3-6] The blood urea nitrogen (BUN) and serum creatinine values should not be used to monitor progression of renal failure, particularly in patients with diabetes.[2] BUN may be low secondary to low protein intake and may not adequately reflect the degree of the renal functional impairment. Serum creatinine may be low due to decreased muscle mass as seen in some women, in the elderly, and in malnourished patients. Hence, serum creatinine concentration may not adequately reflect the degree of the renal functional impairment.

The estimation of V (total body water) by any formulae has not been validated in children with renal failure. Thus, the use of K_rt/V_{urea} as an indication for the initiation of PD is recommended considering this caveat. Creatinine clearance as a means of assessing RRF for purposes of initiation of dialysis should be normalized to body surface area (BSA).

An increasing body of evidence[1,7-10] suggests that K_rt/V_{urea} is a reliable predictor of outcome in PD and that weekly values in the range of 2.0 provide adequate therapy (see Guideline 15: Weekly Dose of CAPD). Although the CANUSA data indicated a linear decrease in modeled mortality rate with increasing $K_{pr}t/V$ up to 2.3, there is some uncertainty about the significance of the high $K_{pr}t/V$ levels achieved in this study.[11]

It has always been a paradox that nephrologists have insisted on optimal therapy once patients are started on dialysis but have accepted much lower levels of renal function, defined as K_rt/V_{urea}, during the predialysis phase of patient management. For example, while we recognize that a weekly $K_{pr}t/V_{urea}$ of 2.0 or higher is associated with improved outcome on PD, dialysis is usually not initiated until weekly K_rt/V_{urea} is in the range of 0.71 to 1.3.[2,12] It is possible that the consequences of delaying initiation of PD may be analogous to the experience of the National Cooperative Dialysis Study, wherein the mortality rate in the year after the study ended was more than twice as high in those randomized to the low dose dialysis protocols, even though they

were returned to standard dialysis after completing 24 weeks in the high BUN (low clearance) arm of the study.[13]

The Work Group feels that the data of Ikizler et al,[4] McCusker et al,[12] and Pollock et al[6] strongly demonstrate the linkage between decreasing kidney function and worsening nutritional status. In the CANUSA study, multiple estimates of nutritional status were associated with two estimates of RKF.[12] Patients who started PD at lower levels of RKF had a worse nutritional status than those who started at a higher level of RRF. CANUSA further demonstrated an association between the relative risk of death and worse baseline serum albumin concentration, worse time-dependent SGA, and worse time-dependent percent lean body mass.[1] While an association between risk of death and nPCR could not be demonstrated in the multivariate analysis, several univariate analyses did demonstrate an association of individual estimates of baseline nutritional status with survival.

These data are consistent with the observations of Bonomini et al[14] who found that patients starting dialysis with a residual kidney creatinine clearance of <5 mL/min had a worse long-term outcome than patients starting incremental hemodialysis with a mean residual kidney creatinine clearance of 11 mL/min.

From these observational data, it seems reasonable to draw the following conclusions:

Once K_rt/V_{urea} falls below 2.0 per week or creatinine clearance falls into the range of 9 to 14 mL/min/1.73 m^2, initiation of dialysis or transplantation[15,16] should be strongly advised. The patient should be considered to be at increasing risk with any further decreases in K_rt/V_{urea} in the absence of renal replacement therapy intervention. If dialysis is not instituted when K_rt/V_{urea} falls below 2.0, it is mandatory to document a negative inquiry for clinical signs or symptoms of uremia and that the following have not occurred: (a) more than a 6% involuntary reduction in edema-free usual body weight (%UBW) or to less than 90% of standard body weight (NHANES II) in less than 6 months; (b) a reduction in serum albumin by greater than or equal to 0.3 g/dL and to less than 4.0 g/dL (see Nutrition Guideline 3), in the absence of acute infection or inflammation, confirmed by repeat laboratory testing; or

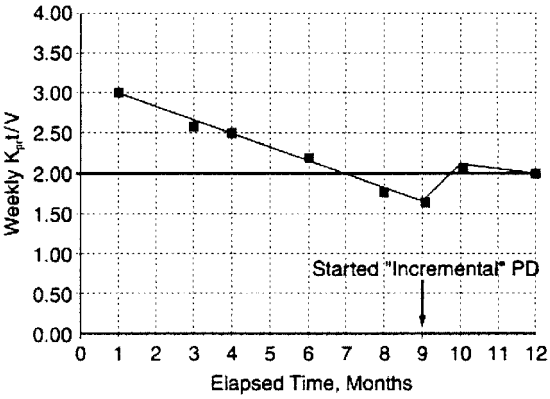

Fig II-1. Solute removal and initiation of PD. Example of tracking solute clearance measurements for a single patient over a 12-month period. The point at which incremental PD was initiated is indicated by the arrow.

(c) a deterioration in SGA by one category (ie, normal, mild moderate, severe; see Nutrition Guideline 9 and Nutrition Appendix VI). When PD is initiated, the K_pt/V_{urea} could be increased incrementally[17-21] such that the combined value of $K_rt/V_{urea} + K_pt/V_{urea}$ does not fall below the target level of 2.0 (see Fig II-1 and Guideline 15: Weekly Dose of PD). Alternatively, the initiation of "full dose" PD may be offered. Since residual kidney function (RKF) is such a crucial component of total solute removal utilizing the incremental initiation approach, more intense scrutiny of RKF is necessary. For initiation with full dose PD, less intense scrutiny of RKF is indicated. This is discussed in Guideline 3: Frequency of Delivered PD Dose and Total Solute Clearance Measurement Within Six Months of Initiation, and Guideline 5: Frequency of Measurement of Kt/V_{urea}, Total C_{Cr}, PNA, and Total Creatinine Appearance, which address frequency of measurements.

In the CANUSA study,[1] the weekly C_{Cr} equivalent to a $K_{pr}t/V_{urea}$ of 2.0 was 70 L/wk/1.73 m^2. As will be clear later in this discussion, a C_{Cr} this high is indicative of residual kidney function, which was clearly present in the CANUSA patients at initiation of PD.

CAPD is the only continuous chronic renal replacement therapy with which to quantitatively compare continuous residual kidney solute clearance. The Work Group strongly supports the opinion that the outcome data for a weekly Kt/V_{urea} of ≥ 2.0 are so compelling that using the

same figure for initiation of dialysis justifies the unknown but presumably small risks of performing peritoneal dialysis. Those risks include infections and the possibility that increasing the length of time on PD contributes to eventual patient "burn-out." If a patient is suspected to be at high risk for these complications, PD may not be the best choice for renal replacement therapy.

The Work Group recognizes that the patient will play a major role in accepting the initiation of dialysis based on a certain "laboratory value." It is the responsibility of the care providers to make clear to the patient the rationale for initiating dialysis when the above conditions become applicable. Reasons to justify a delay in initiating dialysis are listed above. These reasons should be documented, if present.

The Work Group also recognizes that for many clinicians, initiating dialysis based on Kt/V_{urea} is a new concept. Therefore, we have attempted to equate this to the traditional measure of urea clearance, creatinine clearance, and GFR (estimated by the arithmetic mean of urea and creatinine clearance).

What follows is an explicit quantitative approach to the concept of renal urea clearance ($K_{r\,urea}$, mL/min). We recommend that adequate PD be considered to require:

$$K_{pr}t/V = 2.0 \text{ per week} \quad \textbf{(1)}$$

where $K_{pr}t$ is total weekly peritoneal plus renal urea clearance. Guideline 15: Weekly Dose of CAPD, explains the rationale for recommending that $K_{pr}t/V$ be 2.0 per week.

For the purpose of this discussion, $K_{r\,urea}$ is considered equivalent to $K_{p\,urea}$ and, therefore,

$$K_{pr}t/V = 1.44*7*K_{r\,urea}/V, \quad \textbf{(2)}$$

where 1.44 converts mL/min to L/day, when Krt/V is 2.0.

$$2.0 = 1.44*7*K_{r\,urea}/V \text{ and} \quad \textbf{(3)}$$

$$K_{r\,urea} = 0.20*V \quad \textbf{(4)}$$

Equation 4 shows that $K_{r\,urea}$ must equal 0.2 times V when $K_rt/V = 2.0$. It is of interest to compare this criterion to those developed independently[22] for hemodialysis (HD). For twice weekly (biw) HD, a coefficient has been developed[22] from urea kinetic modeling to convert $K_{r\,urea}$, mL/min, to L of equivalent urea clearance during each twice weekly dialysis. The twice weekly adequate level of Kt/V_{urea}[23] in HD is 1.85 (double pool) and the coefficient to convert $K_{r\,urea}$ to equivalent urea clearance during dialysis is 9.0 with units of L/treatment/mL $K_{r\,urea}$. Therefore,

$$1.85 = 9.0*K_{r\,urea}/V \text{ or} \quad \textbf{(5)}$$

$$K_{r\,urea} = 0.20*V \quad \textbf{(6)}$$

Equation 6 for biw HD is identical to Equation 4 for PD. For thrice weekly (tiw) HD the (double pool) coefficient previously developed[22] is 5.0, therefore,

$$1.0 = 5.0*K_{r\,urea}/V \text{ or} \quad \textbf{(7)}$$

$$K_{r\,urea} = 0.20*V \quad \textbf{(8)}$$

Since Equations 4, 6, and 8 are identical, it is apparent that PD, biw HD, and tiw HD should all be started when $K_{r\,urea} = 0.20*V$. For an average patient with V = 35 L, this defines a level of $K_{r\,urea}$ = 7.0 mL/min. There are constraints on the lower level of $K_{r\,urea}$ for biw HD.[22] As Fig II-1 suggests, treatment could be started incrementally once weekly K_rt/V_{urea} falls below 2.0. Typically, this would involve a single overnight exchange, intended to restore Kt/V_{urea} to 2.0 per week. Ultrafiltration would not be needed since at this level of K_rt/V_{urea} urine volumes are usually adequate.

Levels of Residual Renal Creatinine Clearance, $C_{r\,Cr}$, mL/min At Which Dialysis Should Be Initiated. There are no $K_{r\,Cr}$ criteria for HD, and the criteria defining the contribution of residual kidney function ($K_{r\,Cr}$) to therapy are different from the criteria defining the contribution of peritoneal creatinine clearance (K_{pCr}) to the dose of therapy. The problem arises from the argument that tubular secretion of creatinine should be subtracted from the total kidney creatinine clearance, and renal function with respect to creatinine clearance is best expressed as "GFR" as developed below. Therefore, the definitions used with respect to $K_{r\,Cr}$ will each be considered separately and related to the level of Kt/V_{urea} for which $K_{r\,urea}$ and $K_{p\,urea}$ are considered simply additive.

In all instances, the total weekly C_{Cr} is normalized to 1.73 m^2 of BSA. In order to compare this to the $K_{pr}t/V_{urea}$, BSA must be normalized rela-

tive to V, eg, based on the Hume equations and taking the mean of the genders, 1.73 m^2 = 35 L.[24] It is also reasonable to extend this as a linear relationship over the domain of patient size although it should also be considered a gender-dependent relationship.

Consideration of Renal Contribution to Dose Expressed as $C_{r\ Cr}$. As noted above, in all cases the dose of total creatinine clearance is expressed as L/wk/1.73 m^2 of BSA. The following will normalize total creatinine clearance to 1.73 m^2 (nBSA) and Kt/V_{urea} to a standard V = 35 L corresponding to 1.73 m^2 of BSA in order to develop constants relating the creatinine and urea-based dosage parameters. To the extent that BSA and V increase and decrease at the same ratio (reasonably valid), the constants developed are generalizable, and therefore, the relation between $K_{r\,Cr}$ and nBSA can be expressed as follows:

$$[K_{r\,Cr}t/nBSA] = 1.44*7*K_{r\,Cr} = 10.1 \cdot K_{r\,Cr} \quad \textbf{(9)}$$

Equation 9 simply describes the total weekly liters of renal creatinine clearance as a function of $K_{r\,Cr}$ and our normalized BSA of 1.73 m^2.

For the Kt/V_{urea} normalized to V = 35, therefore,

$$K_rt/nV_{urea} = 1.44*7*K_{r\,urea}/35 = 0.29*K_{r\,urea} \quad \textbf{(10)}$$

and, therefore,

$$K_{r\,urea} = 3.47*K_rt/nV_{urea} \quad \textbf{(11)}$$

Assuming

$$K_{r\,Cr} = 2*K_{r\,urea}, \quad \textbf{(12)}$$

we can substitute Equation 11 into Equation 12 to show

$$K_{r\,Cr} = 2*3.47*K_rt/nV = 6.94*K_rt/nV_{urea} \quad \textbf{(13)}$$

Substituting now Equation 13 into Equation 9 yields the following equation:

$$[K_{r\,Cr}t/nBSA] = 10.1[6.94(K_rt/nV)] = 70(K_rt/nV) \quad \textbf{(14)}$$

Equation 14 shows that if we define the renal contribution to PD therapy by $K_{r\,Cr}$, the level of weekly $K_{r\,Cr}$ per 1.73 m^2 must be 70 times the K_rt/nV_{urea} so at K_rt/nV_{urea} of 2.0, $K_{r\,Cr}$ t/1.73 m^2 is 140. For the average patient with V = 35 L and BSA = 1.73 m^2, the required level of $K_{r\,Cr}$ = 14 mL/min.

Consideration of Renal Contribution to Dose Expressed as "GFR." In this case the effective renal creatinine clearance, $eK_{r\,Cr}$, is defined as:

$$eK_{r\,Cr} = GFR = [K_{r\,Cr} + K_{r\,urea}]/2 \quad \textbf{(15)}$$

Therefore,

$$[eK_{r\,Cr}t/nBSA] = 1.44*7(K_{r\,Cr} + K_{r\,urea})/2 = 5.0*K_{r\,Cr} + 5.0*K_{r\,urea} \quad \textbf{(16)}$$

Substituting from Equations 11 and 13, yields

$$[eK_{r\,Cr}t/nBSA] = 5*6.94(K_rt/V) + 5*3.47(K_rt/V) = 52(K_rt/V) \quad \textbf{(17)}$$

Equation 17 shows that if the renal contribution to PD therapy is defined as GFR, which is equivalent to "effective" creatinine clearance or $eK_{r\,Cr}$, the total weekly $eK_{r\,Cr}$ required relative to K_rt/V_{urea} is 52 L/week/1.73 m^2 per unit of K_rt/V_{urea}. It can also be noted that in all instances these equations also relate to $K_{pr}t/V_{urea}$ and K_pt/V_{urea} since we have defined $K_r = K_p$.

Consideration of Peritoneal Creatinine Clearance to PD Dose. In this case, the dose must be expressed directly in terms of peritoneal creatinine clearance (K_{pCr}) and by definition,

$$[K_{pCr}t/nBSA] = 1.44*7*K_{pCr} = 10.1\ K_{pCr} \quad \textbf{(18)}$$

The average relationship between K_{pCr} and K_p urea in CAPD is

$$K_{pCr} = 0.8*K_{p\,urea} \quad \textbf{(19)}$$

Since $K_{p\,urea} = K_{r\,urea}$ and $K_{p\,urea}t/nV = K_{r\,urea}t/nV$, Equations 18, 19, and 11 can be combined to derive

$$[K_{pCr}t/nBSA] = 28[K_{p\,urea}t/nV] = 28[K_{r\,urea}t/nV] \quad \textbf{(20)}$$

Equations 14, 17, and 20 show that the Creatinine Dose Equivalency with respect to the single urea $K_{pr}t$ /V criterion will vary widely depending on how RRF is defined. The relationships are plotted in Fig II-2: Dose of PD With Respect to Weekly Creatinine Clearance Relative to Weekly $K_{pr}t/V$, where the weekly creatinine clearance required per 1.73 m^2 corresponding to a weekly $K_{pr}t$ /V_{urea} of 2.0 ranges from 140 to 56 L,

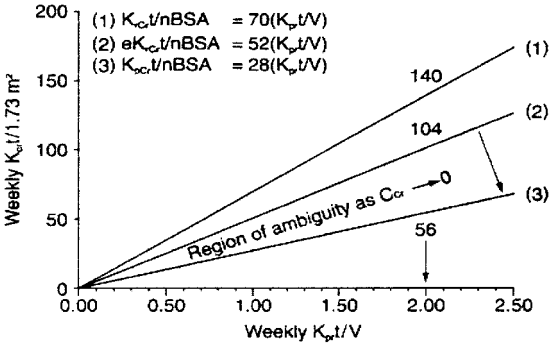

Fig II-2. Dose of PD with respect to weekly creatinine clearance relative to weekly $K_{pr}t/V$. The dose of PD with respect to weekly creatinine clearance relative to weekly $K_{pr}t/V$ varies widely depending on the definition of renal creatinine clearance.

depending on the definitions used. There is no problem in either the case of pure residual kidney function with no PD therapy or the case of pure peritoneal dialysis with no residual kidney function present. The problem arises when one attempts to sum residual kidney creatinine clearance with peritoneal creatinine clearance. In this common circumstance, the dialysis dose relationship will be bounded by regression lines 2 and 3 in Fig II-2.

For line 1, which defines creatinine clearance as the uncorrected (for secretion) creatinine clearance, the creatinine clearance that is equivalent to a Kt/V_{urea} of 2.0 is 140 L/wk/1.73 m^2. Line 2 defines creatinine clearance as the mean of urea and creatinine clearance, and the equivalence to a Kt/V_{urea} of 2.0 is 104 L/week/1.73 m^2. Line 3 represents all clearance from PD (complete absence of residual kidney function). Under this condition a Kt/V_{urea} of 2.0 is equivalent to a creatinine clearance of 56 L/wk/1.73 m^2.

This creates an irreconcilable ambiguity with respect to the creatinine and urea dosage criteria for defining optimal dialysis and the study of outcome as a function of dose. Because the practice of PD has used both C_{Cr} and Kt/V to quantify delivered dose and there is a large body of literature describing outcomes related to C_{Cr}, the Work Group recommends continuing to use both measures (see Guideline 4: Measures of PD Dose and Total Solute Clearance). However, in view of this ambiguity, the Work Group recommends that if only one measure is to be utilized, use $K_{pr}t/V_{urea}$ rather than $K_{r\,Cr}t$ (see Guideline 15: Weekly Dose of CAPD). Nonetheless, creatinine kinetics as discussed in Guidelines 4, 6, and 17 are useful for estimating edema-free, fat-free body mass, compliance with dialysis prescription, and some programs may prefer it for quantification of delivered dose of PD. Thus, total creatinine excretion is valuable.

Finally, it is worth emphasizing that the basic relationship between the level of residual $C_{r\,Cr}$ to $K_{r\,urea}$ for initiation of dialysis will be the same for all of these creatinine dosage criteria. They are related to $K_{pr}t/V$ since $K_{r\,Cr} = 2\ K_{r\,urea}$ and all of the expressions ultimately reduce to this relationship.

Another way to view the creatinine clearance at which to initiate dialysis is to extrapolate backward from the CAPD target of 60 L/week/1.73 m^2 (see Guideline 15: Weekly Dose of PD). This approximates a purely filtered only creatinine clearance of 6 mL/min. Since at this level of residual renal function much of the creatinine appearing in the final urine is from tubular secretion, 60 L/wk/1.73 m^2 approximates a total residual renal creatinine clearance of 9 to 14 mL/min.

Peritoneal Dialysis and Residual Kidney Function Equivalency. Quantitative replacement of renal urea clearance by peritoneal clearance is based on the assumption that the two clearance parameters confer equal clinical benefit with respect to control of uremic morbidity. Thus, we can write the relationship

$$K_{pr}t/V_{urea} = K_pt/V_{urea} + K_rt/V_{urea}, \qquad \textbf{(21)}$$

where K_pt/V_{urea} is total daily or weekly peritoneal urea clearance normalized to V; K_rt/V_{urea} is total daily or weekly renal urea clearance normalized to V.

Solution of Equation 21 for K_pt/V_{urea} with the assumption that adequate weekly $K_{pr}t/V_{urea}$ is 2.0 results in

$$K_pt/V_{urea} = 2.0 - K_rt/V_{urea} \qquad \textbf{(22)}$$

Equation 22 provides a quantitative guideline for replacing residual renal urea clearance by peritoneal clearance such that the sum of weekly K_pt/V_{urea} and K_rt/V_{urea} remains 2.0.

The equivalence of peritoneal and residual renal clearance is controversial. Current data suggest inconsistent conclusions. There is a strong suggestion that protein metabolism in CAPD

patients is similar to that in patients with chronic kidney failure.[24] Peritoneal clearance has been shown to predict survival.[25,26] However, a large retrospective analysis suggested that peritoneal clearance was not predictive of survival, while residual renal clearance was[27] and indirect observations seem to corroborate that. Thus, the Work Group will continue to equate residual renal and peritoneal clearance. To that end, the preservation of residual renal clearance is paramount and strategies to achieve this have recently been described.[28]

Hemodialysis and Residual Kidney Function Equivalency. Compared to CAPD it is more complex to calculate incremental doses of HD such that the sum of intermittent dialyzer clearance (K_dt/V_{urea}) and continuous K_rt/V_{urea} remain constant at a level equivalent to a weekly K_rt/V_{urea} of 2.0. However, the dose and frequency of HD which provide therapy equivalent to continuous K_pt/V_{urea} can be calculated using the fundamental assumption underlying CAPD therapy: the level of continuous K_pt/V_{urea} required for treatment which is clinically equivalent to intermittent HD is that K_pt/V_{urea} which results in a steady state BUN equal to the average predialysis BUN with any specific intermittent HD treatment schedule at the same nPCR.[29-32] From this basic assumption and the urea kinetic model[19] the dose and frequency of HD required for incremental replacement of K_rt/V_{urea} as it falls below 2.0 can be readily calculated, as depicted in Fig II-3.

The dose of intermittent HD is expressed in Fig II-3 as eK_dt/V_{urea}, which is the equilibrated, delivered, and normalized hemodialysis dose (see the NKF-K/DOQI Clinical Practice Guidelines for Hemodialysis Adequacy for further discussion of eK_dt/V_{urea}). The equilibrated measure is utilized here because in peritoneal dialysis, transcellular urea equilibration is achieved, and therefore, it makes conceptual sense to think in terms of equilibrated values. From preliminary data of the HEMO study, eK_dt/V is approximately 0.21 lower than that computed from immediate post-HD BUN sampling, using single-pool, variable volume kinetic modeling.[33] The dashed line depicts incremental increase in daily K_pt/V_{urea} as K_rt/V_{urea} falls in accordance with Equation 22. Model solutions are shown for once, twice and

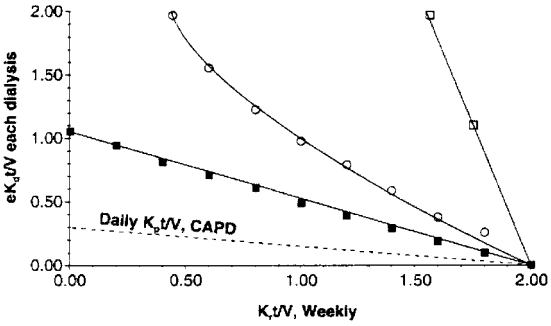

Fig II-3. Equivalent total dialysis doses for incremental replacement of $K_{pr}t/V_{urea}$. Assumptions are made that the K_r, K_p, and K_d are clinically equivalent clearance items. Another assumption for this particular model is that an equal nPCR, the CAPD steady-state BUN equals the average prehemodialysis BUN. Thus, the intermittent hemodialysis dose can be related to the continuous dialysis (CAPD) by the various curves. N = (□) 1, (○) 2, or (■) 3 refers to once, twice, or thrice weekly hemodialysis treatments, respectively. The vertical axis is the equilibrated (double pool) delivered and normalized hemodialysis dose. Equilibrated Kt/V is about 0.21 lower than single pool and is necessary to use here because the CAPD steady-state is equilibrated.

thrice weekly hemodialysis (N = 1, 2, and 3, respectively). The model solutions are limited to $eK_dt/V_{urea} \leq 2.0$ since it is unrealistic to prescribe $eK_dt/V_{urea} > 2.0$. Such a dose would correspond to single pool K_dt/V_{urea} values of 2.8 and 2.3 with treatment times (t) of 2.0 and 4.0 hours, respectively. It can be seen that when N = 1, $eK_dt/V_{urea} = 2.0$ when $K_rt/V_{urea} = 1.6$. Thus, the option for once weekly hemodialysis is limited to a weekly $K_rt/V_{urea} \geq 1.6$. If $K_rt/V_{urea} = 0.5$ and N = 2, the eK_dt/V_{urea} for each HD treatment must be 2.0 to achieve a weekly continuous Kt/V_{urea} equivalent to 2.0. Therefore, for a weekly $K_rt/V_{urea} < 0.5$, more than twice weekly HD will be necessary. Finally, in the case of N = 3, eK_dt/V_{urea} increases linearly to 1.05 as K_rt/V_{urea} falls to zero. The eK_dt/V_{urea} of 1.05 corresponds to single pool K_dt/V_{urea} values of 1.46 and 1.20 at treatment times of 2.0 and 4.0 hours, respectively.

There is emerging evidence that RRF is better preserved in patients undergoing HD with the use of more biocompatible membranes.[34]

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Appendix B

The original PD Adequacy Guideline 2 and Appendix B have been replaced by Guideline 27 of the Nutrition Guidelines. Members of both the PD Adequacy and the Nutrition Work Groups developed the updated Guideline. The Guideline is reproduced as Guideline 2 of the updated PD Adequacy Guidelines without the reference citations which are given in the Nutrition guidelines. Therefore, the reader is encouraged to read the Nutrition Guidelines to obtain the references.

Appendix C: Detailed Rationale for Guideline 6

GUIDELINE 6

Assessing Residual Kidney Function (Evidence)

Residual kidney function (RKF), which can provide a significant component of total solute and water removal, should be assessed by measuring the renal component of Kt/V_{urea} (K_rt/V_{urea}) and estimating the patient's glomerular filtration rate (GFR) by calculating the mean of urea and creatinine clearance.

Rationale The contribution of RKF to total solute and water clearance is significant (30% to 50%), especially during the first few years of dialysis therapy. Assessment of RKF is important for several reasons. A substantial fraction (30%) of the total renal replacement therapy may be provided by RKF when a patient begins PD.[1] After 2 years of PD, the RKF may still contribute about 15% of the total Kt/V_{urea}. Since the RRF contribution will be added to that of PD, it will be measured in the same units and for the same solutes.

Preservation of RKF may be of particular importance to the effectiveness of long term PD therapy. There is a progressive decline of RKF over time with both HD and PD. Several studies have compared the rate of decline of RKF with the two dialytic modalities[2-8] and demonstrated that RKF is preserved better in patients undergoing PD therapies compared to HD. In a study of 25 CAPD patients and 25 HD patients, the rate of decline of creatinine clearance was significantly slower over the first 18 months of dialysis in the CAPD patients.[2] The PD patients started dialysis with an uncorrected C_{Cr} of 4.4 mL/min, and after 18 months it was 4.0 mL/min. In the HD patients, C_{Cr} at initiation was 4.3 mL/min, and after 18 months it was 1.3 mL/min ($P < 0.01$ compared to PD).

Similar differences were observed in patients with diabetes.[8] In another study comparing the urine output and C_{Cr}, the urine output dropped significantly in HD patients at the end of 1 year compared to 3 years in CAPD patients.[3] The mean annual decline of C_{Cr} was identical in HD and CAPD for patients with primary glomerulopathy. However, in the groups with nephrosclerosis and tubulointerstitial nephritis, the rate of decline of C_{Cr} was significantly slower in CAPD compared to HD patients. In another retrospective study of 4 years duration which compared 55 CAPD patients to 57 HD patients, the rate of decline in the HD group was twice that of the CAPD group.[4] This difference persisted after adjustment for age, gender, hypertensive status, and the use of ACE inhibitors. Children have a better preservation of urinary volume, but not GFR, in those receiving PD.[7]

Despite their limitations, these studies generally demonstrate a slower rate of decline of RKF in patients on PD compared to HD. They also demonstrate that the rate of the decline varies from patient to patient. The faster rate of decline of RKF in HD is speculated to be due to repetitive hypotensive episodes, possibly complement activation and cytokine release, and the possibility that the more efficient HD may remove GFR stimulatory factors.

Several methods for measuring the C_{Cr} component of RKF are available. These include the uncorrected C_{Cr}, a flat percentage of uncorrected C_{Cr} as an estimate of GFR, or the average of creatinine and urea clearance also as an estimate of GFR.

While each method has its particular merits, the Work Group recommends using the arithmetic mean of creatinine and urea clearances to determine the RKF component to C_{Cr} and as an estimate of GFR. Therefore, the C_{Cr} component of RKF will subsequently refer to residual renal

C_{Cr}, corrected for secretion by taking the arithmetic mean of urea and creatinine clearances. This method was selected for several reasons. First, it was used in some of the major outcome studies used in establishing these guidelines (see Guideline 15: Weekly Dose of CAPD). Second, the corrected C_{Cr} correlates better with Kt/V_{urea} than the uncorrected C_{Cr}.[9] Third, it makes conceptual sense because the peritoneal transport of creatinine is by diffusion and convection, not secretion. The correction process addresses this.

The MDRD study derived two equations which may approximate GFR,[10] one utilizing demographic, serum, and urine variables:

$$\text{GFR in mL/min per } 1.73\ m^2 = 198 \times (\text{serum creatinine concentration in mg/dL})^{-0.858} \times (\text{age})^{-0.167} \times (0.822 \text{ if patient is female}) \times (1.178 \text{ if patient is black}) \times (\text{serum urea nitrogen in mg/dL})^{-0.293} \times (\text{urine urea nitrogen in g/day})^{+0.249}$$

and the other equation using demographic and serum variables only:

$$\text{GFR in mL/min per } 1.73\ m^2 = 170 \times (\text{serum creatinine concentration in mg/dL})^{-0.999} \times (\text{age})^{-0.176} \times (0.762 \text{ if patient is female}) \times (1.180 \text{ if patient is black}) \times (\text{serum urea nitrogen in mg/dL})^{-0.170} \times (\text{serum albumin concentration in g/day})^{+0.318}$$

However, the Work Group recommends using urea clearance, normalized to total body water, ie, K_rt/V_{urea}, as the key measure to follow serially to determine whether urine collections need to continue (see Guideline 11: Dialysate and Urine Collections). This is termed the renal Kt/V_{urea} or K_rt/V_{urea}. This recommendation was made to simplify the concept of a residual kidney component to the total renal replacement dose. Kt/V_{urea} is believed to be the more valuable measure of renal replacement therapy and the Work Group carried this thinking through to using K_rt/V_{urea} in both initiation of dialysis and for following RKF changes over time.

K_rt/V_{urea} as a measure of RKF is recommended because total Kt/V_{urea} is associated in a clinically important and statistically significant way with patient survival[1,11,12] (see Guideline 15: Weekly Dose of CAPD). The peritoneal clearance of creatinine is about 80% of the urea clearance, while at end-stage the kidney clearance of creatinine is about 1.5 to 2 times that of urea. Perhaps as a consequence of this physiological phenomenon or for other reasons, there is a discrepancy between total Kt/V_{urea} and total C_{Cr} normalized to 1.73 m^2 BSA (see paragraphs below). In the case of discrepancy, Kt/V_{urea} is preferentially recommended to determine PD adequacy, because it is more predictable and reproducible and is independent of the confounding effects of renal secretion of creatinine. A retrospective study of PD adequacy demonstrated an association between Kt/V_{urea} and outcomes.[13]

This emphasis on using K_rt/V_{urea} is not intended to detract from the utility of C_{Cr}. In terms of validity, total C_{Cr} normalized to 1.73 m^2 BSA is predictive of patient survival, technique survival, and hospitalization.[1] The creatinine generation rate is useful for assessment of nutritional status, in particular, in measuring fat-free, edema-free body mass. Total C_{Cr} may also be useful for assessment of compliance.

C_{Cr} as an index of PD adequacy is associated statistically with both morbidity and mortality[1] and correlates with urea clearance.[14] Discrepancies between the two clearances may be found in approximately 20% of PD subjects.[15,16] The main reasons for the discrepancies are the presence of substantial RKF, which tends to cause disproportionately high C_{Cr} values, and low peritoneal solute transport type, which tends to cause disproportionately low C_{Cr} values.[15,16] C_{Cr} values corresponding to a weekly Kt/V_{urea} of 2.0 differ between CAPD subjects with and without RKF (see Fig II-2, referenced previously in Appendix A: Detailed Rationale for Guideline 1). In patients with RKF the mean C_{Cr} corresponding to a Kt/V_{urea} of 2.0 weekly is between 60.5[14] and 67.6[15] L/wk/1.73 m^2. In anuric CAPD subjects, the mean C_{Cr} corresponding to a Kt/V_{urea} of 2.0 weekly is 52.1 L/wk/1.73 m^2.[16]

In the case of a discrepancy, the Work Group recommends the use of Kt/V_{urea} as an immediate

guide of dialysis adequacy because it directly relates to protein metabolism. However, if there is a discrepancy between C_{Cr} and Kt/V_{urea}, the patient must be observed closely because initially it may not be clear why the discrepancy exists and the reason may be important. This is discussed in Guidelines 1, 7, and 15.

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Appendix D: Detailed Rationale for Guideline 8

GUIDELINE 8

Reproducibility of Measurement (Opinion)

Accurate measurement of total Kt/V_{urea} and total creatinine clearance (C_{cr}) requires collection and analysis of urine, dialysate, and serum in a way that yields reproducible and valid results. Dialysate creatinine concentration must be corrected for the presence of glucose in some assays. Peritonitis precludes reliable measurement of delivered PD dose for up to 1 month. Compliance with complete collections is mandatory. For patients who void $\geq$3 times per day, a 24-hour urine collection is sufficient. For patients who void less frequently, a 48-hour collection is recommended. For CAPD patients, the serum sample can be obtained at any convenient time. For NIPD patients, the serum sample should be obtained at the midpoint of the daytime empty period. For CCPD patients, the serum sample should be obtained at the midpoint of the daytime dwell(s).

Rationale To be clinically useful, measurement of PD dose must be performed in a valid and reproducible fashion. The following factors influence the validity and reliability of Kt/V_{urea} and total C_{Cr} as measures of PD dose.

Dialysate glucose. Dialysate creatinine concentration should be corrected for the presence of glucose, which interferes with *some* creatinine measurement methodologies.[1] Each facility must determine this by specifically inquiring of its

laboratory whether the creatinine assay used by that lab is altered by high glucose concentrations. Each laboratory should establish its own correction factor and should reestablish the correction factor if the laboratory's methodology changes. The Work Group does not recommend using correction factors from the literature.

Peritonitis. Peritoneal solute transport increases during peritonitis and usually recovers some time after resolution of peritonitis, with a reported recovery time between 3 days[2] and 1 month.[3]

Patient compliance with the dialysis prescription. Following creatinine appearance in dialysate and urine longitudinally is an objective method to evaluate the degree of compliance (see Guideline 7: PD Dose Troubleshooting). Clinical tools for evaluating compliance are in the process of development.[4]

Variability of residual renal function (RRF). Day-to-day total clearances can vary greatly in PD. The major portion of this variance is caused by changes in measured RKF,[5] although creatinine generation may vary in apparently stable PD patients.[6]

Completeness of urine collection. To avoid sampling errors, urine should be collected over 48 hours in patients who void infrequently (<3 times in 24 hours). A 24-hour urine sample can be used for all other patients. The urine collection should be performed on the same day as the dialysate collection. In children, the urine collection period may be reduced to a minimum of 12 hours.

Dialysate and urine collection for PD adequacy studies. Two methods of dialysate sampling predominate. In the first method, for CAPD, all effluent bags in a 24-hour period are brought to the center. While this "batch" method is simple in concept, it is difficult to carry out because it means transporting all the dialysate bags, which are heavy and bulky.

The second method is referred to as the "aliquot" method. In this approach, each bag of effluent dialysate is shaken vigorously for a few seconds, then is emptied into a measuring container accurate to an error of <50 mL per 2,000 mL. The volume for that bag is recorded in mL and the decimal point is moved three places to the left. The resulting figure is the number of mL which must be drawn from the dialysate effluent in the measuring container and placed in the laboratory red top test tube, provided by the dialysis center. For example, if the effluent volume for the CAPD bag is 2,450 mL, moving the decimal point three places to the left means that 2.45 mL of this fluid is put in the test tube (or other small collection container). Each bag for the 24-hour interval is handled this way. The aliquots are measured by syringes; usually a 5-mL syringe is accurate enough. The aliquots can be mixed in the same container, because the sampling proportion from each original bag is constant at 1/1,000. The total effluent is recorded, and that figure plus the small container with all the collected aliquots are brought to the dialysis center. Some dialysate manufacturers have developed special aliquoting exchange bags that separate an aliquot as part of the exchange.[7]

The collection of effluent dialysate from automated PD is conceptually similar to that described above. The effluent drained via a cycler is quantified automatically by the cycler and generally pools in one collection container or, if in several containers, free mixing is possible. Since the effluent volume is known and the containers are allowed to mix freely, a sample of any reasonable volume (eg, 10 mL) can be brought to the dialysis unit. If several containers are used with equal filling, an equal volume aliquot from each container can be pooled. The total effluent volume must be known and recorded. If the effluent bags are not freely mixing, then a sample from each bag is required, as well as the exact volume of the container from which the sample was drawn. One cannot extrapolate from one container (bag) to the next.

No matter what method is used for dialysate, a complete and accurately timed urine collection is necessary. The urine volume is more easily managed since it is much smaller than the dialysate volume. The longer the collection interval, the more reliable are the collections, assuming patient compliance. A timed collection of 12 to 48 hours is recommended, depending on how frequently the patient voids. Polyuric patients, particularly children, or patients with a short attention span, may void frequently enough that a supervised 12-hour collection is accurate. As for any urine collection, the bladder should be emp-

tied and the urine discarded moments before the start of the collection period. Then, moments before the end of the collection period, the patient empties the bladder, and this urine, plus all that has been collected in the interval, completes the collection. The patient should try to delay the final voiding until just before the interval ends. Three or more bladder voidings generally are necessary for urine collections. For patients who make little urine and hence void infrequently, 48-hour collections may be more informative.

Serum samples. In CAPD, serum concentrations of urea and creatinine are relatively constant, and thus blood samples can be drawn at any convenient time for clearance determinations. For the asymmetric therapies (NIPD and CCPD), blood concentrations are lowest at the end of the cycling period and highest prior to the next cycling period. Theoretically, the best time to draw these blood samples is half way between the lowest and highest times. For NIPD patients, the serum sample should be obtained at the midpoint of the daytime empty period. For CCPD patients, the serum sample should be obtained at the midpoint of the daytime dwell. For most NIPD and CCPD patients, this time point conveniently occurs in the early afternoon.

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Appendix E: Detailed Rationale for Guideline 9

GUIDELINE 9

Estimating Total Body Water and Body Surface Area (Opinion)

V (total body water) should be estimated by either the Watson[1] or Hume[2] method in adults using actual body weight, and by the Mellits-Cheek method[3] in children using actual body weight.

Watson method[1]:

$$\text{For Men: } V(\text{liters}) = 2.447 + 0.3362*Wt(kg) + 0.1074*Ht(cm) - 0.09516 \cdot \text{Age (years)}$$

$$\text{For Women: } V = -2.097 + 0.2466*Wt + 0.1069 \cdot Ht$$

Hume method[2]:

$$\text{For Men: } V = -14.012934 + 0.296785*Wt + 0.192786*Ht$$

$$\text{For Women: } V = -35.270121 + 0.183809*Wt + 0.344547*Ht$$

Mellits-Cheek method for children[3]:

$$\text{For Boys: } V(\text{liters}) = -1.927 + 0.465*Wt(kg) + 0.045*Ht(cm), \text{ when Ht} \leq 132.7 \text{ cm}$$

$$V = -21.993 + 0.406*Wt + 0.209*Ht, \text{ when height is} \geq 132.7 \text{ cm}$$

$$\text{For Girls: } V = 0.076 + 0.507*Wt + 0.013*Ht, \text{ when height is} \leq 110.8 \text{ cm}$$

$$V = -10.313 + 0.252*Wt + 0.154*Ht, \text{ when height is} \geq 110.8 \text{ cm}$$

Body surface area (BSA) should be estimated by either the DuBois and DuBois method,[4] the Gehan and George method,[5] or the Haycock method[6] using actual body weight.

For all formulae, Wt is in kg and Ht is in cm:

DuBois and DuBois method: $BSA(m^2) = 0.007184 * Wt^{0.425} * Ht^{0.725}$

Gehan and George method: $BSA(m^2) = 0.0235 * Wt^{0.51456} * Ht^{0.42246}$

Haycock method: $BSA(m^2) = 0.024265 * Wt^{0.5378} * Ht^{0.3964}$

Rationale The practical methods described in the literature to estimate V include a fixed fraction of body weight (0.60 in males and 0.55 in females, or 0.58 in all subjects) and anthropometric formulae based on sex, age, height, and weight.[1-3] The fixed fraction method is inaccurate, as it overestimates total body water even in overhydrated PD subjects.[7] Therefore, the Work Group recommends that this method not be used.

Both the Watson[1] and Hume[2] formulae were derived by comparing anthropometric measurements to measurements of body water by indicator dilution techniques. An advantage of these formulae is that they were derived in populations which included obese subjects and, therefore, can account for obesity. Estimates from the Watson and Hume formulae are, in general, close to isotopic body water measurements in PD patients.[7] The error of the estimates based on these formulae can increase in subjects with abnormalities in body water (hydration), because such subjects were systematically excluded from the studies used to derive the formulae.[8] Indeed, both the Watson and Hume formulae tend to consistently underestimate isotopic body water in both lean and obese PD patients with overhydration.[7] The formulae are recommended as a reasonable approximation with systematic error, but acceptable based on ease of determination. A proposed correction of the formulae for edema requires careful assessment of the dry weight. The correction considers actual weight at the edematous state as the sum of two weights: the dry weight plus the weight gain secondary to edema. V is the body water at dry weight obtained from the Watson or Hume formulae plus, in its totality, the weight gain secondary to edema.[8] The Watson and Hume formulae provide similar estimates of V.[9] Both formulae provide unrealistic estimates of V in subjects whose height and/or weight differ greatly from the ordinary.[9] The Mellits-Cheek formulae were derived from subjects aged 1 month to 34 years for males and 1 month to 31 years for females. In each case, the measurement of total body water was performed in normal subjects by the use of deuterium oxide distribution with simultaneous measurement of weight and height.[3]

Body surface area is derived from anthropometric variables.[4-6] While the formulae were derived in normal subjects, the influence of clinical conditions on the variability of the calculations are much less than that noted for total body water calculations.

Unfortunately, the relationship between the calculations for V and BSA is not linear.[10] When BSA increases linearly as obesity develops, V increases exponentially. There are gender differences in these relationships as well. For the same height and BSA, males have a larger V than females. Future investigations should apply the same size indicator normalization factor to both solutes.

The Work Group considered the special case of the malnourished, underweight patient. Severe malnutrition is associated with low levels of RKF in patients who did not increase the dose of PD to compensate for the loss in renal function.[11] This evidence suggests that the loss in kidney function may have caused underdialysis as $K_{pr}t/V_{urea}$ decreased. Underdialysis then caused uremia with anorexia and weight loss, which, in turn, resulted in lower V and higher $K_{pr}t/V_{urea}$. Thus, while $K_{pr}t/V_{urea}$ may be in the "acceptable" range in underweight, malnourished individuals, improved nutrition and weight gain is of paramount importance in these individuals. If this aim is fulfilled, V will increase and $K_{pr}t/V_{urea}$ will decrease to the previous levels, which were inadequate. Therefore, it is recommended in such individuals to provide a dose of PD which will result in adequate $K_{pr}t/V_{urea}$ when they reach their desired weight without changing the dialysis prescription. For malnourished patients defined by SGA or Table II-3 below, provide a PD dose to achieve a weekly Kt/V_{urea} of 2.0 for the volume of the patient at desired weight. The calculation of the target $K_{pr}t/V_{urea}$ in malnourished CAPD subjects equivalent to a weekly

Table II-3. Median (50th Percentile) Body Weight (kg)

Age Range	Males			Females		
18.0-24.9						
Frame index	<38.4	38.4-41.6	>41.6	<35.2	35.2-38.6	>38.6
Median body weight (kg)	68.3	71.5	74.7	55.1	58.1	62.9
25.0-29.9						
Frame index	<38.6	38.6-41.8	>41.8	<35.7	35.7-38.7	>38.7
Median body weight (kg)	71.8	75.9	82.2	55.6	58.6	68.7
30.0-34.9						
Frame index	<38.6	38.6-42.1	>42.1	<35.7	35.7-39.0	>39.0
Median body weight (kg)	74.6	72.8	85.4	57.6	60.7	72.7
35.0-39.9						
Frame index	<39.1	39.1-42.4	>42.4	<36.2	36.2-39.8	>39.8
Median body weight (kg)	75.9	80.4	84.1	59.5	61.8	76.7
40.0-44.9						
Frame index	<39.3	39.3-42.5	>42.5	<36.7	36.7-40.2	>40.2
Median body weight (kg)	76.1	79.3	84.9	59.1	62.8	77.1
45.0-49.9						
Frame index	<39.6	39.6-43.0	>43.0	<37.2	37.2-40.7	>40.7
Median body weight (kg)	76.2	79.8	84.0	60.3	63.4	76.8
50.0-54.9						
Frame index	<39.9	39.9-43.3	>43.3	<37.2	37.2-41.6	>41.6
Median body weight (kg)	74.7	78.3	83.1	60.3	64.4	77.7
55.0-59.9						
Frame index	<40.2	40.2-43.8	>43.8	<37.8	37.8-41.9	>41.9
Median body weight (kg)	74.8	77.9	84.5	59.9	66.3	77.6
60.0-64.9						
Frame index	<40.2	40.2-43.6	>43.6	<38.2	38.2-41.8	>41.8
Median body weight (kg)	73.4	76.3	80.7	60.9	64.5	76.8
65.0-69.9						
Frame index	<40.2	40.2-43.6	>43.6	<38.2	38.2-41.8	>41.8
Median body weight (kg)	70.3	74.5	78.9	60.2	64.9	74.5
70.0-74.9						
Frame index	<40.2	40.2-43.6	>43.6	<38.2	38.2-41.8	>41.8
Median body weight (kg)	70.1	72.6	76.7	60.2	62.9	74.5

Obtained from the NHANES Data as reported by Frishanco.[19] Frame Index has no units and is calculated as follows: [Elbow Breadth (mm)/Height (cm)] × 100.

Reprinted with permission.[12]

$K_{pr}t/V_{urea}$ of 2.0 at desired weight is as follows: If V_{actual} is body water obtained from the Watson or Hume formulae using the actual weight and $V_{desired}$ is body water obtained by the same formulae using the desired weight, then for malnourished subjects $V_{actual} < V_{desired}$. The target CAPD weekly $K_{pr}t/V_{desired}$ is 2.0 (for CCPD 2.1 and NIPD 2.2). If $K_{pr}t/V_{actual} = x$, then for the CAPD patient:

$$(K_{pr}t/V_{desired})/(K_{pr}t/V_{actual}) = 2.0/x \text{ or} \quad \textbf{(1)}$$

$$2.0*V_{desired}/V_{actual} = x, \text{ and } x \text{ is the new target } Kt/V_{urea} \quad \textbf{(2)}$$

Equation 2 can be used to calculate the target $K_{pr}t/V_{urea}$ in malnourished CAPD subjects. For example, if V_{actual} is 35 L and $V_{desired}$ is 40 L, then the weekly target $K_{pr}t/V_{actual}$ is 2.0 times 40/35 or 2.29. In essence, the target of 2.0 is modified upward by a factor of $V_{desired}/V_{actual}$. The recommendation to increase the target $K_{pr}t/V_{urea}$ in malnourished PD subjects is based on indirect evidence.

The above water volume estimations are used in the Kt/V_{urea} measure. Target Kt/V_{urea} is modified (Equation 2). The same principle applies if C_{Cr} is used. The normalization of C_{Cr} by BSA should correct $weight_{actual}$ for $weight_{desired}$ in the formula used to determine BSA. This is further discussed in Guideline 15: Weekly Dose of CAPD.

The concept above is intended to deliver a

Table II-4. Fraction of Weight and BSA Corresponding to Amputated Limbs

Body Part Amputated	% Loss in Weight[14]	% of BSA to Subtract[16]
Foot	1.8	3.5
Leg below knee	6.5	10.0
Leg above knee	8.0	12.5
Leg at hip	18.5	18.0
Hand	0.8	2.5
Arm at elbow	3.1	6.0
Arm at shoulder	6.6	10.0

dose of PD considered adequate for the patient at a "desired" weight. Defining a "desired" weight can be subjective, but objective definitions are available. One preferable method is that proposed by a broad collaborative "glossary" group where the "desired" weight described in this rationale is the glossary group's "normal weight," defined as the median body weight of normal Americans with the same age, height, sex, and skeletal frame as the patient in question.[12] Table II-3 from the glossary details these weight ranges based on the input parameters of the patient in question.

Alterations Caused by Amputation. The anthropometric formulae for total body water calculate that as obesity develops and body weight increases, V also increases, but body water content (the ratio V/weight) decreases. This is consistent with the known fact that water content of fat tissue is low. Calculations of V in amputees by uncorrected anthropometric formulae (using the actual postamputation weight and height in the calculations) distorts the relationship between V and weight. In this case, body water content is not consistent with the degree of obesity.[13,14] The anthropometric formulae can be corrected in a way that restores the relationship between body water content and degree of obesity in three steps:

Step A: The fraction of body weight lost to amputation (f_w) is obtained from a nomogram[15] (see Table II-4). The fraction of weight loss (f_w) is the percent loss in weight from Table II-4 divided by 100. The hypothetical nonamputated weight at the same body composition would be equal to actual weight/$(1 - f_w)$.

Step B: V at the hypothetical nonamputated weight ($V_{non\text{-}amputated}$) is calculated from the Watson formula. Body water content is $V_{non\text{-}amputated}/Weight_{non\text{-}amputated.}$

Step C: Actual V is calculated by multiplying the actual postamputation weight by $V_{non\text{-}amputated}/Weight_{non\text{-}amputated}$. This correction makes the assumption that amputation per se will not change body water content.[14]

The calculations for body surface area (BSA) in amputees should be also corrected, because of inconsistent results obtained with the uncorrected calculation of BSA.[16] The correction requires also three steps:

Step A: Same as step A in the correction of V in amputees.

Step B: BSA at the hypothetical nonamputated weight is calculated by one of the three BSA formulae above.

Step C: The fraction of BSA corresponding to the amputated limb(s) (f_{BSA}) is obtained from Table II-4 derived from Herndon. The fraction (f_{BSA}) lost is the percent loss from Table II-4 divided by 100. Corrected BSA is $BSA_{non\text{-}amputated}$ times $(1 - f_{BSA})$.[17]

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Appendix F: Detailed Rationale for Guideline 12

GUIDELINE 12

Assessment of Nutritional Status (Opinion)

Nutritional status of adult PD patients should be assessed on an ongoing basis in association with Kt/V_{urea} and C_{Cr} measurements using the Protein equivalent of Nitrogen Appearance (PNA) and Subjective Global Assessment (SGA). For pediatric PD patients, nutritional status should be assessed using the PNA and other standard nutritional assessments (see Guideline 14 of the Clinical Practice Guidelines for Peritoneal Dialysis Adequacy and the Clinical Practice Guidelines for Nutrition in Chronic Renal Failure).

Rationale Although nutritional status depends on many nondialysis-related factors, appetite suppression, nausea, and vomiting are major clinical features of inadequate dialysis. Therefore, nutritional status is also an important measure of PD adequacy. Of the available measures of nutrition, PNA is recommended because it provides an estimate of protein catabolic rate (PCR) and other protein losses. The SGA is recommended because it is a clinical assessment of patient nutritional status and is strongly associated with patient survival. Both measures are discussed in detail below.

Protein Equivalent of Nitrogen Appearance (PNA). PNA is a useful tool for monitoring the absolute level of changes in dietary protein intake. Nitrogen intake is almost entirely (95%) in the form of protein. Therefore, total nitrogen excretion in stable humans multiplied by 6.25 (there are approximately 6.25 grams of protein per gram of nitrogen) should be a good estimate of protein intake.[1] This relationship does not hold true for: individuals in a state of catabolism where body cell mass may be contributing to nitrogen excretion; conditions of anabolism where the opposite occurs; and inconsistencies in absolute or time-averaged blood concentrations of BUN or creatinine.

In normal humans and in dialysis patients in nitrogen balance who have no direct protein losses in urine, dialysate or feces, the total daily excretion of nitrogen in urine, dialysate, feces, breath, and skin losses is in the form of low molecular weight nitrogenous metabolites (such as urea, creatinine, urate, amino acids, ammonia, and peptides).[1]

The excretion of nitrogen as low molecular weight metabolites multiplied by 6.25 approximates the amount of nitrogen in ingested protein. This calculation has been termed the protein catabolic rate (PCR).[1,2] PCR actually represents the net amount of protein catabolism exceeding protein synthesis required to generate an amount of nitrogen equal to that excreted. The nitrogen in ingested protein enters the body nitrogen pools; nitrogen excreted in urine, feces, breath, skin, and dialysate represents the metabolism of a variety of body substances in these pools, such as creatine and purine, in addition to body proteins. Thus, although PCR is a reasonable estimate of protein intake, not all excreted nitrogen comes

directly from protein. The protein catabolic equivalent of nitrogen excretion is actually a net catabolic equivalent, rather than an absolute. It relates directly to the contribution of protein catabolism to uremic toxicity.

In patients on hemodialysis, nitrogen balance studies have been performed to estimate total nitrogen output or appearance (skin losses were estimated and breath losses were ignored).[2] The relationship of urea nitrogen appearance to total nitrogen output was assumed to be fixed and a formula was developed, known as the Borah equation, to calculate the PCR directly from urea nitrogen appearance[2]:

$$\text{PCR (g/d)} = 6.49*\text{UNA} + 0.294*\text{V} \quad \textbf{(1)}$$

where UNA represents the net production or appearance of urea nitrogen in body fluids (any increase in body fluid nitrogen concentration times body water volume) and all measurable outputs in g/d; V is the volume of distribution of urea in liters. In hemodialysis patients with no direct protein losses in dialysate or urine, this PCR also represents an estimate of dietary protein intake and is the protein equivalent of total nitrogen appearance (PNA).

In dialysis patients with substantial urinary or dialytic protein losses (>0.1 g/kg), the direct protein losses must be added to the PCR to yield the true PNA as an estimate of dietary protein intake.[3,4] Thus, in PD:

$$\text{PNA} = \text{PCR} + \text{protein losses} \quad \textbf{(2)}$$

Nitrogen balance studies have also been performed in PD patients; the measured total nitrogen output (appearance) included estimates of skin and fecal nitrogen losses plus measurement of all nitrogen (including protein nitrogen) in dialysate and urine.[4,5] The average daily dialysate protein loss in the CAPD patients was 7.3 grams. Urine protein losses were <1 g/24 hours. A formula for the calculation of PNA from UNA was developed:

$$\text{PNA (g/d)} = 10.76*(0.69*\text{UNA} + 1.46) \quad \textbf{(3)}$$

This calculation incorporates the average dialysate protein loss of 7.3 g/d.

Calculations of PNA in PD patients with Equations 2 and 3 have been shown to yield nearly identical results.[3-5] Also, subtracting protein losses in dialysate from Equation 3 yields values nearly identical to the PCR calculated by Equation 1, as developed in HD patients.[4]

If daily peritoneal dialysate protein losses exceed 15 grams, PNA calculated from Equation 2 will exceed PNA calculated from Equation 3 by approximately 0.1 g/kg standard body weight.[5] High transporters lose more protein into effluent dialysate than other PD patients.[7,8] Therefore, in high transport patients it is best to measure protein losses in dialysate directly, and if dialysate protein losses exceed 15 g/d (found in <10% of peritonitis-free patients), calculate PNA from Equation 2.[5] For patients who lose large amounts of protein from any nonperitoneal source (eg, nephrotic syndrome), Equation 2 should be used.

Equations 2 and 3 have been validated with nitrogen balance studies only in CAPD and not in other therapies such as NIPD.[3-5] However, since CAPD and HD patients have similar PCR values (PNA − protein losses) at any given UNA, the intermittent nature of NIPD would seem unlikely to alter the relationships. Furthermore, the daily protein losses on NIPD are similar to those of CAPD.[9] As more patients and different operating variables were studied, the accuracy of formulae to predict the nPNA matured. The Bergstrom method is to obtain the nPNA surrogate for dietary protein intake by:

$$\text{PNA (g/24 hours)} = 15.1 + (6.95 \times \text{urea nitrogen appearance in g/24h}) + \text{dialystate and urine protein in g/24 hours}$$[6]

In the absence of direct measurement of urinary and dialystate protein losses, this less accurate formula may be used:

$$\text{PNA (g/24 hours)} = 20.1 + (7.50 \times \text{urea nitrogen appearance in g/24 hr})$$

When protein losses are high, this second formula should not be used. Both formulae will require normalization to body mass in kg. These Bergstrom formulae were preferred in a small study from Italy.[10]

In summary, the most accurate determination of PNA in patients undergoing PD uses Equation 2, but this requires measurement of UNA and dialysate protein losses. Equation 3 is a suitable substitute and requires only measurement of

UNA. However, if dialysate protein exceeds 15 g/d (many high transporters may fall into this category) and in all pediatric patients, Equation 2 is preferred.

Methods of normalizing PNA are still under debate. The Work Group recommends normalization by standard weight, which has been applied extensively. Standard weight is equal to V/0.58.[11] PNA normalized by either standard weight or actual weight tends to be high in malnourished, underweight PD subjects.[12] Normalization of PNA to fat-free, edema-free body mass provides appropriately low nPNA values in underweight individuals.[13] The Work Group recommends that fat-free, edema-free body mass, estimated from creatinine kinetics (see Section II: Measures of PD Dose) should be used, in addition to standard weight, to normalize PNA in underweight PD subjects, defined by Table II-3 in Appendix E. Normalizing is important for patient-to-patient comparisons and to follow PNA measurements serially in an individual patient whose weight may change. If weight is stable, normalization is less important in serial measurements for an individual patient. See Guideline 14 for PNA discussion on pediatric patients.

Subjective Global Assessment (SGA). The SGA is a valid estimate of nutritional status for patients treated with PD.[13] Furthermore, it is associated with the probability of patient survival.[14] The SGA was developed as a clinical estimate of pre-operative nutritional status.[15] For two physicians, the interobserver agreement was 72% greater than would have been predicted by chance alone. Validity was based on correlations with three measures of postoperative hospital morbidity (incidence of infection, use of antibiotics and length of stay).[15] A detailed description of the SGA was provided by Detsky in 1987.[16]

The SGA was originally developed as a clinical assessment of preoperative nutritional status for patients prior to gastrointestinal surgery.[15,16] When applied to CAPD patients,[13] validity testing reduced the number of items to four (weight loss, anorexia, loss of subcutaneous tissue, and muscle mass). To increase the ability of the SGA to detect a change in nutritional status, the scoring scale was increased from a 3-point to a 7-point scale. During the development phase, the SGA was determined by physicians, research nurses, and nurse clinicians[16] but was determined by dialysis nurses and dietitians when used in the CANUSA study.[14]

The SGA, as modified for use in CAPD patients,[13] uses a 7-point scale[14] which any healthcare professional can apply following a short training period.

The four items used to assess nutritional status in CAPD patients are: weight change, anorexia, subcutaneous tissue, and muscle mass.

Weight change is addressed by the question, "What was the patient's weight change over the past 6 months?" Ideally, this should be documented by the actual weights, but historical information from the patient is acceptable. A loss of $>$10% is severe and 5% to 10% is moderate, while 5% is mild. This is rated subjectively on a scale from 1 to 7, where 1 or 2 is severe malnutrition, 3 to 5 is moderate to mild malnutrition, and 6 or 7 is mild malnutrition to normal nutritional status. If the weight change was intentional, the weight loss would be given less subjective weight while edema might obscure greater weight loss.

Anorexia is addressed by the question, "Has the patient's dietary intake changed?"

Supplemental questions determine whether a decrease in dietary intake is by prescription or due to decreased appetite. Nausea and vomiting are adverse factors for this item. Again, the interviewer will rate intake on the 7-point scale with higher scores indicative of better dietary intake, better appetite, and the absence of nausea and vomiting.

Subcutaneous tissue (fat and muscle wasting) can be examined in many areas. A very detailed and illustrated brochure is available from Baxter Healthcare (publication #BRU-008-312-2000). Although the history-taking format is more detailed than required, the description of how to determine muscle wasting and subcutaneous tissue is excellent.

Subcutaneous fat can be assessed by examining the fat pads directly below the eyes and by gently pinching the skin above the triceps and biceps. The fat pads should appear as a slight bulge in a normally nourished person but are "hollow" in a malnourished person. When the skin above the triceps and biceps is gently pinched, the thickness of the fold between the examiner's fingers is indicative of the nutritional

status. The examiner then scores the observations on a 7-point scale.

Muscle mass and wasting can be assessed by examining the temporalis muscle, the prominence of the clavicles, the contour of the shoulders (rounded indicates well-nourished; squared indicates malnutrition), visibility of the scapula, the visibility of the ribs, and interosseous muscle mass between the thumb and forefinger, and the quadriceps muscle mass. These are scored on a 7-point scale.

The four item scores are then aggregated into a global score. The global score is not a simple arithmetic average of the four items. The examiner can apply different weights to the items. For example, if the physical examination items clearly indicate severe malnutrition, but the patient indicates only a moderate decrease in weight and a good appetite, the examiner might weight the physical examination items higher than the historical items.

In 23 CAPD patients four items were statistically associated with the SGA: weight loss, anorexia, loss of subcutaneous tissue, and loss of muscle mass (muscle wasting).[13] Evidence for validity was provided by the correlations with serum albumin concentration, bioelectrical impedance, anthropometric measurements and normalized protein catabolic rate.

Using the SGA as originally described,[16] 59% of prevalent CAPD patients were well-nourished.[17] Mild and severe malnutrition was reported in 33% and 8% of the patients, respectively. In 263 hemodialysis patients and 224 CAPD patients[18] the SGA covaried with low visceral (ie, serum) protein concentrations, midarm muscle circumference (somatic protein mass), and body fat stores.

In the CANUSA study of peritoneal dialysis,[14] weight loss, anorexia, loss of subcutaneous tissue, and loss of muscle mass (muscle wasting), as identified above as being statistically associated with the SGA,[13] were used to generate the SGA for the CANUSA study. To make the scale more discriminative, the 3-point scale was expanded to a 7-point scale, with 1 and 2 corresponding to severe malnutrition, 3 to 5 corresponding to mild to moderate malnutrition, and 6 to 7 corresponding to mild malnutrition to normal nutritional status. In a multivariate analysis, a higher SGA was associated with a lower relative risk of death. A one unit increase on the 7-point scale was associated with a 25% decline in the relative risk of death (relative risk, 0.75). During the first 6 months of dialysis, the mean SGA increased 0.72 units. There was a statistically significant correlation between the increment in adequacy due to the addition of peritoneal clearance (Kt/V_{urea} and C_{Cr}) to RRF. Over the next 12 months, there was a small decrease in SGA and this correlated with loss of RRF estimated by C_{Cr}, but not with Kt/V_{urea}.[19]

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Appendix G: Detailed Rationale for Guideline 15

GUIDELINE 15

Weekly Dose of CAPD (Evidence)

For CAPD, the delivered PD dose should be a total Kt/V_{urea} of at least 2.0 per week and a total creatinine clearance (C_{Cr}) of at least 60 L/wk/1.73 m^2 for high and high-average transporters, and 50 L/wk/1.73 m^2 in low and low-average transporters.

Rationale The evidence supporting this guideline is derived from theoretical constructs and cohort studies which use either univariate or multivariate statistical analyses.

The original description of CAPD[1] suggested that an anephric 70 kg patient with a total body water of 42 L would remain in nitrogen balance with a daily dialysis prescription of 10 L given as five 2-L exchanges. Full equilibration of urea between plasma and dialysate and 2 L/day of net ultrafiltration were assumed. This would produce a daily urea clearance of 12 L or a weekly urea clearance of 84 L. For a patient with a total body water of 42 L, this corresponds to a weekly Kt/V_{urea} of 2.0. Others, using the concept of the Dialysis Index, suggested that a similar patient would require 13.5 L daily of equilibrated drained dialysate to maintain nitrogen balance, and this would produce a weekly Kt/V_{urea} of 2.25.[2] The difference between these two projections is due to the higher target protein intake used in the latter calculation. Using the peak urea concentration hypothesis, a weekly Kt/V_{urea} of 2.0 is equivalent to a single pool hemodialysis Kt/V_{urea} of 1.3 for patients receiving thrice weekly dialysis.[3] These theoretical constructs suggest that a weekly Kt/V_{urea} of 2.0 to 2.25 would be appropriate.

Validation of these theoretical constructs requires clinical study. A series of cohort studies addressed this issue.[4-8] Initially no relationship was found between urea clearance and patient survival,[6] but a reanalysis, using an anthropometric[9] estimate for total body water, found that patients with a weekly Kt/V_{urea} <1.5 had an increased risk of death compared to patients with a weekly Kt/V_{urea} ≥ 1.5. In another study[10] a mean weekly Kt/V_{urea} >1.89 was associated with a decreased risk of death compared to patients with less dialysis, while yet another[4] reported that patients surviving for a 12-month follow-up had a mean weekly Kt/V_{urea} of 2.0 compared to a mean of 1.7 among those who did not survive for 12 months. A Belgian group reported that 16 patients surviving 5 years on CAPD had a mean weekly Kt/V_{urea} of 2.0.[5] These studies all used univariate analysis and therefore did not simultaneously evaluate the association between other important variables (eg, age, diabetes, cardiovascular disease) and patient survival.

Several studies have used multivariate statistical analysis to evaluate the association between adequacy of PD and survival while controlling for other variables.[7,8,11,12] In one such study a lower serum albumin concentration, increased age, greater time on dialysis, and lower weekly Kt/V_{urea} were associated with a decreased probability of patient survival.[11] A French group

reported that patients with a weekly Kt/V_{urea} >1.7 and a weekly C_{Cr} of >50 L/1.73 m^2 at initiation of dialysis had better survival than those with lower values at initiation.[7] However, these investigators did not evaluate the effect of changes in adequacy over time due to loss of RKF, nor did they attempt to evaluate any association of higher weekly Kt/V_{urea} or C_{Cr} with survival. An Italian group evaluated the association between estimates of adequacy and patient survival in a cohort of 68 prevalent continuous PD patients followed over 3 years.[8] A mean weekly Kt/V_{urea} of 1.96 was associated with better survival than lower values. No further benefit was observed with a Kt/V_{urea} higher than 1.96. Among these patients, a weekly Kt/V_{urea} of 1.96 corresponded to a weekly C_{Cr} of 58 L/1.73 m^2.

The Canada-USA (CANUSA) study evaluated the association between adequacy of PD and patient survival, technique survival, and hospitalization among 680 incident patients (new to starting PD) treated with continuous PD.[12] A decrease of 0.1 in weekly Kt/V_{urea} was associated with a 5% increase in the relative risk of death, and a decrease of 5 L/1.73 m^2/wk in C_{Cr} was associated with a 7% increase in the risk of death. The risk of technique failure increased with decreased creatinine clearance, but was not associated with Kt/V_{urea}. Hospitalization increased with decreased C_{Cr}. Using data derived from the multivariate analysis, the predicted 2-year survival associated with a constant weekly Kt/V_{urea} of 2.1 was 78%. The corresponding weekly C_{Cr} was 70 L/1.73 m^2.

Thus, there is both a theoretical rationale and convincing evidence supporting an association between greater clearance of urea and creatinine and better patient survival. There is also evidence supporting an association between greater C_{Cr} to longer technique survival and less hospitalization. In summary, theoretical constructs[1-3] suggest that the minimum weekly Kt/V_{urea} should be 2.0. Cohort studies using univariate statistical analysis support this "target."[4-8,11,12] The CANUSA study predicts, among North American patients, a 78% 2-year survival with a weekly Kt/V_{urea} of 2.1.[12]

There are no theoretical data to support a specific C_{Cr} target. The C_{Cr} which corresponds to a weekly Kt/V_{urea} of 2.1 in the CANUSA study was 70 L/1.73 m^2/wk. The Italian group found that a weekly Kt/V_{urea} of 1.96 corresponded to a weekly C_{Cr} of 58 L. The CANUSA study involved incident patients with significant RKF, while the Italian study evaluated prevalent patients with much less RKF.[8] The target of 60 L/1.73 m^2/wk was selected by the Work Group because it is more relevant to patients with diminished renal function.

Even after controlling for delivered dose, low and low-average transporters have better patient and technique survival outcomes than do high and high-average transporters.[13] In the absence of adequate residual renal function, low and low-average transporters may not be able to achieve a C_{Cr} of 60 L/wk/1.73 m^2 on any reasonable dialysis prescription. However, because urea clearance is less affected than creatinine clearance by transport status, low and low-average transporters can achieve a weekly Kt/V of 2.0. Therefore, it seems reasonable to lower the C_{Cr} target in low and low-average transporters without jeopardizing the outcomes. These patients must be observed closely for evidence of inadequate dialysis.

There are few data to address the issue of adequate compared to optimal dialysis. The latter is defined in part as the dialysis dose above which the incremental clinical benefit is not justified by the social cost to the patient or the financial cost to society. Whether or not increased weekly Kt/V_{urea} greater than 2.0 will be associated with improved clinical outcomes requires further study.

The relative importance of RKF compared to peritoneal clearance and the relative importance of urea compared to C_{Cr} are important and interrelated issues. The convention has been to consider RKF and peritoneal clearance to be equivalent and therefore additive. Some believe that renal clearance is more important, but in the absence of data establishing the magnitude of that difference, the assumption of equivalence was adopted by the Work Group. C_{Cr} appeared more important than urea clearance in the CANUSA study.[12] The former was associated with patient survival, technique survival, and hospitalization, while the latter was associated only with patient survival. One potential explanation for

this finding is that C_{Cr} is more strongly associated with better RKF than was Kt/V_{urea}. This explanation is based on the assumption that RKF is better than peritoneal clearance, an opinion not yet supported by evidence.

The equivalence of peritoneal and residual kidney clearance is controversial. Current data suggest inconsistent conclusions. There is a strong suggestion that protein metabolism is similar in patients with progressive chronic kidney disease.[14] Peritoneal clearance has been shown to predict survival.[15,16] However, a large retrospective analysis suggested that peritoneal clearance was not predictive of survival, while residual kidney clearance was.[17] Thus, the Work Group has adopted the position that until more definitive data are available to direct us, the simplest solution is to continue to equate residual kidney and peritoneal clearance. To that end, the preservation of kidney clearance is paramount and strategies to achieve this have recently been described.[18]

Until evidence to the contrary is available, the Work Group recommends that kidney and peritoneal clearances be considered equivalent. If there is discordance between achieving the target Kt/V_{urea} and C_{Cr}, the Kt/V_{urea} should be the immediate determinant of adequacy since it reflects protein catabolism. However, the reason for the discrepancy should be sought and the patient monitored closely for clinical signs of underdialysis.

A special case is the underweight patient, defined in Table II-3, Appendix E. Successful efforts to restore weight to a normal level in such a patient will result in a rising V, and consequently in a proportionally declining $K_{pr}t/V_{urea}$. To provide a weekly $K_{pr}t/V_{urea}$ of 2.0 at the final increased weight, the weekly target $K_{pr}t/V_{urea}$ provided during the malnourished state must be greater than 2.0. The Work Group recommends that the target $K_{pr}t/V_{urea}$ should be raised in a malnourished CAPD patient to the level that would provide a weekly $K_{pr}t/V_{urea}$ of 2.0 for that patient if he or she was at normal weight. That level is calculated by multiplying the target of 2.0 for CAPD times the ratio of $V_{desired}/V_{actual}$. This is described in detail in Appendix E: Detailed Rationale for Guideline 9, and discussed in Guideline 17: PD Dose in Subpopulations. The same upward target adjustment would be made in C_{Cr}. The target C_{Cr} should be increased by a factor of $BSA_{desired}/BSA_{actual}$.

Clinical judgment suggests that the target doses of PD for children should meet or exceed the adult standards. However, there are currently no definitive outcome data in pediatrics to suggest that any measure of dialysis adequacy is predictive of well-being, morbidity, or mortality. There are limited data regarding the real protein needs of children, especially young children, on dialysis. It is the opinion of the Work Group that the nutritional requirements per kilogram of body weight are higher in children than in adults. Therefore, PD doses in children, and especially small infants who have very high protein intakes, may have to be higher than PD doses in adults.

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Appendix H: Detailed Rationale for Guideline 19

GUIDELINE 19

Identify and Correct Patient-Related Failure to Achieve Prescribed PD Dose (Opinion)

Potential patient-related causes of failure to achieve prescribed peritoneal dialysis dose should be investigated and corrected. These include:

- Failure to comply with the prescription.
- Lack of understanding of the importance of adherence to the full prescription.
- Sampling and collection errors.

Rationale It is the opinion of the Work Group that to increase the likelihood of achieving a prescribed dose of PD, it is necessary to elucidate the patient-related causes of failure to achieve a prescribed dose. Selection of inappropriate candidates for PD may result in failure to achieve a prescribed dose due to medical, technical, and/or psycho-social reasons. The issue of medically appropriate patient selection is dealt with at length in Section VIII: Suitable Patients for PD. In addition to the medical reasons for selecting patients for PD or HD discussed in Section VIII, patient compliance is of paramount importance and should be explored.

Failure to Comply With the Prescription. Patients may decrease the delivered dose of PD in several ways. Some of the ways are listed below:

- Skipping exchanges.
- Shortened exchange times.
- Dialysate dumping: too much flushing resulting in too little fill.[1]
- Delayed dumping: This is achieved by partially draining before the dwell is completed.
- Reduction of total cycler time.
- Unscheduled dry days on CCPD.

A validated method to measure patient compliance is not currently available. Methods proposed for evaluating compliance include monitoring for variations in creatinine output in dialysate and urine[2] as detailed in Guideline 7: PD Dose Troubleshooting. Evidence for this recommendation is currently not available. The recommendation represents, therefore, the opinion of the Work Group members.

In the absence of a validated method to measure patient compliance, its prevalence in the PD population is not known. Preliminary data from the USRDS DMMS Wave II project show that 487 CAPD patients self-report full compliance with 82.8% of their exchanges.[3] One exchange/week is missed by 11.5% of patients and 2 to 3 exchanges/week are missed by 4.5% of patients, all self-reported. Other estimates vary between 5% and 38%.[4] Thus, noncompliance is a major cause of a delivered PD dose being less than the desired dose and is potentially preventable.

Lack of Understanding of the Importance of Adherence to the Full Prescription. Medical literature about conditions associated with noncompliance in PD is inadequate. The Work Group reviewed published information on compliance in hemodialysis[5-8] and in drug treatment for chronic illness.[9-11] The Work Group believes that some of the conclusions in this literature may be applicable to PD. An important conclusion of the

studies on drug compliance is that lack of education regarding the importance of adherence to the full prescription partially contributes to compliance failure. Compliance with the drug prescription improves when the patient is convinced that the diagnosis is accurate, the reasons for the prescribed treatment are correct, and the prescribed treatment is beneficial.[11] Some contend that patients on dialysis are more likely to follow the prescribed treatment if they can be convinced that adherence to the prescription is in their own interest.[8] By not understanding the significance, importance, value, or relevance of the collections or the exchanges, noncompliance could occur without patient concern. Therefore, proper education about the treatment may increase compliance in many PD patients. Patients should be educated that dialysis prescription may change over time (different modality and/or increase in the number or volume of exchanges) due to loss of residual renal function (see Guideline 6: Assessing Residual Renal Function). The method of education should emphasize the expected positive results (improved survival, well-being) of adherence to the PD prescription, rather than the negative outcomes (morbidity, mortality) of nonadherence, to prevent the development of excessive anxiety, which has adverse effects on compliance.

Patient education should be continuous throughout the course of PD. Patients should be told the results of the repeated clearance measurements and should be aware of the target values for $K_{pr}t/V$ and C_{Cr} and of the clinical significance of these clearances. Prevention of noncompliance should include monitoring the patient's psychological status. In studies on compliance to drugs, certain psychiatric conditions, such as hostility toward authority, depression and memory impairment, financial problems, impaired mobility, and language or ethnic barriers, have been associated with poor compliance.[11] In addition, complexity of the prescription[9] and chronicity of the treatment[11] increased noncompliance. In the case of prolonged treatment, repetition of the teaching at 6-month intervals improved compliance.[11] In studies on compliance in HD, male gender[12] and young age[13] were predictors of poor compliance with different aspects of HD prescription. Preliminary information suggests that a general negative attitude of the patients predicts noncompliance in PD.[14] Finally, drug compliance improves with better education of the providers about compliance issues.[10] The Work Group thinks that all of these issues are relevant to PD. The psychological profile which is predictive of noncompliance and the best method of characterizing this profile should be a subject for research in the future. For the present, the Work Group's opinion is that monitoring of patients' psychological status should be aimed at detecting conditions associated with increased risk of noncompliance, and particularly at detecting a negative patient attitude towards PD. Teaching patients about their PD prescription should be repeated at intervals of 6 months or less.

Sampling and Collection Errors. Sampling and collection errors committed by patients during the clearance study preclude accurate measurement of clearance. Such errors include:

- Batch method: the patient may not recognize the importance of accidentally spilled dialysate.
- Aliquot method: Inaccurate weighing of drain volumes which may be the result of inaccurate scales or misreading. Disproportionate filling of the syringe with dialysate.
- Errors in weighing bags for variable fill volumes: for example, when (due to cost issues) 3-L bags are being used and only 2.5 L are exchanged.
- Incomplete urine collections for the RRF determination.

Many of these errors can be prevented by careful patient instruction about the details and significance of the clearance procedure.

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XI. Biographical Sketches of the NKF-K/DOQI Peritoneal Dialysis Adequacy Work Group Members

The following are brief sketches that describe the professional training and experience, as well as principal business affiliations of the Work Group members. All Work Group members completed a disclosure statement certifying that any potential conflict of interest would not influence their judgment or actions concerning the NKF-K/DOQI.

Thomas A. Golper, MD, FACP (*Work Group Chair*), is Medical Director of the Medical Specialties Patient Care Center at Vanderbilt University Medical Center in Nashville, TN. He still practices nephrology and continues to serve as the Senior Medical Officer of Renal Disease Management, Inc, a disease management company headquartered in Youngstown, Ohio. Dr. Golper has been working to improve patient outcomes for the past 23 years. He serves as a CQI advisor to industry and has participated in guideline development for the management of peritonitis since 1986. Dr. Golper has published 136 articles and currently directs research on topics such as peritoneal fluid-drug interactions, peritonitis in PD, and atherosclerotic/thrombotic risk factors in ESRD. Active in many professional societies, he previously served on the Board of Directors for the Renal Physicians Association and currently serves on the Board of Directors and Executive Committee of the American Association of Kidney Patients. Dr. Golper also serves on the Advisory Board of K/DOQI and on several RPA Committees.

David Churchill, MDCM, FRCPC, FRCP (Edin) *(Work Group Vice-Chair)*, is Professor of Medicine at McMaster University in Hamilton, Ontario, Canada. His funded clinical research activities have included urolithiasis research, polycystic kidney disease, quality of life in ESRD, economic analysis, erythropoietin in ESRD, and adequacy of peritoneal dialysis. He is co-principal investigator of the Canada-USA study (CANUSA) on the adequacy of peritoneal dialysis. He has over 100 peer-reviewed publications. Dr. Churchill has served on the scientific review panels for the NIH, Kidney Foundation of Canada, and the Ontario Ministry of Health, as well as on advisory committees for erythropoietin and dialysis services in Ontario. He has a cross-appointment in the Department of Clinical Epidemiology and Biostatistics, with a focus on evidence-based medicine.

Peter Blake, MB, FRCPC, FRCPI, is Director of Peritoneal Dialysis at the London Health Sciences Centre, London, Ontario, Canada and Associate Professor of Medicine at the University of Western Ontario. Dr. Blake is also Chair of the Canadian Society of Nephrology Workgroup of Peritoneal Dialysis and also Course Director of the US National Kidney Foundation course on Peritoneal Dialysis. His clinical research focuses on the areas of adequacy and nutrition in peritoneal dialysis and also in the management of chronic kidney failure in the predialysis phase. He has written or co-authored more than 50 publications in the area of dialysis. He is on the editorial board of the *Journal of the American Society of Nephrology*, *Peritoneal Dialysis International*, and *Advances in Renal Replacement Therapy*. He is also co-editor of the Third Edition of handbook of Dialysis.

John Burkart, MD, is Associate Professor of Internal Medicine/Nephrology and Director of Outpatient Dialysis Services (CAPD and HD) for the Section of Nephrology at Wake Forest University/Bowman Gray School of Medicine in Winston-Salem, North Carolina. Dr. Burkart has been an active clinical nephrologist for 11 years and manages a large nephrology and dialysis practice. He currently cares for 70 end-stage renal disease patients and participates in a group practice serving more than 250 dialysis patients. He serves as a consultant to industry and has actively participated in clinical trials and educational workshops. Dr. Burkart has written or co-authored more than 90 publications, and is currently involved in research related to adequacy of peritoneal dialysis, improving outcomes on peritoneal dialysis, and alternative osmotic agents for peritoneal fluid. He is a co-investigator in the Hemodialysis Study and serves on the editorial boards of *Peritoneal Dialysis International* and *Advancement of Renal Replacement Therapy*. Dr Burkart reported an affiliation with Baxter Healthcare.

Dinesh K. Chatoth, MBBS, is Assistant Professor of Medicine at the University of Arkansas

for Medical Sciences and Medical Director of Dialysis Services for the John L. McClellan Veterans Affairs Medical Center in Little Rock, Arkansas. Dr. Chatoth received the JD Chastain Research Award in 1998 from the National Kidney Foundation of Arkansas. His main research interests are related to cardiovascular disease in peritoneal dialysis, pre-ESRD education and incremental dialysis, and sustained low efficiency dialysis in acute renal failure.

Catherine Firanek, RN, CNN, MBA, is Global Senior Clinical Marketing Manager for Baxter Healthcare Corporation's Renal Division which develops, manufactures and markets hemodialysis and peritoneal dialysis products and services. She currently focuses on establishing clinical educational programs and marketing activities related to dialysis therapy development around the world. For the past 18 years, Ms. Firanek has been involved with peritoneal dialysis program establishment, patient care, research and educational development at Rush-Presbyterian St. Luke's Medical Center/Circle Medical Management in Chicago, IL. Both locally and nationally, Ms. Firanek has been actively involved with the National Kidney Foundation serving in several positions related to nursing educational development, board of directors and now as co-editor of the joint council quarterly publication and CNNT council member at a national level. She was a member of the DOQI PD Adequacy workgroup established in 1993. She has served in advisory and research roles related to industry and has published numerous articles in areas of peritoneal dialysis including urban population experience, peritonitis incidence and adequacy.

Denis Geary, MB, MRCP(UK), FRCPC, is Associate Professor, Department of Pediatrics, at the University of Toronto, and Chief of Nephrology at the Hospital for Sick Children in Toronto, Canada. Dr. Geary's clinical training took place in the United States, United Kingdom, and Ireland. He has practiced as a staff physician in pediatric nephrology for 15 years. Dr. Geary's publications involve the subjects of dialysis, and the growth and development of children with chronic kidney disease.

Frank Gotch, MD, is a consultant to the Renal Research Institute in New York and is Associate Professor of Medicine at UCSF. Dr. Gotch has worked in clinical dialysis and dialysis research , particularly quantification of therapy, for 30 years. He chaired the NIH Hemodialyzer evaluation Study Group which sets standards for dialyzer performance in 1972 and the National NIH conference on Adequacy of Hemodialysis in 1975. He served on the planning committee and as kinetic consultant to the National Cooperative Dialysis Study and serves on the Steering Committee of the current HEMO study and was Co-Principal Investigator of a Cooperative study of Randomized Peritoneal Dialysis Prescriptions and Clinical Outcome. He has over 100 publications and provides consultation in dialysis kinetics and dialysis systems development to industry. His current research interests are primarily concerned with modeling dialysis technology.

Alan S. Kliger, MD, FACP, is Clinical Professor of Medicine at Yale University School of Medicine and Director of the New Haven CAPD. He currently chairs the ESRD Network of New England, the Quality Improvement Committee of the Forum of ESRD Networks, and the Quality Patient Care Committee of the Renal Physicians Association. Dr. Kliger also serves on the National Kidney Foundation's K/DOQI Support Group.

Stephen M. Korbet, MD, is Professor of Medicine at Rush Medical College and Associate Director of the Section of Nephrology at Rush-Presbyterian-St. Luke's Medical Center in Chicago Illinois. He also serves as Medical Director of Circle Medical Management Dialysis Facility. Dr. Korbet is currently a member of the International Society of Peritoneal Dialysis Committee on Education and Standards and Baxter's International Ad Hoc Committee on Ultrafiltration Management in Peritoneal Dialysis. Active in research, Dr. Korbet's interests include nephrotic syndrome, focal segmental glomerulosclerosis, and peritoneal dialysis. He has served on the editorial board of the *American Journal of Kidney Disease*, and currently serves on the editorial boards of the *Journal of Nephrology*, and *Peritoneal Dialysis International*.

Antonios Tzamaloukas, MD, FACP, is Chief of the Renal Section of the New Mexico VA Health Care Center and Professor of Medicine at the University of New Mexico School of Medicine. Dr. Tzamaloukas has been on the faculty of

the University of New Mexico for 25 years. He has had a major interest in peritoneal dialysis for the past 15 years. He has more than 230 scientific publications and is a member of the editorial board of the International Journal of Artificial Organs, Peritoneal Dialysis International, Kidney International, and American Journal of Kidney Diseases. He is active in several professional societies. His main research interest is in adequacy and nutrition of dialysis patients.

Bradley Warady, MD, is Chief of Nephrology and Director of Dialysis and Transplantation at The Children's Mercy Hospital, and Professor of Pediatrics at the University of Missouri – Kansas City School of Medicine. Dr. Warady's clinical and research focus is end-stage renal disease, with particular emphasis on peritoneal dialysis. He established the Pediatric Peritoneal Dialysis Study Consortium and currently co-directs research projects on a number of topics including: growth hormone usage in pediatric dialysis patients; peritoneal dialysis adequacy in children; and intravenous iron therapy in pediatric patients receiving hemodialysis. He co-edited the book "CAPD/CCPD in Children" and has published more than 150 articles. Dr. Warady currently serves on the executive committees of the American Society of Pediatric Nephrology and the Nephrology section of the American Academy of Pediatrics. Dr. Warady also sits on the Editorial Board for the *Advances of Renal Replacement Therapy.*