

**I. NKF-K/DOQI CLINICAL PRACTICE GUIDELINES FOR
HEMODIALYSIS ADEQUACY:
UPDATE 2000**

NOTE: The citation for these guidelines should read as follows: National Kidney Foundation. K/DOQI Clinical Practice Guidelines for Hemodialysis Adequacy, 2000. Am J Kidney Dis 37:S7-S64, 2001 (suppl 1)

Acronyms and Abbreviations

Abbreviation	Term
AAMI	Association for the Advancement of Medical Instrumentation
BUN	blood urea nitrogen
CKD	chronic kidney disease
EDW	estimated dry weight
ESRD	end-stage renal disease
GFR	glomerular filtration rate
HCFA	Health Care Financing Administration
HD	hemodialysis
HEMO	HEMOdialysis Study
NCDS	National Cooperative Dialysis Study
NPCR	normalized protein catabolic rate
PRU	percent reduction of urea
QALE	quality-adjusted life expectancy
RPA	Renal Physicians Association
TCV	total cell volume
TMP	transmembrane pressure
UFR	ultrafiltration rate
UKM	urea kinetic modeling
URR	urea reduction ratio
USRDS	United States Renal Data System

Introduction

APPROXIMATELY 284,000 Americans suffered from end-stage renal disease (ESRD) in 1996,¹ of whom 62% were treated by maintenance hemodialysis (HD).² Despite a longer life expectancy for the general population of the United States in comparison to that of most other industrialized nations, several analyses have reported that the gross and adjusted annual mortality of Americans with ESRD greatly exceeds the analogous rates observed in other countries.³⁻⁸ Several explanations have been proposed for these differences in ESRD patient outcome, including:

1. The acceptance of patients for maintenance dialysis in the United States who are relatively older and/or have more comorbidity than dialysis patients in other countries.^{9,10}
2. Genetic differences between the prevalent patient populations in the United States and abroad that confer differing risks for comorbid conditions such as cardiovascular disease.¹¹
3. The prevalent practice in the United States of dialyzer reuse (81% of dialysis centers in 1996) that may expose hemodialysis patients to toxic chemicals, increased risk of infection, and/or less effective dialysis due to compromised dialyzer function.¹²⁻¹⁷
4. The lower tendency in the United States to adequately meet the nutritional needs of hemodialysis patients.¹⁸⁻²¹
5. The incomplete and/or inaccurate reporting of relevant patient comorbidity and outcomes by non-US ESRD registries.^{7,22-25}
6. The lower tendency to deliver an adequate dose of hemodialysis to patients in the United States.^{14,18,19,26-32}

Regardless of the precise reasons for the apparent difference in outcome between Americans with ESRD and patients from other industrialized nations, it is indisputable that the delivered dose of hemodialysis is a significant predictor of patient outcome^{19,33-42} and that the dose of hemodialysis provided to many American patients can and should be increased.^{19,27,29-31,43} This assertion is based on several premises, including:

1. The dose of hemodialysis can be measured precisely, reproducibly, and routinely in the clinical setting.^{19,34,42-50}

2. A scientific consensus exists on what constitutes an adequate dose of hemodialysis.^{51,52}
3. Many patients do not receive that dose of hemodialysis.^{19,31,43,53-57}
4. Reasons for deficiencies in the delivered dose of dialysis can be identified and redressed.^{35,51,53-55,58-61}

The Renal Physicians Association's (RPA) 1993 *Clinical Practice Guideline on Adequacy of Hemodialysis** describes acceptable methods for measuring hemodialysis adequacy and defines a minimum acceptable delivered dose of hemodialysis for adults (>18 years old) with ESRD who have negligible residual kidney function and are receiving outpatient hemodialysis three times per week. Specifically, the RPA recommended that the variable volume, single-pool model of urea kinetic modeling (Kt/V_d) should be measured monthly to assure the adequacy of hemodialysis (HD), such that patients receive the full benefit of HD for ESRD. The recommended Kt/V_d should be at least 1.2 (urea reduction ratio $\geq 65\%$). When the Kt/V_d falls below this level, corrective action should be undertaken.⁵¹

The NKF-K/DOQI HD Adequacy Work Group identified several topics pertinent to implementing and maintaining adequate hemodialysis that had received limited attention in the RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis*. As a result, the NKF-K/DOQI Work Group summarized data and developed recommendations that supplement the RPA guideline in the following areas:

1. Optimum hemodialysis dose.
2. Adequacy of hemodialysis for pediatric patients.
3. Blood sampling to measure the hemodialysis dose.
4. Reuse of hemodialyzers.
5. Patient comfort and adherence.

* To obtain a copy of the RPA guideline, see ordering information in Appendix A.

Optimum Hemodialysis Dose

The RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis* described a minimum delivered dose of hemodialysis for adults with no residual kidney function who were receiving hemodialysis three times per week. In this respect, the RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis* did not describe a dose of hemodialysis that maximizes the survival, health, and quality of life of ESRD patients. In the absence of financial constraints, a dose of dialysis that maximizes patient outcomes is the optimal dose of hemodialysis and is a more appropriate target for prescribed dialysis therapy than a minimum adequate dialysis dose. The HD Adequacy Work Group examined peer-reviewed literature published since the release of the RPA guideline in an attempt to define an optimal delivered dose of hemodialysis. Because of changes in the demographics of the ESRD population, eg, an aging ESRD population, an increasing prevalence of patients with diabetes mellitus,¹ the HD Adequacy Work Group considered what constitutes a minimum adequate dose for different subpopulations. Selected patient subsets (blacks and diabetics) were examined to determine if the minimum hemodialysis dose for them should differ from that for the rest of the dialysis population.

Because of inappropriate timing of acquisition of the postdialysis blood urea nitrogen (BUN) sample in many patients, some of the apparent improvement in hemodialysis adequacy that has been reported may be spurious.⁶²⁻⁶⁴ Therefore, significant opportunities for improvement still exist. The HD Adequacy Work Group developed an algorithm that details recommended procedures for identifying and correcting deficiencies in the delivered dose of dialysis. The intent of the algorithm is to help dialysis care teams:

1. recognize deficiencies in the delivered dose of hemodialysis.
2. identify the cause(s) of inadequate delivered dose of hemodialysis.
3. correct the cause(s) of inadequate delivered dose of hemodialysis.

Adequacy of Hemodialysis for Pediatric Patients

Pediatric patients comprise less than 1% of the total hemodialysis patient population, even in

industrialized countries with established pediatric ESRD treatment capabilities. In the United States, the point prevalence of ESRD patients less than 20 years of age was 4,777 per million in 1994-1996. Eighteen percent of ESRD patients less than 20 years old received maintenance hemodialysis.^{1,65} There are two predominant reasons for the small number of pediatric as compared with adult patients. First, ESRD is not a common pediatric disorder. Its incidence in pediatric patients is just over 15 new patients per million per year. In contrast, incidence rates are 122/million/yr for people 20 to 44 years of age.^{1,65} Second, most children spend a relatively short time on dialysis, typically only the time awaiting kidney transplantation. As a result, even the largest pediatric hemodialysis programs are quite small by adult program standards and rarely exceed 10 to 15 patients per facility.

There are few reports in the medical literature of studies involving pediatric hemodialysis patients and no data on outcomes as a function of hemodialysis dose in children. Previous efforts to develop guidelines for hemodialysis, including the RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis*, did not address pediatric patients. The HD Adequacy Work Group recognized the paucity of data on adequacy of hemodialysis in pediatric patients, and decided that it was desirable and possible to extend the guideline development process to children. All available pediatric hemodialysis literature was reviewed; where pediatric data were lacking, the Work Group extrapolated from adult patient data. Thus, the NKF-K/DOQI *Clinical Practice Guidelines for Hemodialysis Adequacy* addresses children as well as adults.

Blood Sampling Procedure

Considerable variability in sampling procedures exists in dialysis practice in the United States. For example, 33% of the hemodialysis units represented by members of the Medical Review Board of the ESRD Network of New England (ESRD Network 1) reported that the samples for testing postdialysis BUN were drawn immediately before the hemodialysis treatment was terminated, 25% obtained samples immediately after the end of the dialysis treatment, and 42% drew the sample 5 minutes after all blood was reinfused into the patient.⁶² Similar proce-

dural inconsistency has been observed in ESRD Network 16. Data for all hemodialysis patients in Network 16 suggest that postdialysis BUN samples were drawn immediately upon the completion of dialysis at 21% of the dialysis facilities, after an interval of 1 to 2 minutes at 52% of the facilities, 2 to 10 minutes after the completion of dialysis at 15% of the facilities, and more than 10 minutes after completion of dialysis at 13% of facilities.⁴³ During 1993, the United States Renal Data System (USRDS) reported that, in the dialysis facilities surveyed, the postdialysis BUN sample was drawn immediately at the end of hemodialysis without changes in the blood flow at 15% of facilities, immediately upon ending hemodialysis with a slowing or stopping of the blood pump at 48% of facilities, 20 to 60 seconds after the end of dialysis at 9% of facilities, 1 to 2 minutes after the end of dialysis at 12% of facilities, 3 to 15 minutes after the end of dialysis at 15% of facilities, and more than 15 minutes after the completion of dialysis at 1% of facilities.⁶⁶ Because of inappropriate timing of the acquisition of postdialysis blood samples, the actual delivered dose of hemodialysis may be overestimated.^{47,58,67,68} A 1995 survey of 195 dialysis units in the United States found that 5% and 42% of the centers used predialysis and postdialysis blood drawing procedures, respectively, that were judged to be erroneous.⁶⁴ Erroneous blood drawing techniques and needless procedural variability compromise the ability to compare the dose of hemodialysis delivered by different dialysis units, even when the same formulae for calculating Kt/V are used. More precise specification of appropriate procedural technique will increase the accuracy and comparability of measured hemodialysis doses. To address this problem, the HD Adequacy Work Group developed supplemental procedural guidelines for predialysis and postdialysis BUN sampling.

Reuse of Dialyzers

Predominantly for economic reasons, reuse of hemodialyzers is a prevalent practice in the United States.^{16,17,69-71} In 1993, approximately 79% of adult hemodialysis patients used reprocessed dialyzers. Data describing the prevalence of dialyzer reuse among pediatric hemodialysis patients are not available. Because the essential

function of a hemodialyzer is to permit the mass transfer of solutes from the patient's blood into the dialysate and vice versa, the solute transport capacity or clearance of a hemodialyzer is a critical variable in writing and delivering an adequate hemodialysis prescription. Reuse of a hemodialyzer can change its solute transport capacity.^{72,73} For this reason, clinicians need an accurate assessment of the solute clearance of the hemodialyzer. In the absence of direct measures of change in solute clearance with reuse, change in the total cell volume (TCV), also described as the fiber bundle volume, has been the conventional surrogate used to monitor changes in solute transport characteristics for hollow fiber dialyzers.^{74,75} Several factors prompted the HD Adequacy Work Group to evaluate the use of TCV as a measure of clearance, including:

- The TCV is an indirect measure of solute clearance.
- Reprocessing techniques have evolved.

The HD Adequacy Work Group examined the peer-reviewed literature and the *Association for the Advancement of Medical Instrumentation Standards and Recommended Practices for Reuse of Hemodialyzers*.⁷⁶

Patient Comfort and Adherence

The HD Adequacy Work Group recognizes that a major barrier to providing adequate hemodialysis is patient nonadherence with the hemodialysis prescription. Patients may confound the health care teams' attempts to provide an otherwise adequate treatment by missing hemodialysis sessions, arriving late for treatments, temporarily interrupting the treatment, or discontinuing the hemodialysis session prematurely.^{32,53,77,78} The RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis* focused on the processes of patient care necessary to provide an adequate dose of hemodialysis, but did not offer clinical strategies and interventions to enhance patient acceptance of the hemodialysis prescription. The HD Adequacy Work Group examined the peer-reviewed literature to identify strategies that minimize patient discomfort during and immediately after hemodialysis treatments. Complications, such as hypotension and cramps, that would compromise patient acceptance of hemodialysis, were a major focus.

In 1997, the NKF-DOQI HD Adequacy Work Group published the initial version of their evidence-based clinical practice guideline for hemodialysis adequacy.⁵² In brief, the guidelines recommended:

1. Preferential use of a single pool, variable volume model for calculating urea distribution and removal during hemodialysis at least once per month;
2. Quantification of urea removal during a single dialysis session using formal urea kinetic modeling for adults and children;
3. Prescription of a Kt/V of ≥ 1.3 , so that the minimum delivered Kt/V would be ≥ 1.2 ;
4. Routine baseline measurement of a hemodialyzer's TCV prior to the first use and prior to each subsequent use;
5. Discarding of a hemodialyzer if its TCV is less than 80% of the original value; and
6. Vigorous effort to ensure patient comfort during hemodialysis by using strategies to minimize cramps and hypotension.

In the years since the RPA and NKF-DOQI recommended how the delivered dose of hemodialysis should be measured and clarified the minimum acceptable dose of hemodialysis, a significant improvement in reported dialysis dose has been reported in the United States.²⁹⁻³¹ In 1993, a population-based cohort study of 13,500 adult ESRD patients noted that only 36% of the patients received a urea reduction ratio (URR) of $\geq 65\%$.¹⁹ *U.S. News and World Reports* described this state of care as "deadly dialysis."⁷⁹ These findings were confirmed and extended by the ESRD Core Indicators Project, a nationwide quality improvement project, and conducted by the Health Care Financing Administration (HCFA) using the ESRD Networks. A random national sample of adult, ESRD patients from October to December 1993 showed that only 43% of the patients had a URR $\geq 65\%$; the mean URR was 62.7%.³¹ The greatest deficiency in URR was observed for blacks, who had a 60% greater likelihood of receiving an inadequate dialysis dose compared with whites.⁸⁰ From 1993 to 1997, the mean URR increased from 62.7% to 68.0%.³¹ Improvement of a similar magnitude was observed in another national data set; the median URR increased from $58.9\% \pm 9.8\%$ to $69.5\% \pm 8.75\%$ from 1990 to 1997, respec-

tively.²⁹ The percentage of patients receiving a benchmark URR $\geq 65\%$ increased from 43% in 1993 to 72% in 1997. The most dramatic improvement in dialysis dose was achieved by blacks, for whom a 92% increase in the number receiving a URR $\geq 65\%$ was achieved.^{31,80} In contrast, there was a 59% increase in the number of whites receiving a URR $\geq 65\%$. As a result, the racial disparity in dialysis dose has narrowed. The odds ratio of achieving an inadequate dialysis dose for blacks compared with whites has declined from 1.6 in 1993 to 1.2 in 1997. Several data sets have demonstrated that the dose of dialysis varies inversely by weight, total body water, body surface area, and body mass index.^{55,57,81} In that all these anthropometric parameters are greater on average in blacks with ESRD than whites, and fixed dialysis doses are prescribed, it may not be inappropriate that the average dialysis dose is lower in blacks than in whites. Patient and/or nephrologist behaviors also seem to be contributing factors.⁵⁵ Thus, the increment in dialysis dose for blacks is all the more significant, since it occurred in the setting of unfavorable anthropometric attributes and treatment compliance for improvement. Blacks with ESRD have greater urea distribution volumes than whites and are more likely to terminate hemodialysis prematurely. If dialysis care teams are offered advice regarding "best" clinical practices, as provided by the RPA and NKF-DOQI's clinical practice guidelines, quality of care can be improved. Translation of some of the NKF-DOQI clinical practice guidelines into national clinical performance measures (CPM) may be helpful.⁸² The national HD adequacy CPM initiative will provide some insights into the potential impact of NKF-DOQI guidelines on hemodialysis adequacy.

Despite these improvements in patient care, many opportunities for significant improvement remain. Firstly, more than 20% of the ESRD patients in the 1996 Core Indicators Project received a Kt/V less than 1.2.³¹ Secondly, procedural problems persist with the sampling method used for obtaining the predialysis and postdialysis blood samples to measure the BUN concentration. Using spline techniques to determine the dialysis dose at which optimal mortality benefit is conferred, a recent analysis suggests that inap-

appropriate timing/technique for acquisition of the postdialysis BUN samples is so prevalent that the potential mortality benefit associated with the apparent increase in dialysis dose may be minimal.⁶³

Because many ESRD patients still do not receive an adequate dose of hemodialysis, and the literature supporting the NKF-DOQI HD Adequacy Guidelines has expanded, the HD Adequacy Work Group has reevaluated the topics addressed in the previous clinical practice guidelines. The NKF-K/DOQI HD Adequacy Work Group focused its efforts on a review of the existing *Clinical Practice Guideline on Hemodialysis Adequacy* and a discussion of operational and clinical issues that may affect the practical acceptance and/or implementation of the RPA and DOQI hemodialysis adequacy guidelines. Three specific Work Group objectives were defined:

1. Review the NKF-DOQI *Clinical Practice Guideline on Adequacy of Hemodialysis*. Based upon this review, develop updates and supplements as needed.
2. Identify barriers to the acceptance and implementation of the NKF-DOQI guidelines for hemodialysis adequacy.
3. Develop strategies for enhancing the implementation of the NKF-DOQI clinical practice guidelines for hemodialysis adequacy.

TOPICS NOT COVERED BY THESE GUIDELINES

Flux of Large Molecular Weight Solutes

The HD Adequacy Work Group recognizes that the clearance of a marker solute, such as urea,^{45,83} is only one of the many parameters that define or are relevant to the global concept of hemodialysis adequacy. Another parameter is membrane flux of larger molecular weight solutes. For example, the use of hemodialysis membranes that have relatively higher clearances for larger molecular weight solutes, such as vitamin B₁₂ and β_2 -microglobulin (molecular weight of 1,355 and 12,500 daltons, respectively), may reduce the likelihood of developing dialysis-associated amyloidosis,⁸⁴⁻⁸⁹ decrease the severity of lipid abnormalities in ESRD patients,⁹⁰ and improve survival.^{87-89,91} However, because of the clinical impact of persistent deficiencies in the

delivered dose of hemodialysis based on urea clearance, a limited literature on the association between patient outcomes and membrane flux, and limited time and resources, the HD Adequacy Work Group focused on the clearance of the more conventional marker solute—urea. The Work Group did not address membrane flux. The ongoing National Institutes of Health *HEMO Study*, a prospective, randomized intervention trial, will evaluate the effect of membrane flux on morbidity and mortality in hemodialysis patients.^{49,92}

Membrane Biocompatibility

Independent of the delivered dose of hemodialysis as measured by urea clearance, hemodialyzers composed of selected membrane materials may interact with the effector limb of adaptive immunity.^{93,94} Described as membrane biocompatibility, interactions between soluble and cellular components of the blood and selected dialysis membrane materials result in perturbations in the complement cascade⁹⁵⁻⁹⁹ and granulocyte number and function.¹⁰⁰⁻¹⁰² As a consequence of these membrane-associated immunologic abnormalities, ESRD patients may be at increased risk of malnutrition, infection, hospitalization, and death.^{93,94,103-107} Because of the extensive scope of this topic, resource limitations, and the focus of the Work Group on small molecular weight solute clearance, membrane biocompatibility was excluded from the literature review.

Appropriate Timing for Initiation of Hemodialysis

Delaying the initiation of dialysis until frank uremia develops is clearly deleterious to the patient's physical and psychological well-being.¹⁰⁸ For patients with less severe degrees of advanced kidney failure (glomerular filtration rate [GFR], 10 to 20 mL/min), the benefit of relatively early dialysis is less clear, however. The HD Adequacy Work Group recognizes that patients who are initiated on hemodialysis relatively early will have greater residual kidney function that will enhance small and large solute clearance over that provided by dialysis alone. However, the Work Group did not undertake a full literature review in an attempt to define an optimal time or clinical setting for the initiation of maintenance hemodialysis because:

1. The preponderance of outcome studies of the impact of hemodialysis dose has excluded patients with residual kidney function or assumed that none was present.
2. Few outcome analyses have been reported that examine the relationship between residual kidney function and mortality/morbidity on maintenance hemodialysis.
3. Residual kidney function declines with increasing vintage on hemodialysis, making it an unstable influence on the delivered dose of dialysis.
4. The Work Group elected to focus resources on the fundamental issue of the impact of small molecular solute clearance on patient outcomes once hemodialysis is initiated.

For dialysis care teams who seek direction on appropriate timing for initiation of dialysis, the NKF-K/DOQI *Clinical Practice Guidelines for Peritoneal Dialysis Adequacy* provide guidance.¹⁰⁹

Hemodialysis Dose and Nutrition

Another topic not reviewed by the HD Adequacy Work Group is the relationship between hemodialysis dose and nutrition. Some investigators have suggested that the dose of hemodialysis and/or the composition of the hemodialyzer membrane affect a patient's dietary protein intake, as measured by the normalized protein catabolic rate.^{110,111} This and other issues related to nutrition in kidney disease patients are addressed in the NKF-K/DOQI Nutrition Guidelines.¹¹²

Quality of Life and Rehabilitation

Although the HD Adequacy Work Group recognizes the importance of the patients' perception of their quality of life as an outcome measurement,^{113,114} this topic was not reviewed. The connection between rehabilitation and adequacy of hemodialysis is likewise important. Adequacy of dialysis is crucial for success in any of these areas. However, the Work Group elected to focus resources on the fundamental issue of the impact of small molecular weight solute clearance on the principal patient outcome of mortality.

PATIENTS TO WHOM THE NKF-K/DOQI HEMODIALYSIS ADEQUACY CLINICAL PRACTICE GUIDELINES APPLY

These guidelines apply to all adult and pediatric hemodialysis patients with ESRD and negligible kidney function (GFR <5 mL/min) who receive outpatient hemodialysis three times per week. These guidelines are not applicable to patients who undergo hemodialysis less than or greater than three times per week, hospitalized patients receiving hemodialysis, patients with a residual GFR $\geq$ 5 mL/min, or patients with a reasonable presumption of recovery of kidney function. The guidelines also may not be applicable to hemodialysis patients outside of the United States and the American Trust Territories (Puerto Rico, Guam, American Samoa, and Saipan) because of substantial international differences in patient mix, processes of patient care, and reimbursement mechanisms for the care of ESRD patients.

EVIDENCE-BASED VERSUS OPINION-BASED CLINICAL PRACTICE GUIDELINES

These guidelines are based on evidence in the published literature and, where evidence is not available, on consensus opinion of the HD Adequacy Work Group based on the available literature. For each guideline, there is a notation of whether the guideline is based on evidence or opinion. It is the intent of the HD Adequacy Work Group that the material provided herein be used solely as recommendations for patient care and not as standards. However, it is the duty of the dialysis patient care team to consider implementing these recommendations on an individual patient basis and, where they are not or cannot be applied, to strive to optimize patient care by offering reasonable and safe alternative processes of care. Furthermore, the Work Group acknowledges its awareness of the financial ramifications of these guideline statements for the providers of hemodialysis care. Successful implementation of the *Clinical Practice Guidelines for Hemodialysis Adequacy* will also depend on payers providing adequate reimbursement for high quality patient care, including the appropriate use of laboratory-based performance measures and requisite dialysis supplies and equipment.

I. Measurement of Hemodialysis Adequacy

GUIDELINE 1

Regular Measurement of the Delivered Dose of Hemodialysis (Evidence)

The dialysis care team should routinely measure and monitor the delivered dose of hemodialysis.

Rationale Numerous outcome studies have demonstrated a correlation between the delivered dose of hemodialysis and patient mortality and morbidity.^{19,33,34,36,38-42,57} The evidence demonstrates that mortality among ESRD patients is lower when sufficient hemodialysis treatments are provided. Because there is poor correlation between the dialysis care team's clinical assessment of hemodialysis adequacy and patients' clinical outcomes, unnecessary risk is placed on the patient unless rigorous methods of evaluation are used. Clinical signs and symptoms alone are not reliable indicators of hemodialysis adequacy.^{115,116} To ensure that ESRD patients treated with chronic hemodialysis receive a sufficient amount of dialysis, the delivered dose should be measured and monitored routinely. Guideline 6: Frequency of Measurement of Hemodialysis Adequacy offers guidance to the dialysis care team about the appropriate frequency for measuring and monitoring the dose of hemodialysis for adult and pediatric patients.

GUIDELINE 2

Method of Measurement of Delivered Dose of Hemodialysis (Evidence)

The delivered dose of hemodialysis in adult and pediatric patients should be measured using formal urea kinetic modeling, employing the single-pool, variable volume model.

Rationale

The HD Adequacy Work Group considered several issues regarding the definition of acceptable and preferred measures of the delivered dose of hemodialysis. These included:

1. The comparative accuracy of alternative methods;
2. The completeness of information provided by alternative methods (eg, does the method support calculation of normalized protein catabolic rate [NPCR], which provides an estimate of the dietary protein intake in

steady-state; will the method account for the impact of residual kidney function on the delivered dose of hemodialysis and NPCR);

3. The availability of dialysis unit staff to properly collect blood samples and record information from the dialysis session, such as the type of dialyzer used, intradialytic weight loss, blood and dialysate flows, true dialysis time, etc; and
4. The time to record, enter, and process this information.

Urea is the substance that is most often monitored in clinical practice as a surrogate for measurement of the clearance of small solutes in general. Reasons for this are that urea is a small, readily dialyzed solute that is the bulk catabolite of dietary protein,^{47,83} constitutes 90% of waste nitrogen accumulated in body water between hemodialysis treatments,^{47,83} is easily measured in blood, and that the fractional clearance of urea in body water correlates with patient outcomes, such as mortality^{19,33,35,36,38,39,42,48,57} and morbidity.^{34,36,39} Conventional methods of quantifying the prescribed or delivered hemodialysis dose begin by estimating the difference in predialysis and postdialysis urea concentration by sampling a patient's blood before and after a single dialysis session.

The dialysate collection method is an alternative approach for quantifying the delivered hemodialysis dose. In this approach, the total dialysate that passes through the dialyzer during a hemodialysis treatment is collected. The total mass of urea removed is then calculated as the product of the urea concentration and the volume of spent dialysate. This method has been considered by some investigators to be the gold standard for urea kinetic analysis.^{45,117-119} Advocates of this method emphasize the advantage of minimizing exposure of patients and staff to blood-borne pathogens. However, the HD Adequacy Work Group recognized that dialysate measurement techniques are not routinely available, are impractical to implement in most hemodialysis units, have not been examined in relation to patient outcomes, and may be associated with the exaggeration of systematic collection errors.^{58,120-123} For example, a 7% error in dialysate collection

can result in a 20% error in the equilibrated Kt/V. Although, the HD Adequacy Work Group also recognizes that dialysate side urea kinetics are best characterized as an equilibrated model, the Work Group thought it was best to focus on single-pool models of urea removal. Therefore, the Work Group focused on blood-based measurements of urea removal.

To normalize for differences in the size and habitus of patients, a dose of hemodialysis (prescribed or delivered) is best described as the fractional clearance of urea as a function of its distribution volume (Kt/V). The fractional clearance is operationally defined as the product of dialyzer clearance (expressed as K and measured in liters per minute [L/min]) and the treatment time (expressed as t and measured in minutes); the volume of distribution of urea is expressed as V and measured in L. Kt/V may be determined by formal urea kinetic modeling (UKM) or by extrapolation from the fractional change in blood urea concentration during a dialysis session. The delivered dose of hemodialysis may also be assessed using the URR.

Based on a review of the literature published prior to and since the release of the RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis*, the Work Group agreed with the RPA's conclusion that formal UKM, based on either two or three BUN samples, was the best method for routine measurement of the dose of hemodialysis for adult and pediatric patients. Of the single-pool, variable volume mathematical analyses for quantitation of urea removal during a single hemodialysis session, formal UKM was considered to be the most accurate and complete. However, it is the least simple to implement.

Recent literature suggests that only one alternative method for calculating Kt/V (Kt/V natural logarithm formula) and one other measurement of the delivered dose of hemodialysis (URR) should be considered for routine use in adults. Respectively, these are:

(1) Kt/V natural logarithm formula⁴⁴

$$\text{Kt/V} = -\text{Ln}(R - 0.008 \times t) + (4 - 3.5 \times R) \times \text{UF/W} \quad (1)$$

in which Ln is the natural logarithm; R is the postdialysis BUN ÷ predialysis BUN; t is the dialysis session length in hours; UF is the ultrafil-

tration volume in liters; and W is the patient's postdialysis weight in kilograms; and

(2) URR¹⁹

$$\text{URR} = 100 \times (1 - C_t/C_0) \quad (2)$$

in which C_t is the postdialysis BUN and C_0 is the predialysis BUN.

Formal urea kinetic modeling. Formal kinetic modeling provides a quantitative method for developing a treatment prescription for a specific patient. Because of the complexity of the formulae that provide the information for calculation of Kt/V by UKM, computational software is necessary to compute Kt/V using formal UKM. Formal UKM can be used to calculate the exact treatment time required to deliver a particular hemodialysis dose at specified blood and dialysate flows with a particular dialyzer. Formal UKM requires accurate measures of:

1. Predialysis and postdialysis BUN for the first dialysis treatment of the week and the predialysis BUN for the second dialysis session of the week in a thrice weekly hemodialysis schedule.
2. Predialysis and postdialysis weights at the time of the first hemodialysis treatment of the week.
3. The actual treatment time, ie, the exact number of minutes during which the hemodialysis treatment was delivered on the first dialysis treatment of the week (not the prescribed length of treatment time or the time elapsed between putting the patient on the machine and taking him or her off).
4. The effective clearance of the dialyzer as measured in the hemodialysis unit (not the in vitro clearance value reported by the manufacturer alone).

Two-sample hemodialysis UKM based on the predialysis and postdialysis midweek BUN has been described and validated for accuracy in comparison to classical three-sample UKM.^{120,124}

Advantages of urea kinetic modeling. When rigorously performed, formal UKM is a reproducible, quantitative method that has several advantages for assessing the adequacy of hemodialysis.^{36,48,124}

Formal UKM can be used to develop an individualized hemodialysis treatment prescription. Hence, using UKM, the dose of dialysis (Kt/V)

can be based on patient-specific parameters, such as residual kidney function and NPCR.^{48,83,126} To develop a hemodialysis prescription, it is necessary to obtain a dialyzer's urea clearance (K) for a variety of blood and dialysate flows in blood/water. In order to provide this information to the dialysis care team, formal UKM uses the dialyzers urea clearance (K) that is provided by the manufacturer (typically derived in aqueous solution in vitro). The computational software for formal UKM then extrapolates a KoA value for that dialyzer that can be applied with a range of blood and dialysate flows. It is important that the urea clearance be calculated in order for the blood/water clearance to more accurately reflect the volume from which urea is removed and into which urea is generated reflected by the NPCR.

Formal UKM calculates the volume of distribution of urea by a complicated mathematical iteration of two formulae that share common terms (see Appendix B). The first formula solves for the end dialysis volume, V_t . The other formula calculates the urea generation rate (G) between consecutive hemodialysis sessions. The computational software repeats these formulae until unique values for V_t and G are found that satisfy both equations. Urea distribution volume can also be derived anthropometrically (see Appendix C). Both the anthropometrically derived urea distribution volume (for normal body composition is approximately $0.58 \times$ body weight) and the kinetic extrapolated volume of distribution for urea are related to the patient's height, weight, gender, and age (age is a variable in the Watson and Chertow formulae only).¹²⁷⁻¹²⁹ This value becomes the initial V for the Kt calculation (clearance $\times$ time).

Once these two parameters are fixed, the treatment time can be calculated easily as follows:

$$\begin{aligned} & [(\text{Desired Kt/V}) (\text{Urea Volume, L}) / (\text{K, L/min})] \\ & = \text{Treatment time, min} \end{aligned}$$

$$\text{Example: } [(1.4)(35/.250)] = 196 \text{ minutes}$$

Various treatment time and blood flow combinations may be calculated by formal UKM and considered by the hemodialysis care team to achieve a desired Kt/V. Thus, the use of formal urea kinetic modeling provides the hemodialysis care team with guidance about which specific

parameters of the prescription to modify to achieve the target hemodialysis dose. Changes in the dialysis treatment time, choice of dialyzers, or operating conditions such as blood and dialysate flows can be calculated to meet the selected prescription goal. The impact of residual kidney function on urea clearance can also be considered (see Appendix D). The latter information is also important for rigorous calculation of NPCR.

Potential prescribing errors. The Work Group noted that prescribing a Kt/V using an assumed volume of urea distribution, or one derived from anthropometric calculations only, has limitations that may compromise patient outcomes by diminishing the accuracy of the Kt/V. Estimates of the volume of distribution of urea (V) that are based on surface area nomograms, or calculations, may underestimate V in very muscular individuals. The erroneous V will lead to a proportional error in the calculated required Kt, which in turn may lead to prescription of a dose of hemodialysis that is too low for these patients.

Errors in prescribing the dose of hemodialysis may also occur using an assumed dialyzer clearance. The use of inaccurate hemodialyzer urea clearance values (K), based on incorrect assumptions from the manufacturers about KoA,¹³⁰ or unappreciated, deleterious effects of hemodialyzer reuse¹³¹ may lead to significant errors in the hemodialysis prescription. The assumed K may overestimate the true clearance of a given device due to lot-to-lot variability (see Guideline 11: Baseline Measurement of Total Cell Volume). Actual dialyzer clearance may be affected by inadequate monitoring of hemodialyzer reuse procedures (see Guideline 13: Minimum Required Total Cell Volume). The failure of the dialysis care team to independently calculate the delivery of the prescribed dose of hemodialysis may permit this deficiency to go unrecognized. The incorporation of an independent method for error checks in formal UKM allows for improved monitoring of the dialysis dose.

Finally, although the HD adequacy guidelines are based on the assumption that no significant residual kidney function exists, the HD Adequacy Work Group agreed with the RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis* statement that the patient's residual kidney function should be accounted for in the hemodi-

alysis prescription. A minority of patients with ESRD have significant residual kidney function (K_r) that, when unaccounted for, may result in an underestimation in the actual total delivered dose of hemodialysis and an underestimation of NPCR (see Appendix D). These effects are a consequence of unaccounted urea removal by endogenous kidney clearance, especially between hemodialysis sessions. Although it has been suggested that the contribution of residual kidney function to Kt/V can be computed by simply calculating the weekly kidney urea clearance and dividing by three, these assumptions are incorrect. Likewise, K_r cannot be simply added to K_t , as this will greatly underestimate the effect of K_r . The single-pool, variable volume model of urea kinetics requires that the combined effects of K_t and K_r be analyzed with both continuous (endogenous) clearance and intermittent clearance (hemodialyzer-dependent) occurring over the treatment cycle. This complicated mathematical task is best performed by the computational software that is necessary for formal UKM (see Appendix D).

Formal UKM provides a mechanism to check for errors in the delivered dose of hemodialysis.

Formal UKM requires measurement of the BUN concentrations pre-hemodialysis and post-hemodialysis, the delivered treatment time, and urea clearance for those blood and dialysate flow rates. Most formal UKM computer programs assume all input data are correct; they calculate the unique volume of distribution for urea in the patient that fits those data. By comparison, the value of V derived from the patient's anthropometric features is only an estimate of urea distribution volume based on body composition analysis.^{127,128} A discrepancy between the kinetically derived V and the V expected from anthropometric calculations is an indicator of potential technical problems with the hemodialysis session. For example, if the kinetically derived V is larger than the anthropometric V , it may indicate under-delivery of the hemodialysis prescription secondary to problems such as:

1. Blood flow from the angioaccess was low.
2. The performance of the dialyzer was inadequate.
3. Dialysate flows during the hemodialysis treatment were less than prescribed.

4. The dialysis machine was programmed incorrectly.
5. The hemodialysis treatment ended prematurely.
6. The predialysis BUN sample was drawn after initiation of hemodialysis.

In the case where the kinetically derived V is larger than the anthropometrically derived V , the delivered dose of hemodialysis will be less than prescribed dose. Possible causes of an error in the kinetically derived volume of distribution of urea can be surmised from the variables that are used in its computation. Less frequently, the kinetically derived V is smaller than the anthropometrically derived V , so that the delivered dose of hemodialysis is greater than the prescribed dose. Some situations in which the postdialysis BUN concentration is incorrectly low and the kinetically derived V is too small include:

1. The postdialysis BUN sample was drawn from the venous blood line.
2. The postdialysis BUN sample was drawn in the setting of significant fistula recirculation.
3. The postdialysis BUN sample was drawn following a very efficient hemodialysis in a patient with a small V (high K/V), resulting in urea disequilibrium in the body water compartment.
4. The postdialysis BUN sample was inadvertently diluted with saline.

Based on the erroneous assumption that the resultant large Kt/V is correct, the dialysis care team may inappropriately advise a reduction in some component of the hemodialysis prescription, such as the duration of the treatment or the blood flow. Furthermore, because such errors are extended to the calculation of the PCR, the NPCR will also be inaccurate. Inappropriate dietary counseling to decrease the dietary protein/caloric intake may result.

Therefore, the Work Group agrees with the RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis* that despite its computational complexity, calculation of the kinetically derived volume is useful. Because errors are unavoidable in assessing the hemodialyzer clearance, treatment time, or BUN concentrations, mathematically fixing the K_t and calculating the effective

volume of distribution for urea allows for the evaluation of the additive effects of all these potential sources of error.

A discrepancy in the volume of distribution of urea should alert the dialysis care team to an unanticipated error in the delivered hemodialysis dose. Formal UKM provides an accurate mechanism to check for errors in the delivered dose of hemodialysis, and it provides the greatest support for continuous quality improvement (CQI) efforts in the delivery of hemodialysis. Optimal quality improvement efforts require that the processes of care affecting patient outcome be routinely measured, individual deficiencies be easily defined, and corrective actions be simply implemented. The rigor of formal UKM supports the prescription of an appropriate dose of hemodialysis and allows errors in the delivered dose of dialysis to be easily recognized. Furthermore, formal UKM facilitates the identification of the variable(s) in the delivery of the hemodialysis prescription that were problematic, if the delivered dose was not the prescribed dose. Therefore, the HD Adequacy Work Group recommends that formal UKM be implemented as a component of a complete CQI program for ESRD care.

Formal UKM permits calculation of the NPCR. The volume of distribution term may be used to calculate the NPCR as follows:

$$\text{NPCR (g/kg/day)} = (\text{PCR, g/day})(\text{mean V}/0.58)$$

Use of the NPCR enables the dialysis care team to perform longitudinal analysis of the patient's nutritional status.^{47,48} The NPCR can be used to identify patients who might benefit from counseling about their dietary protein intake. Furthermore, it can be used to determine whether the hemodialysis dose needs to be escalated because of sustained high protein intake. (Calculation and use of the NPCR are discussed in greater detail in the RPA's 1993 *Clinical Practice Guideline on Adequacy of Hemodialysis*⁵¹ and in the NKF-K/DOQI *Clinical Practice Guidelines for Peritoneal Dialysis Adequacy*.¹⁰⁹)

Disadvantages of urea kinetic modeling. The disadvantages of formal UKM are logistical. For example, the complexity of the calculations requires the use of computational devices and software. Physical parameters, such as the K and V, are difficult to measure and to monitor, and the

actual treatment time can be difficult to determine. In addition, the time required for the dialysis unit staff to accurately collect and adequately process all patient information to support these calculations can be significant in large dialysis units. Finally, although the cost of the computers and software is low, it is a factor for some dialysis centers. Despite these relatively minor limitations of formal UKM, the Work Group agreed with the RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis* about the necessity of formal UKM. It is the most rigorous method for prescribing dialysis treatment and evaluating the consistency with which the prescribed treatment is delivered to the patient.⁵¹

Measuring delivered dose of hemodialysis in pediatric patients. Formal 2- and 3-point urea kinetic modeling can be reliably performed in pediatric hemodialysis patients.¹³²⁻¹³⁷ Despite wide variability in body size, Kt/V calculations using formal urea kinetic modeling are accurate and reproducible in pediatric patients. To date, there have been no studies of the dose of hemodialysis as a predictor of outcomes in pediatric patients.^{136,138} However, there is no reason to assume that the diligence in monitoring or the achievement of benchmarks should be modified for children. Although a small recent analysis demonstrated that the measured dialysis dose was equivalent whether using formal urea kinetic modeling or the Kt/V Ln formula,¹³⁶ the HD Adequacy Work Group favors use of formal urea kinetic modeling to derive the Kt/V.

Other methods for measuring delivered dose of dialysis for adults and children. Recognizing that computational software to support the calculation of the Kt/V using formal UKM may not be available to all hemodialysis providers, several alternate methods for calculating Kt/V were examined by the HD Adequacy Work Group. Of these, the second generation logarithmic estimate, described as the Kt/V natural logarithm formula, provides the closest approximation to the single-pool, variable volume Kt/V derived from formal UKM.⁴⁴

- **Kt/V natural logarithm (Ln) formula.** The Kt/V Ln formula, which accounts for intradialytic volume changes secondary to ultrafiltration and the resultant convective solute transport (solute clearance via ultrafiltra-

tion), is accurate over the full range of single-pool, variable volume Kt/V values (range, 0.7 to 2.1).^{44,45,119,139} The Work Group endorses this method as the best alternative for dialysis providers who are unable or unwilling to perform formal UKM for their adult or pediatric patients.

However, the HD Adequacy Work Group does not recommend this method for primary use because it has several important limitations compared to formal urea kinetic modeling. First, the Kt/V Ln formula alone does not support the calculation of the NPCR. An NPCR can be derived from a nomogram that uses patient-specific parameters and the Kt/V Ln formula,^{46,120} or by a described equation.^{139,140} However, these approaches have not been subjected to extensive comparative analysis. Second, the Kt/V Ln formula does not permit the rigorous, quantitative analysis of the hemodialysis prescriptions described earlier for formal urea kinetic modeling. For example, if the delivered Kt/V is observed to be too low, the natural logarithm Kt/V does not provide insight into how therapy should be altered (eg, dialysis time, blood and dialysate flows, and dialyzer).

- **URR.** The HD Adequacy Work Group acknowledges the ease of calculation and resultant popularity of the URR.^{31,66} Of the three methods that the HD Adequacy Work Group considered appropriate for measuring the delivered dose of hemodialysis, the URR is the simplest to execute. The URR has been shown to be a statistically significant predictor of mortality for ESRD patients.^{19,40}

However, the Work Group agreed with the limitations of the URR as a measure of hemodialysis adequacy as delineated in the RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis*. Most important among these is that the URR does not account for the contribution of ultrafiltration to the final delivered dose of dialysis, in contrast to formal UKM and the Kt/V Ln formulae.¹⁴⁰⁻¹⁴² This is because the convective transfer of urea that occurs by ultrafiltration does not result in a decrease in the BUN concentration, although urea removal into the dialysate has occurred. The result is that the URR is less accurate in estimating the delivered dose of he-

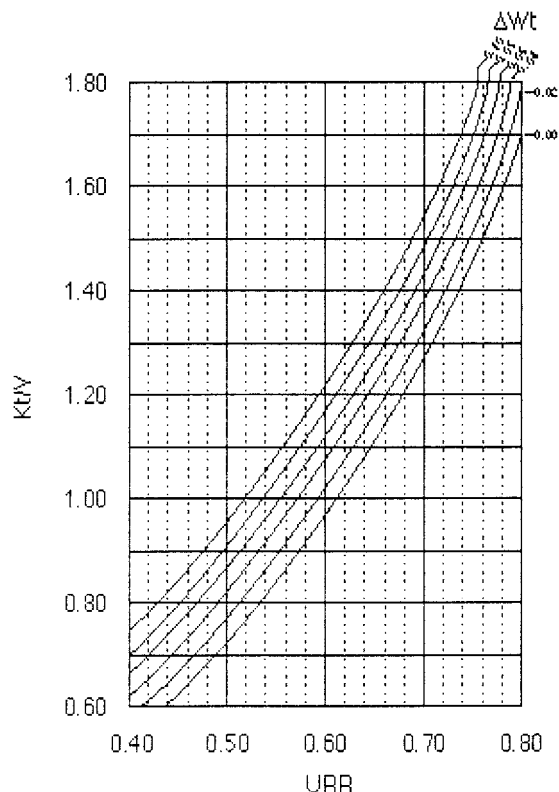


Fig I-1. Impact of solute clearance through ultrafiltration losses on the delivered dose of hemodialysis as measured by the Kt/V. The curves are derived from formal urea kinetic modeling assuming a 3-hour hemodialysis, no residual kidney urea clearance, and a volume of distribution of urea of 58% of body weight. Wt refers to net ultrafiltration losses as a fraction of final body weight. Reprinted with permission.¹⁴²

modialysis than the single-pool, variable volume Kt/V calculated by formal UKM. For example, a patient with a large ultrafiltration requirement (as a percentage of body weight) will have a Kt/V that may be 0.2 or more greater than a patient with the same URR, but no ultrafiltration requirement.¹⁴² The result is that, at any given prescribed URR, the actual delivered dose of hemodialysis may vary substantially because of different ultrafiltration volumes. As shown in Fig I-1, a URR of 65% may correspond to a single-pool Kt/V (Kt/V_{sp}) of as low as 1.1 in the absence of ultrafiltration or can be as great as a Kt/V_{sp} of ~ 1.35 when ultrafiltration of 10% of body weight occurs.

Furthermore, errors in the delivered dose of hemodialysis may be particularly difficult to detect in the target range of URR of $\geq 65\%$ ⁵² where a curvilinear relationship exists between URR

and Kt/V .¹⁴² As a consequence of this nonlinear relationship, modest alterations in the URR can result in large clinically significant changes in the Kt/V . For example, assuming ultrafiltration losses of 2% of body weight during hemodialysis, a decrease in URR from 70% to 65% corresponds to a reduction in the Kt/V from 1.32 to 1.15.

The likelihood of error in the delivered dose of hemodialysis as measured by the URR is increased by its inability to support calculations of V for comparison to anthropometric values. In addition, like the Kt/V Ln formula, correcting observed deficiencies in URR requires empirical modification of the components of the treatment prescription. Similarly, the URR does not support calculation of the NPCR and ignores the contribution of residual kidney function to urea clearance. Thus, while the URR is a practical measurement tool for epidemiological outcome studies,^{19,40} its relative inaccuracy, and the incomplete information provided, compromise its use as the sole measure of delivered doses of dialysis in individual ESRD patients. Dialysis doses measured by URR have not been validated for pediatric patients. Routine substitution of this measure may thus be especially problematic for this patient subset. Children have a smaller body and relatively higher total body water and are therefore at increased risk for significant amounts of urea rebound.

- Kt/V derived from the percent reduction of urea (PRU). The HD Adequacy Work Group reviewed literature on the accuracy of Kt/V calculations from the PRU that were published since the RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis*. The PRU formulae were derived by linear correlation to the Kt/V derived from total dialysate collection and from formal UKM.^{117,118} However, because the Kt/V derived from the PRU can be incorrect by approximately 20% in comparison to more rigorous measures of Kt/V ,^{44,143} the Work Group felt that these formulae were not adequate for routine clinical use in measuring the delivered dose of hemodialysis and concluded that they should not be used.
- Urea (or solute) removal index and alternative methods of measurement. A less com-

mon method of expression of hemodialysis adequacy, the solute (or urea) removal index (SRI), is defined as the percentage of total body urea nitrogen content that is removed by a dialysis treatment. This measure could not be evaluated by the HD Adequacy Work Group because of the lack of clinical experience with this method.^{116,119,123} There are other promising methods under study, such as the use of devices that directly quantify urea removal during a hemodialysis session as the measure of intradialytic clearance,^{122,144-146} but judgments about their accuracy and routine utility cannot be made at this time.

- Kt. Recent reports that have described counterintuitive relationships between hemodialysis dose measured as URR and/or unequilibrated Kt/V and patients' outcomes. First, when grouped by weight for height percentile, a progressive deterioration of survival was observed for patients with the greatest URR and the lowest percentile weight for height.¹⁴⁸ Second, another report described increasing mortality risks when the URR exceeded 70%, and so described a reverse j-shape for the URR-death risk profile. A similar mortality profile has been depicted by other investigators.^{40,149,150,186,189,191} By adjusting for TBW measured by bioelectrical impedance, the reverse j-shape can be eliminated, so that mortality benefit is seen over the entire spectrum of URR values.¹⁸⁶ An explanation offered was that a low TBW was reflective of poor nutrition, which was not overcome by a greater dialysis dose. An alternative interpretation was that patients with low TBW experienced greater urea rebound and hence received a clinically deleterious lower dose of dialysis than was appreciated by URR measurements alone. Third, although blacks receive lower dialysis doses than whites, their adjusted survival on hemodialysis is better.^{6,31,55,57} Blacks with ESRD have greater serum creatinine and albumin concentrations and anthropometric attributes than whites.^{57,152} This disparity in survival is negated by multivariable models in which the serum creatinine concentration, a laboratory-based surrogate of somatic nutrition, is included.¹⁵² Last, using

data from a US Renal Data System special study, the relationship between the equilibrated Kt/V, patients' anthropometric attributes, and mortality was examined.¹⁵⁴ Kt/V and body size were both independently and significantly related to mortality after adjustment for patients' characteristics and comorbid conditions.

These findings have been interpreted as being consistent with an independent beneficial effect of nutrition on survival for hemodialysis patients, which is reflected in their anthropometric attributes and hence measures like the urea distribution volume. In the urea kinetic constructs for dialysis dose, such as Kt/V or URR, whereby one measure ($K \times t$) is divided by another (V, a proxy of lean body mass and nutrition), paradoxical relationships to outcome may be observed. For example, increasing the V, which is reflective of better nutritional health, may be associated with lower reported dialysis doses. This is unsurprising since many dialysis care teams prescribe relatively uniform dialysis doses with different patient weights. The findings reported above suggest that patient mortality is more reflective of the effect of V, than of the Kt/V.¹⁸⁹ This hypothesis is supported by the finding that V, total body water, body weight, and body mass index are independent predictors of mortality risk for hemodialysis patients.¹⁸⁹ Higher values predict better outcomes. Therefore, it has been suggested that disaggregating Kt/V and using the Kt alone offers a more clinically relevant strategy to measure the dose of hemodialysis.^{156,189} Based on cross-sectional data, minimum Kt thresholds of 40 to 45 L per treatment for female and 45 to 50 L per treatment for male ESRD patients have been suggested.¹⁵⁶ Alternative theories have been posited to explain the more complex interactions described herein in which V is both an independent outcome predictor and the measure of the volume of distribution for the target solute, urea.¹⁵⁸ The HD Adequacy Work Group does not feel there is sufficient evidence to advocate the substitution of Kt for Kt/V, but anticipate that the longitudinal design of the HEMO Study, with its well characterized patient cohort, will facilitate the examination of these complex interactions.⁹²

- Duration of dialysis treatment. Some clinical researchers contend that the hemodialysis treatment time alone, independent of the Kt/V or URR, can be used as a measure of hemodialysis adequacy. Arguably, longer hemodialysis times may enhance patient survival.^{18,27,147} However, other investigators have observed that when the dose of hemodialysis was controlled, no relationship was demonstrable between the prescribed duration of hemodialysis and patient outcomes.^{19,34,40,149,151} Most of these studies have examined the prescribed treatment time instead of the delivered dialysis time; this discrepancy needs to be considered.¹⁵³

The proponents of time as a measure of hemodialysis adequacy argue that the duration of hemodialysis is a surrogate for increased clearance of solutes other than urea that are not accounted for by urea-based kinetic models. Arguably, because this group of putative uremic toxins is much larger than urea,^{88,89,91,107} their clearance is less dependent on diffusion for blood-side removal, if conventional (low flux) dialyzers are used. Proponents also claim better control of other parameters that affect patient outcome, such as blood pressure.^{39,147,155,157} Conceivably, patients with longer hemodialysis treatments have fewer complications secondary to ultrafiltration and thus are more likely to routinely achieve their estimated dry weight. As a result, they suffer fewer cardiovascular complications secondary to hypertension and/or hypervolemia.¹⁵⁹⁻¹⁶² (see Guideline 15: Optimizing Patient Comfort and Adherence, and Guideline 16: Strategies to Minimize Hypotensive Symptoms). Some Work Group members felt that independent of the delivered dose of hemodialysis calculated using a single-pool, or equilibrated, variable volume model of urea kinetics, the duration of hemodialysis should not be permitted to fall below a particular threshold value (<2.5 hours). In the absence of empirical data, disagreement existed among the Work Group members with respect to this issue, and consensus could not be reached.

However, the Work Group agreed that the dialysis care team should be alert for the potential consequences of implementation of the prescribed treatment time derived from formal UKM, particularly for small-statured patients with a

small V. If dialyzers with high urea clearance are used, the suggested treatment time to achieve the target Kt/V may be unacceptable to comfortably meet the patients needs for ultrafiltration (see Guideline 15: Optimizing Patient Comfort and Adherence). For example: (1) Patient V = 25L; (2) prescribed Kt/V=1.2; and (3) dialyzer urea clearance of 350 mL/min or 0.35 L/min, resulting in a treatment time of only 86 minutes (calculated based on $1.2 \times 25 / 0.35$). Such short treatment times in the setting of large K and small V may also result in inadequate delivered doses of hemodialysis secondary to urea compartmentalization.^{163,164}

Single-pool versus double-pool effects in adult and pediatric patients. No single-pool, variable volume model for UKM accounts for the different rates of urea transfer between fluid compartments, commonly termed the double-pool effect. With increased dialyzer efficiency, urea removal from the extracellular compartment (K_p) can exceed its diffusive transfer rate from the intracellular compartment to the extracellular compartment (K_c),¹⁶⁵ which is estimated at 800 mL/min.¹⁶⁶ Although higher K_c values have been observed,^{168,171} the relative impedance of urea movement from the cells to the interstitium and blood effectively render the intracellular compartment an unequilibrated reservoir of urea that is not accounted for by single-pool models of urea kinetics.^{45,168-170} According to this model (commonly termed the diffusion model), release of the sequestered urea continues for 30 to 60 minutes after completion of the hemodialysis session, a process nonspecifically described as urea rebound.^{67,119,163,171} Thus, the effective delivered dose of hemodialysis will be overestimated if this sequestered urea pool is large and is not considered (kinetic underestimation of true V).^{45,164,170,171} The use of dialyzers with high K, especially in patients with a small V, that permit short dialysis times such as pediatric patients (increased K/V), increases the risk of significant double-pool effects.^{132,133,174}

Since the publication of the RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis*, another major factor contributing to urea rebound has been characterized: the relative disequilibrium between cardiac output and blood flow to various vascular beds.¹⁷⁵ Even if there is

no impedance to the movement of urea from the intracellular to the extracellular compartment, organs with relatively low blood flows, such as skin, bone, and muscle, may serve as reservoirs for urea. Seventy percent of the total body water is contained in organs that receive only 20% of the cardiac output (flow-volume disequilibrium). Because these tissues receive relatively less blood flow, their contribution to the total plasma urea content entering the extracorporeal hemodialysis circuit is less than that of tissues that receive more blood flow. Therefore, during the course of a hemodialysis session, flow-volume disequilibrium for urea between vascular beds results in the preferential loss of urea from the well-perfused, but relatively urea-depleted vascular beds. This compartmentalization of urea results in an increase in the BUN concentration over the 60 minutes after the completion of hemodialysis.

The extent of urea rebound varies greatly among adult patients. In one study, the mean amount of urea rebound, measured as the percent increase in postdialysis BUN concentration immediately after dialysis versus 30 minutes after dialysis was 17%.¹⁶³ However, in some patients, the literature describes the occurrence of as much as 45% rebound¹⁷¹ or 19% to 75% error between single-pool and double-pool Kt/V.¹⁷⁰ On average, the equilibrated Kt/V (Kt/V_{equil}) is 0.2 units less than the single-pool Kt/V,^{176,177} but can be as great as 0.6 units less. For most patients, urea rebound is nearly complete 15 minutes after hemodialysis, but for a minority of patients, it may require up to 50 to 60 minutes.⁶⁷ As stated above, the severity of urea rebound is partially a function of the K/V.^{67,163,164,171,174} Therefore, the degree of rebound may be exaggerated in ESRD patients who are small-statured^{132,170} and during hemodialysis sessions that are complicated by intradialytic hypotension.¹⁷⁸

Because of the inability to predict which patients will have significant urea rebound, and in view of the potential deleterious impact of urea rebound on calculations of the delivered dose of hemodialysis,^{119,132,133,170} the Work Group examined the applicability of the double-pool, variable-volume urea kinetic model. Although this model may more accurately quantify intradialytic urea removal^{67,170,171} and may result in a more precise NPCR because of the more accurate assess-

ment of V (in comparison to an anthropometric value),^{169,179} the need to obtain the postdialysis BUN sample 30 to 60 minutes after the completion of hemodialysis (equilibrated postdialysis BUN sample) makes it impractical in the conventional outpatient hemodialysis setting. In an attempt to overcome this practical problem, a mathematical algorithm that estimates the dose of hemodialysis from the predialysis BUN concentration (C_0) and the equilibrated postdialysis BUN concentration (C_{eq}) has been developed (Smye formula).^{119,133,170} The C_{eq} is calculated by:

$$C_{eq} = C_0 \times \text{Exp}(-[T/(T - T_s)]) \times \text{Ln}[C_s/C_t]$$

in which C_{eq} is the equilibrated postdialysis BUN; C_0 the predialysis BUN; C_s is the mid-dialysis BUN concentration (usually obtained after 70 minutes of hemodialysis); C_t is the BUN concentration at the end of hemodialysis; T is the duration of hemodialysis; and T_s is the time at which C_s is drawn. Exp and Ln are the exponential and natural logarithm of the bracketed terms, respectively. The resultant C_{eq} is used to calculate the Kt/V_{equil} . In a small study using this formula to generate a calculated equilibrated Kt/V , the average error was only 13%, in comparison to a measured equilibrated value.¹⁷⁰

An alternative and more accurate approximation of the equilibrated Kt/V has been developed based on the aforementioned variable organ perfusion, double-pool model (Daugirdas rate formula).¹⁷⁴ Assuming all other variables are equivalent, the impact of urea rebound may be much less when using a venovenous angioaccess than with an arteriovenous access ($\leq 30\%$)¹⁸⁰ (see Guideline 8: Acceptable Methods for BUN Sampling). Thus, the mathematical relationship between the equilibrated and the single-pool Kt/V will vary depending upon the location of the angioaccess and the site from which the postdialysis BUN sample was obtained. Kt/V_{sp} , calculated using an arterial postdialysis BUN sample from an arteriovenous angioaccess (art Kt/V), will be greater than that calculated from a mixed venous postdialysis BUN, drawn through a venovenous angioaccess (ven Kt/V).¹⁸¹ The corresponding equilibrated Kt/V values are calculated by:

$$\text{art } Kt/V_{equil} = \text{art } Kt/V_{sp} - (0.6 \times \text{art } Kt/V_{sp}/T) + 0.03 \quad (1)$$

$$\text{ven } Kt/V_{equil} = \text{ven } Kt/V_{sp} - (0.47 \times \text{ven } Kt/V_{sp}/T) + 0.02 \quad (2)$$

in which T is the dialysis treatment time in hours and t is the dialysis time in minutes.¹⁷⁷ The comparative accuracy of the Smye versus the Daugirdas formulations has been determined. In a report from the National Institutes of Health's Hemodialysis Pilot Study that compared the accuracy of blood side measures of the Kt/V_{equil} , the rate formula was found to more closely correspond to the equilibrated Kt/V calculated using a 30-minute postdialysis BUN sample ($r = 0.85$).¹⁷⁷ An apparent operational advantage of the Daugirdas formula is that it only requires two blood samples, instead of the three samples for Smye. An alternative, but less well validated two blood sample approach to calculating an equilibrated Kt/V , is to obtain a BUN concentration 30 minutes prior to the completion of dialysis and substitute this value for the postdialysis BUN. This approach is based on the observation that the 30-minute postdialysis BUN concentration is not statistically different than the intradialytic concentration 30 minutes before the end of hemodialysis.¹⁸²

Using Formula 1 for calculating art Kt/V_{equil} , the impact of the duration of hemodialysis on the single-pool, variable volume Kt/V is presented in Table I-1. For any Kt/V_{sp} , shortening the duration of hemodialysis reduces the equilibrated Kt/V . For example, the Kt/V is reduced by >0.18 with a reduction in hemodialysis time from 5.0 to 2.0 hours for all single-pool Kt/V values of 1.0.

Double-pool effects of urea removal can substantially reduce the accuracy of single-pool urea kinetic calculations. Thus, some patients whose dialysis dose is measured by the single pool model alone may be at risk for unappreciated underdelivery of hemodialysis. For this reason, the HD Adequacy Work Group encourages the use of equilibrated Kt/V measurements, especially in patients with a large K/V .¹⁸³ Use of Kt/V_{equil} is considerably easier now that the Daugirdas rate formula has been validated.¹⁷⁷ The use of two-compartment urea kinetic models to calculate the delivered dose of hemodialysis is a

Table I-1. Relationship Between Single-Pool (spKt/V) and Equilibrated (eKt/V) as a Function of Treatment Time (t)

spKt/V	eKt/V						
	2.0 hrs	2.5 hrs	3.0 hrs	3.5 hrs	4.0 hrs	4.5 hrs	5.0 hrs
1.0	0.73	0.79	0.83	0.86	0.88	0.90	0.91
1.1	0.80	0.87	0.91	0.94	0.97	0.98	1.00
1.2	0.87	0.94	0.99	1.02	1.05	1.07	1.09
1.3	0.94	1.02	1.07	1.11	1.14	1.16	1.17
1.4	1.01	1.09	1.15	1.19	1.22	1.24	1.26
1.5	1.08	1.17	1.23	1.27	1.31	1.33	1.35
1.6	1.15	1.25	1.31	1.36	1.39	1.42	1.44

useful adjunct to a complete kinetic modeling program, especially for patients at risk for significant amounts of urea rebound. However, the HD Adequacy Work Group does not yet endorse the substitution of two-compartment urea models for single-pool models in adults on hemodialysis for the following reasons:

1. Two-compartment models based on calculations using the postdialysis BUN sample taken more than 30 minutes after completion of dialysis are impractical in the outpatient hemodialysis setting.
2. Despite theoretical dosing inaccuracy that may result from the failure to take into account the extent of urea rebound, most studies have shown a relationship between doses of hemodialysis estimated by single-pool, variable volume models and patient survival. These studies were the basis of the Work Group's recommendations about minimal adequate hemodialysis dose.
3. The Work Group was uncertain of the longitudinal validity of either of the mathematical approximations of the equilibrated Kt/V as the patient's years of survival on hemodialysis increased and/or the patient's nutritional and cardiac function changed.
4. At this time, there are no prospective outcome studies in adult ESRD patients based on two-pool models. However, at the completion of the HEMO Study, definitive evidence will be provided of the appropriate dialysis dose using equilibrated urea kinetics and will demonstrate its relationship to patients' mortality and morbidity.⁹² Similarly, there are no data that address the use of double-pool urea kinetics to predict outcomes in children undergoing hemodialysis.

RECOMMENDATIONS FOR RESEARCH

1. Data from ongoing prospective, randomized studies, such as the National Institutes of Health HEMO Study,⁹² that employ double-pool, variable volume models should be used to evaluate the advantages and limitations of double-pool modeling and to clarify its ability to predict patients' outcomes.
2. The applicability and long-term validity of the formulae that approximate the equilibrated Kt/V need to be determined by observational study.
3. The validity of single-pool, variable volume models and double-pool, variable volume models as outcome predictors needs to be evaluated to a greater extent among pediatric hemodialysis patients.
4. A prospective, multicenter study of the effects of dialysis dose on outcomes in pediatric dialysis patients should be undertaken.
5. Dialysate side and alternative methods of monitoring the delivered dose of hemodialysis, such as online urea measuring devices and direct measures of clearance, need to be developed further and ultimately correlated with patient outcomes in a prospective manner.

GUIDELINE 3

Uniformity of Method of Measurement (Opinion)

All patients receiving hemodialysis in the same dialysis facility should have the delivered dose of hemodialysis measured using the same method.

Rationale Adoption of the same method of measurement of hemodialysis dose for all pa-

tients in a given facility will enhance consistency in procedures and permit meaningful comparisons of data for a single patient over time between patients and among different hemodialysis facilities. Therefore, the HD Adequacy Work Group strongly urges that the governing body or equivalent administrative authority within the hemodialysis facility formally adopt a uniform method of measuring the delivered dose of hemodialysis for all its patients.

The adoption of such a primary procedure does not preclude the use of supplemental measures of the delivered dose of hemodialysis for some or all patients. For example, some Work Group members felt that monthly URR measure-

ments may be supplemented by less frequent formal UKM. Additional modeling data are certainly not discouraged. However, there should be a single, consistent, and therefore, comparable adequacy measurement for all hemodialysis patients.

If multiple methods of measurement are used within a hemodialysis facility, the method used to quantify the dose of hemodialysis delivered to a given patient should be documented, and the method used to calculate delivered dose of hemodialysis for a given patient should be consistent over time. In the absence of such consistency, longitudinal comparisons of the delivered dose of hemodialysis for a given patient cannot be made.

II. Hemodialysis Dose

GUIDELINE 4

Minimum Delivered Dose of Hemodialysis (Adults Evidence, Children Opinion)

The dialysis care team should deliver a Kt/V of at least 1.2 (single-pool, variable volume) for both adult and pediatric hemodialysis patients. For those using the URR, the delivered dose should be equivalent to a Kt/V of 1.2, ie, an average URR of 65%. However, URR can vary substantially as a function of fluid removal.

Rationale Numerous peer-reviewed studies have confirmed the association between the adequacy of the delivered dose of hemodialysis and patient outcome.^{19,33,34,36,38-42,57} At the time of its publication in 1993, the RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis* defined adequate hemodialysis as the recommended quantity of hemodialysis delivered which is required for adequate treatment of ESRD such that patients receive full benefit of hemodialysis therapy. At that time, the 15-year-old National Cooperative Dialysis Study (NCDS) was the sole prospective, randomized, controlled trial to provide data concerning the relationship between the fractional clearance of urea and patient outcome.³⁴ Reanalysis of the primary data from the NCDS showed that Kt/V <0.8 was associated with a relatively high rate of patient morbidity, whereas Kt/V values between 1.0 and 1.2 were associated with a low rate of morbidity.⁴⁸

Extrapolating from the NCDS data to current dialysis practice is difficult for several problems. The NCDS was performed prior to the widespread dissemination of current hemodialysis technologies such as ultrafiltration control, bicarbonate dialysate, variable dialysate sodium programming, and biocompatible dialysis membrane materials. Furthermore, patients with demographic characteristics similar to those of many current ESRD patients were not eligible for participation in the NCDS. For example, diabetics and patients over the age of 70 were excluded from the NCDS. Finally, morbidity, not mortality, was the principal outcome.³⁴ Thus, the RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis* stated that the NCDS alone was not an appropriate guide regarding what constitutes the minimum dose of hemodialysis. The authors of the RPA's *Clinical Practice Guideline*

on Adequacy of Hemodialysis found that uncontrolled retrospective studies suggested an improved survival with greater delivered doses of hemodialysis (up to Kt/V >1.2 and URR of 65%).^{19,51,147}

Because literature available at the time of the RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis* was not definitive, a decision analysis was performed using available data.¹⁸⁴ The initial analysis used a probabilistic model to assess how variables in the dialysis prescription affect a patient's quality-adjusted life expectancy (QALE). In a complementary analysis, lifetime costs and QALE were modeled to determine the marginal cost-effectiveness of the components of the dialysis prescription. On the basis of this analysis, the RPA recommended that the delivered Kt/V should be at least 1.2. For those using URR, this value should be at least 65%. The RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis* noted that the QALE increases with increasing Kt/V to a tested level of 2.0. However, at Kt/V >1.3, a rapid increase in outpatient costs to achieve the higher dose of hemodialysis occurred in conjunction with improvements in QALE. Thus, the final RPA recommendation reflected a balance of concerns regarding the patients quality-adjusted life expectancy and marginal cost-effectiveness.

The HD Adequacy Work Group reviewed the literature available after the release of the RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis* and found no convincing basis for recommending a higher minimum dose of hemodialysis. Most of the published reports supporting the suggestion that hemodialysis patients benefit from higher minimum values of Kt/V or URR are retrospective observational analyses from self-selected hemodialysis centers, which could lead to selection bias and inability to generalize to other populations.^{33,40,41,147} Limitations of these reports include the comparison of patient outcomes to uncontrolled historical standards,^{41,147} lack of patient randomization,^{33,36,40} patient profiles that did not match prevalent ESRD patients,³⁶ lack of standardization for collecting BUN samples,^{33,40} use of relatively broad categories of Kt/V or URR for analysis,^{33,40} or major differences in clinical practice and patient

behaviors compared to those in the United States.¹⁴⁷ Although one of these studies was prospective, patient randomization was not performed; several factors other than the dose of hemodialysis varied simultaneously; and the only comparison made was between an adequate and inadequate hemodialysis dose ($Kt/V = 1.3$ versus 0.8, respectively), ie, a minimum target Kt/V was set at the start of the study.³⁶ The Work Group also felt that much of this literature was compromised by the longitudinal averaging of hemodialysis doses, rather than accounting for repeated measures within a single individual. In addition, the ability to draw conclusions from these studies is limited by their use of mean data.⁴² If the improvement in survival for ESRD patients occurs as a step function above some minimum Kt/V , increasing the dialysis dose for the population of patients will result in a decrease in mortality for the group. With a normal distribution, increasing the group mean minimizes the number of patients at risk, so the false impression of continued benefit from higher dialysis doses is portrayed. Furthermore, not all study results suggested that patient survival improved with delivered hemodialysis doses higher than Kt/V of 1.2 (URR of 65%).¹⁹ A recent retrospective analysis of data from the Case Mix Adequacy Database, which used both single-pool (sp) and double-pool (dp) urea kinetic models, found no improvement in survival for a Kt/V_{sp} of 1.2 to 1.4 or a Kt/V_{dp} of 1.0 to 1.2.¹⁸⁵

In the absence of clear and consistent data demonstrating a clinical outcome advantage associated with a higher minimum dose of hemodialysis, the Work Group cannot advise that the minimum hemodialysis dose recommended in the RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis* be changed for adult patients with ESRD. However, dialysis care teams are not discouraged from establishing greater minimum levels of hemodialysis dose for their patients. In fact, because of variability in the measurement of delivered dose,¹⁸³ as discussed in greater detail in Guideline 5: Prescribed Dose of Hemodialysis, higher minimum prescribed hemodialysis doses are encouraged. The HD Adequacy Work Group acknowledges concerns that some patients with a small V may develop deleterious metabolic disturbances in the setting of a high Kt/V or URR.¹⁸⁶

Table I-2. The Correlation of URR to Kt/V Corrected for Ultrafiltration

$\Delta Wt/BWt$, %	URR Values at Kt/V							
	0.8	0.9	1.0	1.1	1.2	1.3	1.4	1.5
0	53	57	61	65	68	71	74	76
1	52	57	61	64	68	71	73	76
2	50	55	59	63	66	69	72	75
3	49	54	58	62	65	68	71	74
4	48	53	57	61	64	67	70	73
5	47	51	56	60	63	67	70	72
6	46	50	55	59	62	66	69	71
7	44	49	53	58	61	65	68	71
8	43	48	52	57	60	64	67	70
8	42	47	51	56	63	65	66	69
10	41	46	50	54	58	62	65	68

NOTE. Calculated from single-pool, variable volume model with a body weight of 67.3 kg, V of 35 L, and NPCR of 1.0. Wt/BWt is the ultrafiltration volume divided by the postdialysis weight multiplied by 100.

Because this scenario has not been validated in outcome studies, and because the risk of inadequate hemodialysis is well-established, the Work Group underscores that these recommendations are minimum, not target values.

Adjustments of URR for ultrafiltration. In determining whether the recommended minimum dose of hemodialysis is delivered, the dialysis care team is reminded that the relationship between Kt/V and URR is affected by the extent of ultrafiltration^{141,142} (see Guideline 2: Method of Measurement of Delivered Dose of Hemodialysis, and Fig I-1). Table I-2 presents these relationships by illustrating the correlation between the single-pool Kt/V and the ultrafiltration volume as a function of the patient's postdialysis weight.

Because of the variability due to ultrafiltration, when URR is used as the method for measuring hemodialysis adequacy, the minimum delivered dose should be equivalent to a Kt/V of 1.2 (ie, an average URR of 65%), but can vary substantially as a function of fluid removal.

Optimal dose of hemodialysis. The Work Group emphasizes that the literature clearly supports delivery of a minimum hemodialysis dose of at least $Kt/V = 1.2$, but does not suggest what constitutes an optimal dose. Identification of an optimal dose of hemodialysis would require evaluation of patient survival, the patient's subjective valuation of quality of life, and the cost-

effectiveness of hemodialysis. Until such data are available, the Work Group emphasizes that the hemodialysis doses recommended herein are minimum values only.

Minimum delivered dose in selected patients. The Work Group also evaluated the issue of defining a minimum dose of hemodialysis for selected patient subsets defined on the basis of demographic characteristics or comorbidity.

- **Diabetics.** The suggestion has been made that ESRD patients with diabetes mellitus experience a reduction in their odds risk of death by approximately 40%, if their minimum delivered Kt/V is increased from 1.0-1.2 to 1.4.³³ In addition to the methodological limitations described earlier for this study, a survival advantage resulting from an increase in the minimum delivered dose of hemodialysis has not been observed uniformly in patients with diabetes.^{40,185} Therefore, the Hemodialysis Adequacy Work Group could not support the recommendation that diabetics should routinely be provided a greater minimum dose of hemodialysis.
- **Blacks.** Because several observational analyses have reported that blacks with ESRD more often receive less hemodialysis than recommended by the RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis*^{43,55,57,187} but have better survival than whites,^{57,188} the suggestion has been made that blacks may require less hemodialysis than has been recommended. A retrospective analysis of mortality by race and gender suggested a relative insensitivity of observed mortality to the delivered dose of hemodialysis in blacks in comparison to whites.⁵⁷ This counterintuitive finding may be a consequence of the mathematical construct of Kt/V, in which V behaves as a biologic-based, independent outcome predictor reflecting the patient's nutritional health.^{57,186,189} The Work Group found no evidence in the literature to suggest that the minimum delivered dose of hemodialysis should be less than that recommended in the RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis* for blacks or other racial subsets.

- **Pediatric patients.** Data regarding the association between delivered dose of hemodialysis and outcomes do not exist for pediatric patients.¹³⁶⁻¹³⁸ In the absence of such data, the opinion of the HD Adequacy Work Group is that the delivered dose of hemodialysis for children should be at least that recommended for adults. Higher Kt/V values, which are relatively easy to achieve in children because of their relatively low V, may facilitate growth.¹³⁷

Other factors related to hemodialysis adequacy. The HD Adequacy Work Group reminds the hemodialysis care team that Kt/V and URR focus on only one of the numerous parameters that operationally define the adequacy of hemodialysis.^{14,39,110,147,159,190-192} Urea is only a marker solute^{47,83} and measures of hemodialysis adequacy, such as the Kt/V or URR, are only surrogates for the clearance of other small molecular weight solutes. As discussed in the introduction, the flux of larger molecular weight solutes and membrane biocompatibility may be equally important issues.^{88,89,91,107} The Work Group recognizes that an increasing body of evidence suggests that the clearance of larger molecular weight solutes may have an independent effect on patient survival that is not fully reflected in the Kt/V_{urea}. Therefore, the Work Group urges clinicians not to base the dose of hemodialysis for an individual patient solely on the minimum acceptable amount of urea removed in a single dialysis session. For example, even when an appropriate minimum Kt/V or URR is routinely delivered, a patient may still be inadequately dialyzed in terms of potassium removal, correction of acidosis, or failure to render the patient a sufficient protein/caloric intake to prevent malnutrition. Similarly, an appropriate minimum Kt/V or URR may be routinely delivered, but the duration of hemodialysis may be too short to remove an adequate volume of fluid to reestablish euvolemia. The issue of more global, outcome-based definitions of hemodialysis adequacy is especially important for pediatric ESRD patients. Attention should be given to the child's school or vocational performance, growth, and emotional development, as well as the Kt/V.

Likewise, the dialysis care team is reminded that within the constraints of the desired Kt/V,

the duration of dialysis should be a matter of shared decision making with the patient. If after full disclosure to the patient of the deleterious outcomes resulting from inadequate hemodialysis, the patient desires a dialysis duration that is insufficient, the dialysis care team should respect the patient's wishes. However, a nonconfrontational dialogue should be continued regarding this topic. If a correctable barrier to adequate dialysis is identified, such as cramps or hypotension (see Guideline 16: Strategies to Minimize Hypotensive Symptoms), it should be addressed.

Twice-weekly hemodialysis. All HD Adequacy Work Group recommendations regarding hemodialysis dose are based on the assumption that hemodialysis treatments are delivered three times per week. Twice-weekly hemodialysis is usually inadequate unless there is a reasonable amount of residual kidney function ($\text{GFR} \geq 5 \text{ mL/min}$). Because residual kidney function declines with time, if a significant amount of kidney function is present at the initiation of hemodialysis, and the patient is undergoing twice-weekly hemodialysis, residual kidney function must be monitored serially. Such diligence guides the appropriate timing of a switch to three times per week hemodialysis. Unless close monitoring of the patient's residual kidney function can be routinely and serially provided, the Work Group recommends hemodialysis three times per week for all patients who require hemodialysis.

GUIDELINE 5

Prescribed Dose of Hemodialysis (Opinion)

To prevent the delivered dose of hemodialysis from falling below the recommended minimum dose, the prescribed dose of hemodialysis should be Kt/V 1.3. In terms of URR, a Kt/V of 1.3 corresponds to an average URR of 70%, but the URR corresponding to a Kt/V of 1.3 can vary substantially as a function of ultrafiltration.

Rationale Not all patients receive their prescribed dose of hemodialysis.^{53-55,81,115,116} Some studies suggested that only 50% of ESRD patients in the United States actually receive their prescribed hemodialysis dose.¹¹⁵ To ensure that patients receive the minimum adequate dose of hemodialysis at all treatments, nephrologists should prescribe doses of hemodialysis that are

higher than the aforementioned minimum delivered levels.

A variety of factors may result in the actual delivered dose of hemodialysis falling below the prescribed dose.^{53-55,60,81,115,116,183,193} Common factors include:

1. **Compromised urea clearance.** Effective urea clearance is a combination of dialyzer membrane permeability and surface area plus blood and dialysate flow rates. Effective clearance may be compromised by:

- Access recirculation, which reduces effective clearance by reducing the concentration gradient in the dialyzer.
- Inadequate blood flow from the vascular access.
- Inaccurate estimation of dialyzer performance, as actual clearance can be substantially less than the manufacturers stated clearances.
- Inadequate dialyzer reprocessing related to inadequate quality control of reuse.
- Dialyzer clotting during dialysis, which reduces effective dialyzer surface area.
- Blood pump/dialysate flow calibration errors, which result in blood and/or the dialysate flow rates that can be less than is assumed and reported.
- Errors in prescribed blood and dialysate flow rates due to variability in blood pump tubing. There may be variation in the extruded internal diameter or collapse of the inlet of a segment of tubing as a result of very high pre-pump extracorporeal negative pressure.
- Dialysate flow rate that is inappropriately set too low.
- Dialysate flow miscalibration.
- Dialyzer leaks.

2. **Reductions in treatment time.** Effective treatment time must accurately reflect the exact amount of time during which diffusion occurred at the prescribed blood and dialysate flow rates. Reasons that effective treatment time may be less than the prescribed time include:

- Inaccurate assessment of effective time, eg, as a result of use of wristwatches, instead of a synchronized dialysis unit clock to measure the hemodialysis time interval or
- Incorrect assumption of continuous treat-

ment time, eg, failure to account for interruptions during treatment due to occurrence of clinical complications during the hemodialysis session, equipment alarms (secondary to improperly set alarm limits or malfunctioning detectors for air), replacement or manipulation of fistula needle(s), pump failure, replacement of dialyzer (secondary to clotting of hemodialyzer during hemodialysis), or dialysate bypass with conductivity or temperature alarms. Such interruptions reduce the actual dialysis time.

- Premature discontinuation of hemodialysis for staff or unit convenience, eg, due to scheduling conflicts.
- Premature discontinuation of hemodialysis to honor patient request/adherence, eg, patient requests early termination of a hemodialysis session.
- Delay in starting dialysis session due to patient tardiness.
- Wrong patient taken off dialysis.
- Time on dialysis calculated incorrectly.
- Time read incorrectly for initiation or completion of hemodialysis.
- Clerical deficiencies, eg, manual documentation that does not capture actual time that hemodialysis was initiated and terminated and thus renders the effective dialysis time unknown.

3. **Laboratory or blood sampling errors.** Predialysis and postdialysis BUN measurements may not reflect the true systemic urea concentration at the time hemodialysis was initiated and terminated, respectively, due to errors in sampling procedure and/or laboratory error. Reasons for errors in measurement of BUN concentration include:

- Dilution of predialysis BUN blood sample with saline, which reduces the true predialysis BUN concentration and results in a smaller intradialytic reduction in BUN concentration and a larger apparent V.
- Drawing predialysis BUN blood sample after the start of dialysis. Once dialysis starts, the BUN concentration is lowered because of solute removal by dialysis, dilution by

recirculated blood if any access recirculation is present, and dilution by cardiopulmonary recirculation.

- Laboratory error due to calibration or equipment problems.
- Drawing postdialysis BUN blood sample before the end of dialysis, which increases the postdialysis BUN concentration and results in a smaller intradialytic reduction in BUN concentration, and a larger apparent V.
- Drawing postdialysis BUN blood sample more than 5 minutes after dialysis, which may result in a BUN concentration that is significantly higher than the value observed immediately after hemodialysis, because of urea rebound.
- Laboratory error in the BUN measurement.

The HD Adequacy Work Group emphasizes that most of the problems pointed out above will result in a discrepancy between the V derived from formal UKM and the V derived from anthropometrics. Therefore, these problems will be readily detected in a dialysis CQI program that uses formal UKM.

The Work Group was particularly concerned about the observed tendency within the nephrology community to implement the minimum Kt/V and URR values from the RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis* as target values. Because of the plethora of variables that adversely affect the delivered dose of hemodialysis, **the deliberate targeting of a delivered Kt/V = 1.2 or a URR = 65% will result in a significant number of hemodialysis sessions in which the Kt/V or URR fall below these threshold values.**

To prevent the Kt/V or URR for any patient from declining to values below the recommended minimum delivered dose, practitioners should prescribe doses of hemodialysis that are greater than these minimum values. A recent survey of hemodialysis practices demonstrated that a low dialysis prescription was one of the strongest predictors of inadequate dialysis dose.⁵³ In the National Institutes of Health's (NIH) HEMO Study, where rigorous implementation of the hemodialysis prescription and measurements of the dose of hemodialysis have been effected,⁹²

Table I-3. Values for Single Pool (spKt/V) Calculated From Equilibrated (eKt/V) and Dialysis Treatment Time (t)

Hours	spKt/V at eKt/V of	
	1.0	1.05
2.0	1.39	1.46
2.5	1.28	1.34
3.0	1.21	1.28
3.5	1.17	1.23
4.0	1.14	1.20
4.5	1.12	1.18
5.0	1.10	1.16

the 90% confidence interval for the single-pool Kt/V of 1.3 is 0.10 units (T. Greene, personal communication, 1999). Therefore, the Work Group suggests that the **prescribed minimum Kt/V be 1.3** for patients dialyzing three times per week. For URR, the HEMO Study observed a 90% confidence limit of 4%. Therefore, nephrologists using URR should set a **minimum target URR of 70%** (T. Greene, personal communication, 1999). Different target values will be needed for patients who dialyze more or less frequently.

Recognizing that some dialysis care teams may prefer to follow hemodialysis dosing using a double pool model for Kt/V, the HD Adequacy Work Group recommends that the **minimum prescribed dose in a double pool model be considered to be 1.05 for patients dialyzing three times per week**. In the HEMO Study, of 426 patients randomized, this minimum target resulted in fewer than 4% of the patients having a single pool Kt/V <1.2. As shown in Table I-3, if a eKt/V of 1.05 is prescribed, the spKt/V does not decrease to <1.2 until the hemodialysis time is increased to >4 hours. On the other hand, if an eKt/V of 1.0 is used, this relationship occurs at dialysis times >3 hours.

Evidence or suspicion that the delivered hemodialysis dose has fallen below the prescribed value should trigger a thorough evaluation of the processes involved in delivering dialytic care. Guideline 14: Inadequate Delivery of Hemodialysis, presents an algorithm for detecting the cause(s) of inadequate delivery of hemodialysis and for implementing corrective action.

GUIDELINE 6

Frequency of Measurement of Hemodialysis Adequacy (Opinion)

The delivered dose of hemodialysis should be measured at least once a month in all adult and pediatric hemodialysis patients. The frequency of measurement of the delivered dose of hemodialysis should be increased when:

1. Patients are noncompliant with their hemodialysis prescriptions (missed treatments, late for treatments, early sign-off from hemodialysis treatments, etc.).
2. Frequent problems are noted in delivery of the prescribed dose of hemodialysis (such as variably poor blood flows, or treatment interruptions because of hypotension or angina pectoris).
3. Wide variability in urea kinetic modeling results is observed in the absence of prescription changes.
4. The hemodialysis prescription is modified.

Rationale Numerous outcome studies have demonstrated a correlation between the delivered dose of hemodialysis and patient mortality and morbidity.^{19,33,34,36,38-42,57} The evidence demonstrates that mortality among ESRD patients is lower when an appropriate minimum dose of hemodialysis is provided. To ensure that ESRD patients treated with chronic hemodialysis receive adequate treatments, the delivered dose of hemodialysis needs to be measured. Clinical signs and symptoms alone are not reliable indicators of dialysis adequacy (see Guideline 1: Regular Measurement of the Delivered Dose of Hemodialysis).

The HD Adequacy Work Group recommends that the dose of hemodialysis be measured at least monthly. There are several reasons for this recommendation. In the studies of the relationship between delivered dose of hemodialysis and patient outcome, the typical frequency of performance of the selected measurement of the delivered dose of hemodialysis was monthly.^{19,33,34,36,38,39,41} Less frequent measurement may compromise the timeliness with which deficiencies in the delivered dose of hemodialysis are detected and, hence, may delay implementation of corrective action. Furthermore, the Work Group noted that most ESRD patients undergo monthly blood-based biochemical evaluations and that the institutional reporting of the results oc-

curs monthly. Therefore, monthly measurement of delivered dose is pragmatic. There is neither evidence nor reason to believe that pediatric and adult patients differ in their need for adequate hemodialysis or their need for at least monthly assessment of the delivered hemodialysis dose.

RECOMMENDATIONS FOR RESEARCH

Observational data should be collected on the relationship between the frequency of measurement of hemodialysis adequacy and patient outcomes and costs of care.

III. Blood Urea Nitrogen (BUN) Sampling

GUIDELINE 7

Blood Urea Nitrogen (BUN) Sampling (Evidence)

Predialysis and postdialysis blood samples for measurement of BUN levels must be drawn at the same hemodialysis session.

Rationale Evaluation of the dose of dialysis delivered during a hemodialysis session must be based on data from that particular treatment. Incomplete information derived from separate hemodialysis treatments provides little meaningful information about the delivered hemodialysis dose. Similarly, the laboratory that is processing the blood samples should analyze both specimens at the same time. This strategy will minimize the variability in the BUN concentration that arises because of interassay variability. In an analysis of individual variability in measures of hemodialysis adequacy that standardized for blood sampling technique (4.0% and 2.4% coefficient of variation for Kt/V and URR, respectively), most of the variation was attributable to variation in the laboratory's BUN measurement.¹⁸³

GUIDELINE 8

Acceptable Methods for BUN Sampling (Evidence)

Blood samples for BUN measurement must be drawn in a particular manner. Predialysis BUN samples should be drawn immediately prior to dialysis, using a technique that avoids dilution of the blood sample with saline or heparin. Postdialysis BUN samples should be drawn using the slow flow/stop pump technique that prevents sample dilution with recirculated blood and minimizes the confounding effects of urea rebound.

Rationale Accurate measurement of the change in BUN concentration that results from a hemodialysis treatment can only be made when blood samples are collected properly. Predialysis and postdialysis sampling techniques must control for the site of the blood draw, needle or catheter preparation, blood and dialysate pump flow rates, ultrafiltration rate, and the timing of the blood sampling with respect to the initiation and completion of hemodialysis.¹³⁹ The ideal and accurate measurement of the delivered Kt/V, URR, and NPCR requires that:

1. Predialysis BUN be measured before hemodialysis begins and be obtained without dilution of the blood sample.¹⁹⁴
2. Postdialysis BUN be measured after hemodialysis ends and angioaccess recirculation has resolved.^{195,196}
3. Laboratory processing of BUN samples is accurate.¹⁸³

Predialysis blood sampling procedures. The predialysis BUN must be drawn before dialysis is started to prevent this sample from reflecting any impact of dialysis.¹⁹⁴ Dilution of the predialysis sample with saline or heparin must be avoided or the predialysis BUN will be artificially low, resulting in a falsely low Kt/V and/or URR, an incorrectly elevated V, and a falsely reduced K.

Recommended method when utilizing an arteriovenous fistula or graft:

1. Obtain the blood specimen from the arterial needle prior to connecting the arterial blood tubing or flushing the needle. Be sure that no saline and/or heparin is in the arterial needle and tubing prior to drawing the sample for BUN measurement.

Purpose: Prevents dilution of the blood sample.

2. Do not draw a sample for use as a predialysis measure of BUN if hemodialysis has been initiated, or if saline or heparin is present in the lines.

Purpose: Prevents sampling of dialyzed blood or dilution of sample, respectively.

Recommended method when utilizing a venous catheter:

1. Withdraw any heparin and saline from the arterial port of the catheter, following the dialysis unit's protocol.

Purpose: Prevents dilution of the blood sample.

2. For adult patients, using sterile technique, withdraw 10 mL of blood from the arterial port of the catheter. For pediatric patients, withdraw 3 to 5 mL, according to the fill volume of the catheter. Do not discard this blood if the intent is to reinfuse it after the sampling is complete (see step 4).

Purpose: To ensure that the blood sample will not be diluted by heparin. Ideally, all the contaminating diluent is removed in step 1. Step 2 provides an additional margin of security. Be-

cause pediatric patients and their catheters are smaller, recommended volumes are reduced.

3. Connect a new syringe or collection device and draw the sample for BUN measurement.

Purpose: Prevents dilution of the sample, and preserves the blood from step 2 for reinfusion, if so desired.

4. Complete initiation of hemodialysis per dialysis unit protocol. (Optional step: reinfuse the blood drawn from step 2.)

Purpose: Reinfusion minimizes blood loss and may be particularly desirable in pediatric patients who have significantly smaller blood volumes.

Postdialysis blood sampling procedure. Proper timing for acquisition of the postdialysis BUN sample is critical.¹⁹⁴ Immediately upon completion of hemodialysis, if vascular access recirculation was present, some of the blood remaining in the angioaccess and extracorporeal circuit is actually recirculated blood. That is, some of the just-dialyzed blood has been routed through the angioaccess and the extracorporeal circuit for hemodialysis without that blood first having passed through waste product-rich tissues. If the blood sample is drawn immediately upon completion of dialysis, just-dialyzed blood that has recirculated into the angioaccess will dilute the sample. The consequence of sampling this admixture is a falsely reduced BUN value and artificially elevated Kt/V and URR.¹⁹⁶ In this situation, the V will be falsely low and the K falsely elevated. Therefore, the amount of dialysis delivered will be overestimated.

Early urea rebound (≤ 3 minutes postdialysis) may be viewed as a two-component process.^{58,197,198} The first component is secondary to blood recirculation within the angioaccess or catheter and is not present in patients without access recirculation. If access recirculation is present, urea rebound from recirculation begins immediately upon completion of hemodialysis and resolves in less than 1 minute, usually approximately 20 seconds. The second component of early urea rebound is cardiopulmonary recirculation that begins approximately 20 seconds after the completion of hemodialysis and is completed 2 to 3 minutes after slowing or stopping of the blood pump.¹⁹⁸ Cardiopulmonary recirculation

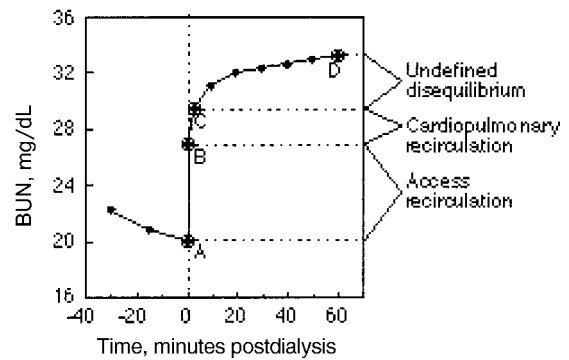


Fig I-2. Components of urea rebound. This illustration shows a total of 65% urea rebound of which over half is secondary to access recirculation (A→B). The contribution from cardiopulmonary recirculation is 15% (B→C), and the remaining 31% (C→D) is a consequence of flow and diffusion limitations. Reprinted with permission.⁵⁸

refers to the routing of just-dialyzed blood through the veins to the heart, through the pulmonary circuit, and back to the angioaccess without the passage of the just-dialyzed blood through any urea-rich tissues.^{169,198,199} The late phase of urea rebound (>3 minutes) is completed within 30 to 60 minutes after the cessation of dialysis. The late phase is a consequence of flow-volume disequilibrium (perfusion or parallel flow model)¹⁷⁵ and/or of delayed transcellular movement of urea (diffusion model)^{67,169} (see Guideline 2: Method of Measurement of Delivered Dose of Hemodialysis, Single-Pool Versus Double-Pool Effects in Adult and Pediatric Patients). These components of urea rebound are schematically presented in Fig I-2.⁵⁸

Because of urea rebound, the post-BUN concentration and the resultant Kt/V, URR, and NPCR will vary greatly depending upon the timing of the acquisition of the blood sample.¹⁹⁴ For example, the postdialysis BUN concentration will be higher, and the resultant Kt/V, URR, and NPCR will be relatively lower, with increased time after the completion of hemodialysis (see Table I-4). Although the most accurate way to resolve this problem would be to uniformly wait 30 to 60 minutes after the completion of hemodialysis before drawing a postdialysis BUN sample, this approach is impractical for patients and busy dialysis facilities.

The HD Adequacy Work Group identified a preferred method for postdialysis BUN sampling that is sufficiently reproducible and simple to be

Table I-4. Effect of Timing of Postdialysis Sampling on BUN and Kt/V or URR

Time After Dialysis Ends (min)	Potential Effect on BUN	Potential Effect on Kt/V or URR	Physiology	Comments
0	Major reduction	Major increase because of sampling of recirculated blood	BUN will be falsely decreased secondary to recirculated blood still present in the angioaccess*	Inappropriate time for BUN sampling for any form of urea kinetic modeling
0.25-0.50	Index	Index	Angioaccess recirculation resolved; urea rebound starting to occur secondary to cardiopulmonary recirculation, flow volume disequilibrium, and delayed diffusion	Most accurate for blood drawing to support formal UKM based on single-pool model; sample timing corresponds to slow flow/stop pump technique
2-3	Increased	Decreased because urea rebound is occurring	Urea rebound is occurring; cardiopulmonary recirculation completely dissipated	Sample timing corresponds to reinfusion technique†
5-10	Increased more	Decreased more	Significant, but incomplete resolution of urea rebound from compartment effects and flow/volume disequilibrium	Sample timing corresponds to reinfusion technique†
30	Greatest increase	Greatest decrease	Complete resolution of urea rebound	Correlates with double-pool model, but time for sampling is clinically impractical

*This is true only if angioaccess recirculation is present.

†Because of the variable timing of blood reinfusion at the end of hemodialysis, the sampling typically occurs 2 to 10 minutes after the completion of hemodialysis.

implemented by different dialysis care teams in varied dialysis settings. This method, called the slow flow/stop pump sampling technique, supports the use of formal UKM to quantitate the delivered dose of hemodialysis.

Recommended method for blood sampling using the slow flow/stop pump sampling technique.

1. At the completion of hemodialysis, turn off the dialysate flow and decrease the ultrafiltration rate (UFR) to 50 mL/h, to the lowest transmembrane pressure (TMP)/UFR setting, or off. If the dialysis machine does not allow for turning off the dialysate flow, or if doing so violates unit policy, decrease the dialysate flow to its minimum setting.

Purpose: Stop the hemodialysis treatment without stopping the blood flow completely. The risk of clotting the extracorporeal circuit is low.

2. Decrease the blood flow to 50 to 100 mL/min for 15 seconds. To prevent pump shut-off as the blood flow rate is reduced, it may be necessary to manually adjust the venous pressure limits downward.

Purpose: Fills the arterial needle tubing and the arterial blood line with non-recirculated blood (in case there is any access recirculation) by clearing the dead space in the arterial needle tubing and the arterial blood line.

At this point, proceed with either the slow flow or stop pump technique:

Slow flow sampling technique.

3. With the blood pump still running at 50 to 100 mL/min, draw the blood sample for postdialysis BUN measurement from the arterial sampling port closest to the patient.

Purpose: Drawing the blood from the arterial sampling port ensures the postdialysis BUN measurement is performed on undialyzed blood.

4. Stop the blood pump and complete the patient disconnection procedure as per dialysis unit protocol.

Stop pump sampling technique.

3. Immediately stop the blood pump.
4. Clamp the arterial and venous blood lines. Clamp the arterial needle tubing.
5. Blood for postdialysis BUN measurement

may be sampled by needle aspiration from the arterial sampling port closest to the patient. Alternatively, blood may be obtained from the arterial needle tubing after disconnection from the arterial blood line and attaching a vacutainer or syringe without a needle.

6. Blood is returned to the patient and the patient disconnection procedure proceeds as per unit protocol.

Successful application of the slow flow/stop pump sampling technique has several advantages. There is minimal technical variability between blood drawing sessions, so that the calculation of the delivered dose of hemodialysis is impacted less by this operation. Therefore, longitudinal comparisons of hemodialysis adequacy more accurately reflect delivered dialysis dose. Furthermore, the use of a single-pool model for formal urea kinetic modeling mandates that postdialysis BUN be measured without the effects of access recirculation and before a significant amount of urea rebound has occurred. The relatively precise timing of the blood sampling (shortly after the cessation of hemodialysis) meets this requirement by minimizing the confounding effects of urea rebound.¹⁹⁹ Lastly, the two recommended formulae for converting the single-pool value of Kt/V to a double-pool measurement require that the postdialysis BUN sample be obtained before urea rebound is completed (see Guideline 2: Method of Measurement of Delivered Dose of Hemodialysis).

There are modest challenges associated with the use of the slow flow/stop pump sampling technique, especially the relative precision required in timing the blood draws and setting the blood and dialysate pumps. Some members of the Work Group expressed concern that in busy hemodialysis units, where the healthcare team is performing multiple tasks at the completion of dialysis, the rigor needed to execute the slow flow/stop pump sampling technique cannot be provided routinely. In addition, the necessity that the slow flow/stop pump sampling technique blood samples be drawn from the arterial port or the arterial needle tubing increases the likelihood of error. Nevertheless, the reproducibility of this technique and its support of the formulae to calculate Kt/V greatly outweigh these potential operational issues.

The HD Adequacy Work Group recognizes the widespread use of an alternative method of postdialysis BUN sampling, the blood reinfusion sampling technique, in which the postdialysis BUN sample is drawn after the patient's blood has been completely reinfused. It is much less reproducible than the slow flow/stop pump sampling technique. The HD Adequacy Work Group identified several potential limitations with this technique. These are:

1. Based on the experience of the Work Group members, it takes at least 5 minutes to return a patient's blood at the end of hemodialysis. Therefore, the blood reinfusion sampling technique allows for the postdialysis BUN sample to be obtained after resolution of cardiopulmonary recirculation (which takes 2 to 3 minutes).^{197,198} By this time, some urea rebound has occurred secondary to compartment equilibration. In effect, the postdialysis BUN sample is a partially equilibrated determination and has a higher BUN level. This relative inaccuracy in V will work in the patient's favor, ie, the measured Kt/V and URR will be lower than they would be otherwise.

2. Obtaining the postdialysis BUN by the blood reinfusion sampling technique does not meet the rigorous requirements of the single-pool, variable volume model of urea kinetics. This is because the BUN obtained ≥ 5 minutes after the completion of hemodialysis is a partially equilibrated sample.

3. The highly variable time necessary to reinfuse the patient's blood between different dialysis sessions, and the lack of uniformity of reinfusion times by different caregivers, introduces unacceptable variability in the postdialysis BUN. The variable time necessary to perform blood reinfusion from different dialysis sessions means that variable amounts of rebound will have occurred.¹⁹⁸ Indeed, variability in the timing of blood reinfusion may introduce enough variation in the postdialysis BUN results to make it difficult to interpret changes in Kt/V or URR. Although this inaccuracy is in the patient's favor because the measured Kt/V and URR will be lower than the unequilibrated values, continuous quality improvement efforts and longitudinal comparisons of delivered dialysis dose will be much less rigorous.⁶³ However, for patients re-

ceiving hemodialysis characterized by a high K/V, who therefore are at risk for significant urea rebound, the blood reinfusion sampling technique partially compensates for the reduced effective delivered dose of hemodialysis, attributable to single urea pool underestimation of the postdialysis BUN.

4. The HD Adequacy Work Group noted that the saline reinfused into the patient at the end of the treatment (approximately 150 to 500 mL, depending upon the volume of the hemodialyzer and blood lines and the rinsing protocol in use) will dilute the plasma and can lower the postdialysis BUN concentration. The extent of lowering may be insignificant if the patient is large. However, for small patients, with a relatively diminished intravascular distribution volume for urea, the impact of the saline infusion can be noteworthy.

The principal advantage of the blood reinfusion sampling technique for obtaining the postdialysis BUN sample is its relative simplicity, which reduces the likelihood of operational error. Unlike the slow flow/stop pump sampling technique, it is not necessary in the blood reinfusion sampling technique for the postdialysis BUN sample to be drawn with the blood pump, dialysate pump, and ultrafiltration controller or TMP/UFR rate at precise settings. Similarly, critical timing and location of the blood draw, the cornerstones of the slow flow/stop pump sampling technique, are not required for the blood reinfusion sampling technique. For example, because the extracorporeal circuit no longer exists after blood reinfusion, the postdialysis blood sample does not have to be drawn from the arterial sampling port or arterial needle tubing. However, based on experience, the Work Group found these issues to be of little concern, if the step by step approach that we have described for the slow flow/stop pump sampling technique is followed.

The HD Adequacy Work Group recognizes that hemodialysis facilities using the blood reinfusion sampling technique to obtain their postdialysis BUN samples may have Kt/V and URR

values that are systematically lower than dialysis units using the slow flow/stop pump sampling technique, even when the amount of delivered dialysis is the same.¹⁹⁵ In addition, because the postdialysis BUN is higher with the blood reinfusion sampling technique, the NPCR will be relatively lower when the blood reinfusion sampling technique is used. Continuous quality improvement initiatives that use the delivered dose of hemodialysis and the NPCR as clinical performance measurements must realize that apparent performance differences between patients and facilities may be due solely to differences in the blood sampling method alone.⁶²

GUIDELINE 9

Standardization of BUN Sampling Procedure (Opinion)

Hemodialysis facilities should adopt a single BUN sampling method. If several different methods are used, the sampling method should be routinely recorded. The sampling method used for a given patient should remain consistent. The predialysis and postdialysis BUN samples for a given patient should be processed in the same batch analysis at the laboratory.

Rationale Implementing a standardized protocol for blood sampling within each hemodialysis facility will promote reproducibility of the measured hemodialysis dose. The use of consistent methodology for a given patient permits longitudinal analysis of treatment effectiveness. In addition, rigor in sampling procedures greatly enhances quality assurance programs related to the dose of hemodialysis.

The HD Adequacy Work Group notes that inaccurate measures of hemodialysis adequacy also can result from improper processing of the BUN samples after they are drawn. Interassay variability in the laboratory measurement of BUN is approximately 3%. This variability can be minimized by requesting that all predialysis and postdialysis BUN samples from a given patient be processed in the same batch analysis at the laboratory.

IV. Hemodialyzer Reprocessing and Reuse

GUIDELINE 10

Use of the Association for the Advancement of Medical Instrumentation (AAMI) Standards and Recommended Practices for Hemodialyzer Reprocessing (Opinion)

When hemodialyzers are reused, they should be reprocessed following the *Association for the Advancement of Medical Instrumentation (AAMI) Standards and Recommended Practices* for reuse of hemodialyzers,⁷⁶ with the exception of the AAMI guideline regarding baseline measurement of the total cell volume (see Guideline 11: Baseline Measurement of Total Cell Volume).

Rationale For economic reasons, reuse of hemodialyzers is a prevalent practice in the United States.^{12,66,70,71} Seventy-three percent of the hemodialysis units in the United States reprocessed dialyzers in 1995. Among dialysis units that reprocess dialyzers, the median of the average number of reuses has increased from 9 in 1986 to 14 in 1994. The median of the maximum number of reported reuses has increased from 23 to 30 over the same interval.⁷¹ Data describing the prevalence of dialyzer reuse among pediatric hemodialysis patients are not available. Recent retrospective information about the impact of dialyzer reuse on the mortality of dialysis patients has been published.^{15,200} These data report a 10% increase in the risk of death among patients who used hemodialyzers reprocessed in selected hemodialysis settings and with the use of certain germicides.¹⁵ It is noteworthy that this report did not control for differences in patient comorbidity or hemodialysis adequacy. Furthermore, this reported finding of increased risk of death has not been observed consistently, even with uniform data set extraction and risk modeling.²⁰⁰⁻²⁰³ To date, no prospective, randomized controlled trial of hemodialyzer reuse has been performed.

A thorough examination of the data concerning the impact of reused dialyzers on patient safety was beyond the scope of the HD Adequacy Work Group. Therefore, the Work Group cannot endorse or condemn the practice of hemodialyzer reuse. However, the impact of reprocessing on dialyzer performance was evaluated and addressed. The Work Group found evidence that hemodialyzer performance, measured as blood

side urea clearance,²⁰⁴⁻²⁰⁶ and the delivered dose of dialysis may decline as a result of dialyzer reuse.⁷² Urea clearance decreased as the number of reuses increased. An extreme example is offered in a study examining polysulfone high flux hemodialyzers reprocessed with formaldehyde and bleach in which urea clearance decreased at least 20% by 10 reuses, even though conventional AAMI dialyzer practices were followed.²⁰⁴ This finding has not been observed universally.²⁰⁵ Furthermore, in a prospective survey of 34 hemodialysis facilities, a correlation was found between the number of dialyzer reuses and the delivered Kt/V. Although the prescribed Kt/V was identical for the high reuse (mean of 13.8) and low reuse (mean of 3.8) groups, the delivered Kt/V for each of the two groups was 1.05 and 1.1, respectively. The Work Group was particularly concerned by the apparent dialysis center-specific effect of reuse on delivered Kt/V, suggesting that the process of hemodialyzer reuse and/or its monitoring may be problematic.

Therefore, the Work Group recommends that hemodialysis facilities who choose to reuse hemodialyzers follow the AAMI recommendations for reprocessing, with the exception of the AAMI recommendation regarding baseline measurement of total cell volume (see Guideline 11: Baseline Measurement of Total Cell Volume). They should remain alert to the possibility that reuse may adversely affect adequacy of the delivered hemodialysis dose. The AAMI recommendations describe practical reuse procedures that have been adopted by the Health Care Financing Administration (HCFA).^{76,207} These recommendations were prepared by a panel of experts and represent the best guidance available on dialyzer reuse procedures.

GUIDELINE 11

Baseline Measurement of Total Cell Volume (Evidence)

If a hollow fiber dialyzer is to be reused, the total cell volume (TCV) of that hemodialyzer should be measured prior to its first use. Batch testing and/or use of an average TCV for a group of hemodialyzers is not an acceptable practice.

Rationale The essential function of a hemodialyzer is to permit the mass transfer of sol-

utes from the patient's blood into the dialysate in order to deliver the prescribed hemodialysis treatment. The solute transport capacity or clearance of a hemodialyzer is a critical variable in writing a hemodialysis prescription and in delivering an adequate treatment. For this reason, the dialysis care team needs an accurate assessment of the solute clearance of the hemodialyzer. In the absence of direct measures of solute clearance, changes in the TCV, also described as the fiber bundle volume (FBV), have been shown to be an adequate index of changes in solute transport characteristics for hollow fiber dialyzers^{74,75,208} (see Guideline 13: Minimum Required Total Cell Volume). The TCV is equal to the volume of saline necessary to fill the blood compartment of the hemodialyzer.

There is considerable variability between the in vitro and in vivo urea clearance of hemodialyzers.¹³⁰ The TCV can vary by 8% to 10% from the TCV stated by the manufacturers.¹³¹ In addition, there is lot-to-lot variability and hemodialyzer-to-hemodialyzer variability within a single lot. Therefore, the HD Adequacy Work Group considered it inappropriate to rely only upon the manufacturer's published TCV alone. The alternative practice recommended by AAMI of averaging the pre-processing volume of approximately 10 hemodialyzers and using this value for the TCV is also unacceptable. For example, if an individual hemodialyzer has a relatively large pre-processing TCV, and this is unappreciated because of the use of a lot average TCV that is lower than the true value for this dialyzer, use of the dialyzer may not be discontinued at the appropriate time. Measurement of TCV prior to hemodialyzer use is recommended in order to provide a baseline value for subsequent monitoring and evaluation of the performance of each individual dialyzer. The Work Group suggests that the actual TCV of each dialyzer be measured. Thus, although the AAMI recommendations permit batch testing and/or the use of an average TCV for a group of dialyzers, it is the opinion of the Work Group that these practices are not acceptable.

GUIDELINE 12

Monitoring Total Cell Volume (Evidence)

During each reprocessing, the total cell volume (TCV) of reused dialyzers should be checked.

Rationale Because of the clotting of individual hollow fibers within a dialyzer, TCV may decline after use. Assuming no change in the geometry and/or permeability of the dialyzer's membrane, a reduction in the TCV may be associated with reduced solute clearance and a decline in the delivered dose of hemodialysis.^{72,204-206,209} Although routine monitoring of the delivered dose of hemodialysis is the gold standard for assessing the performance of a hemodialyzer, it is likely that the solute clearance rate (KoA) of a hemodialyzer could decline significantly in the interval between measures of hemodialysis adequacy and therefore go unrecognized. The use of a surrogate measure for the hemodialyzer's potential performance, such as the TCV, after each use and reprocessing will help clarify the safety of continuing to reuse the hemodialyzer.⁷³

It is noteworthy that a case report describes that careful monitoring of TCV did not preclude the reuse of hemodialyzers having unacceptable clearance characteristics.²⁰⁹ This situation may arise because the in vitro measure of TCV may mask the intradialytic loss of fibers secondary to thrombosis. The procedure sequence for dialyzer reprocessing mandates flushing the dialyzer with a pressurized solution to displace any clots from the lumen of the fibers. Because the TCV is measured thereafter, the loss of fibers during hemodialysis will not be appreciated. Using a novel dilution technique for in vivo determination of FBV, conventional volumetric measurements of TCV were observed to be substantially greater.²¹⁰

GUIDELINE 13

Minimum Required Total Cell Volume (Opinion)

Dialyzers having a total cell volume (TCV) <80% of original measured value should not be reused.

Rationale Solute clearance must be maintained within acceptable limits to ensure that hemodialysis is adequate. The use of a hemodialyzer with reduced clearance without appropriate

compensatory changes in other components of the dialysis prescription (such as increasing dialysis time) will reduce the delivered dose of hemodialysis. Therefore, it is necessary to monitor the TCV and define a threshold TCV at which use of reprocessed dialyzers is discontinued.

Because the relationship between the decline in TCV and solute clearance is nonlinear, the decrease in TCV must be evaluated relative to the original volume of the hemodialyzer. Small reductions in TCV may not significantly reduce dialyzer clearance. If the residual TCV of a hollow-fiber dialyzer is 80% of the hemodialyzer's original TCV, it is estimated that the relative decrease in urea clearance will be approximately 10%.⁷³ Reductions in TCV of more than 20% from the original baseline TCV compromises the effectiveness of the hemodialyzer and, thus, may affect the adequacy of the hemodialysis treatments.^{*,208}

RECOMMENDATIONS FOR RESEARCH

1. With continued economic pressure to reuse hemodialyzers, more research needs to be done

regarding the association between dialyzer reuse, hemodialyzer performance, and patient safety. The HD Adequacy Work Group believes that an observational analysis that controls for comorbid factors, the delivered dose of hemodialysis, and reprocessing techniques would be useful to clarify the safety of current hemodialyzer reuse procedures. Such an analysis is currently underway by the USRDS, and results are expected to be available soon.

2. The HD Adequacy Work Group recommends that further studies be performed to develop a better measure of dialyzer performance than TCV.

3. Data on the rate of hemodialyzer performance failure as a cause of inadequate dialysis dose should be collected, specifically:

- Frequency of hemodialyzer performance failure as a cause of inadequate dialysis dose.
- Effect of reductions in TCV on the solute clearance of hemodialyzers made by various manufacturers.
- Clarification of the relationship between the number of reuses and dialyzer clearance, by brand.
- Impact of reduced TCV on the clearance of high-flux hemodialyzers.

* Pages 106-107 of *The Association for the Advancement of Medical Instrumentation (AAMI) Standards and Recommended Practices* for reuse of hemodialyzers detail the relationship between TCV and dialyzer clearance.⁷⁶

V. Hemodialysis Dose Troubleshooting

GUIDELINE 14

Inadequate Delivery of Hemodialysis (Opinion)

If the delivered Kt/V falls below 1.2, or the URR declines to <65%, on a single determination, at least one of the following actions should be performed:

1. Investigate potential errors in the delivery of the prescribed hemodialysis dose (see Table I-5);
2. Empirically increase the prescribed dose of hemodialysis; and/or
3. Suspend use of the reprocessed hollow fiber hemodialyzer.

The impact of these corrective interventions should be followed by performing more frequent measurements of Kt/V or URR.

Rationale Every effort should be made to ensure that patients receive adequate hemodialysis at each treatment (see Guideline 4: Minimum Delivered Dose of Hemodialysis). Whenever the delivered dose of dialysis falls below the minimum acceptable level ($Kt/V = 1.2$ or $URR = 65\%$), a systematic investigation should be initiated promptly to identify why the delivered dose has declined to that level. The HD Adequacy Work Group developed an algorithm (see Table I-5) that can be used to identify the causes of inadequate delivery of hemodialysis and to implement corrective actions. The algorithm is based on the following assumptions:

1. It is unrealistic to expect dialysis care teams to immediately identify and correct problems

that result in inadequate hemodialysis. Some delay in identifying a problem typically will occur. For example, with routine blood sampling, there is usually a delay of several days to 1 week between blood sampling and the delivery of the lab report that signals a problem. Over that interval, up to three hemodialysis treatments will have occurred. There will be additional delays as the potential causes of the problem are investigated. A prompt corrective response will minimize inadequate treatments.

2. More frequent measurements of Kt/V or URR will assist in identifying the problem(s), the underlying cause(s), and the necessary corrective action(s).

3. Hemodialysis units and clinicians should strive to categorize failures and to identify specific causes, eg, procedural errors by staff, equipment problems, deficient reprocessing techniques/systems, patient nonadherence, etc.

4. Increasing the prescribed hemodialysis dose until appropriate minimum targets are reached will improve patient outcomes.

5. Inadequate performance of reprocessed dialyzers may be associated with reductions in the delivered dose of hemodialysis.^{72,204-206,209}

6. Prudent clinical judgment requires that use of a potentially inadequate hemodialyzer be suspended until the specific etiology of the insufficiency of delivered dose can be identified. If other factor(s) explaining the deficiency are identified, the dialyzer can be returned to use.

Table I-5. Error Analysis for Deficiencies in Delivered Kt/V or URR

Because of the complexity and technological nature of the hemodialysis procedure, deviations from the prescription may occur. It is important to evaluate potential technical problems that may result in significant deviation(s) between the prescribed and delivered dose. For this reason, a clinical algorithm has been developed to assist in the elucidation of potential technical problems. The algorithm has been organized such that the initial assessments focus on elements of the dialysis treatment that can be evaluated immediately using available information and without additional costs. A second level of assessments includes techniques or investigations which may be invasive, require more time, or incur costs to the dialysis center and/or patient (see Appendices E and F).

When investigating potential technical problems, it is useful to remember that there are four primary treatment variables that determine the actual delivered Kt/V. These include the clearance of hemodialyzer, treatment duration, and the flows of blood and dialysate. Any of these elements may vary for a given hemodialysis treatment. Therefore, small deviations in delivered Kt/V are common and should be evaluated within the constraints of time. Significant underdelivery of the hemodialysis prescription by >20% should initiate attempts to determine the cause(s). Errors that contribute to an apparent delivery of hemodialysis that is significantly greater than prescribed should also be investigated. Since the response of many dialysis care teams is to actively decrease the dose of hemodialysis by prescribing less hemodialysis, erroneous reports of overdelivery of this sort are potentially dangerous.

Error analysis algorithm

Initial Assessments Elements of hemodialysis treatment* to evaluate/correct immediately. These elements can be assessed noninvasively, using available data, and/or without incurring cost.

Clearance (K) less than assumed. Elements of the hemodialysis procedure affecting clearance include: dialyzer permeability (KoA), effective dialyzer surface area, blood flow, and dialysate flow.

1. Assess fistula integrity to determine if there may be recirculation.
 - Perform hydraulic compression test during next dialysis.
 - Review A/V needle placement, proximity, and orientation with patient care staff and patient.
 - Verify graft flow configuration.
2. Review written documentation of hemodialysis treatment when Kt/V or URR was measured.
 - Review hemodialyzer reuse log to evaluate total cell volume (TCV).
 - Review maintenance log for machine to check last calibration date and results.

- Review hemodialysis log to compare prescribed versus actual parameters, including:
 - a. Recorded blood flow rate (Q_b)
 - b. Dialysate flow rate (Q_d)
 - c. Type of hemodialyzer
 - d. Extracorporeal pressures compared to previous sessions with prescribed Q_b
 - Were prepump arterial pressures 200 mmHg?
 - Were prepump arterial or venous pressures close to upper limit per dialysis unit policy?
- Review dialysis log for clinical events, eg, hypotension, muscle cramps or chest pain that may have resulted in a change in treatment parameters (blood flow).

Effective hemodialysis treatment time (T_d) less than prescribed. Hemodialysis treatment time is the total time at the prescribed blood and dialysate flow rates with the prescribed dialyzer, or is the dialysis time determined to provide an equivalent Kt/V at the prevailing blood and dialysate flow rates for a particular hemodialyzer.

1. Review written documentation of total duration of the dialysis treatment for determination of any of the following:
 - Patient arrived late for hemodialysis treatment

* The hemodialysis care team should note that list is not all-inclusive. However, the elements provided are the most common sources of error.

Table I-5. (Cont'd)

- Facility/staff late starting dialysis without compensatory extension of time
- Patient requested early termination of hemodialysis treatment
- Clinical events (eg, hypotension, muscle cramps, chest pain, etc) that may have caused premature discontinuation or interruption of hemodialysis
- Hemodialyzer blood leak
- Needle problems or need for recannulation of angioaccess
- Extracorporeal pressures close to alarm limits

Errors in blood sampling or processing for BUN Concentration.

Predialysis BUN sample concentration is low.

- Check with patient care provider about whether needles were saline-filled or if blood sample was drawn after initiation of dialysis.
- Consider asking lab to rerun sample.

Postdialysis BUN sample concentration is high.

- Review with patient care staff whether the postdialysis blood sample was drawn at end of dialysis or after reinfusion of blood.

Secondary Assessments Evaluation of these elements of hemodialysis treatment requires further investigation. These investigations may be invasive, require more staff time or equipment maintenance, and/or are cost generating.

Clearance (K) less than assumed.

1. If hydraulic compression test is positive, perform measurement of recirculation in fistula using slow flow/stop pump sampling technique.⁵¹
2. Determine if dialyzer clearance is overestimated by reviewing urea kinetic modeling

results on other patients using same dialyzer model and same prescribed Kt/V.

3. Review dialyzer clotting. May warrant review of anticoagulation protocol.
4. Determine if blood pump calibration was inaccurate by reviewing kinetic modeling results on other patients using same equipment.
5. Review hemodialysis log for extracorporeal pressures (particularly prepump arterial pressure) for values ≥ 200 mmHg.
6. For delivery systems with computers, review the total liters of blood processed.
7. Empirically recalibrate blood pump and dialysate flow rate.

Effective hemodialysis treatment time (Td) less than prescribed.

1. Review patient arrival time in unit and transportation needs.
2. Evaluate repetitive early termination with patient and patient care staff.
3. Review understanding of treatment components with patient and patient care staff.

Errors in sampling or processing for BUN concentration.

Postdialysis BUN sample concentration is low (Kt/V is significantly greater than prescribed).

- Review sampling procedure with patient care staff with focus on the following areas:
 - a. Using slow flow/stop pump sampling technique for postdialysis BUN sampling to avoid recirculation contamination
 - b. Avoiding sample dilution from saline reinfusion before sampling
 - c. Preventing sampling from venous instead of arterial bloodline

Repeat predialysis and postdialysis BUN sampling to determine Kt/V or URR.

VI. Maximizing Patient Adherence to the Hemodialysis Prescription

GUIDELINE 15

Optimizing Patient Comfort and Adherence (Opinion)

Without compromising the delivered dose of hemodialysis, efforts should be undertaken to modify the hemodialysis prescription to prevent the occurrence of intradialytic symptoms that adversely affect patient comfort and adherence.

Rationale Based on clinical experience, the HD Adequacy Work Group recognizes that a major barrier to providing adequate hemodialysis is patient nonadherence. Patients may confound attempts to provide an otherwise adequate treatment by missing hemodialysis sessions, arriving late for treatments, temporarily interrupting the treatment, or leaving the hemodialysis session prematurely.^{32,53,54,77,78,113,211} The reasons for patient nonadherence can be varied. Hence, an assessment by the dialysis care team should be undertaken to determine the cause(s); interventions should be planned and executed accordingly. The Work Group was impressed by the number of patients reported to have discontinued hemodialysis treatments prematurely because of complications occurring during the treatment. In a large observational study of this problem, 55% of the premature terminations were because of medical reasons.⁷⁷ Within this category, 70% were because of cramps, 48% were a consequence of feeling sick, and 15% were secondary to symptomatic hypotension. Intradialytic hypotension and/or cramps thus can adversely affect the delivered dose of hemodialysis.

Because of physical discomfort associated with hemodialysis treatments, many patients miss sessions more often and/or terminate their dialysis sessions prematurely.^{77,114,193} Hemodialysis adequacy is further compromised by the response that is taken when these adverse symptoms occur. Many hemodialysis healthcare teams respond to hypotensive or cramping patients by decreasing the blood flow and ultrafiltration rate. In this situation, the patient may receive less than the prescribed hemodialysis dose and not meet the ultrafiltration goal. Lastly, protracted hypotension during a hemodialysis session may exaggerate urea rebound.¹⁷⁸ Therefore, if possible, repeated symptomatic hypotension and cramps should be avoided.

Some members of the Work Group were especially concerned about the clinical practice of routinely and deliberately provoking hypotension to operationally define a patient's estimated dry weight (EDW).*

The literature does not support the notion that hypotension is a reasonable clinical indicator of the achievement of EDW. Based on invasive measures of intravascular volume, such as right heart catheterization with or without pulmonary capillary wedge measurements, patients who are hypotensive during hemodialysis may be intravascularly euvoletic, hypovolemic, or hypervolemic.²¹²⁻²¹⁵ This finding is not surprising in view of the contradictory literature describing the association between intravascular volume, intradialytic hypotension and/or cramps, and the volume of fluid removed.²¹⁶⁻²²¹

The Work Group was unable to find a practical clinical measure of EDW. Typically, the degree of volume expansion is defined historically. It is based on the increase of the patient's weight above the value at discharge from the previous hemodialysis session. However, this assumes that the previous discharge weight was appropriate. For many patients, this assumption is incorrect.²¹⁶ For example, the historical EDW may change because of unappreciated alterations in the patient's nutritional status. Alternatively, the historical dry weight may have been erroneous but well tolerated.^{213,215}

In view of the difficulty in establishing a value for EDW, and considering the deleterious consequences of hypotension and cramps on the delivery of hemodialysis, the Work Group suggests that clinicians modify the dialysis prescription for patients whose hemodialysis treatments are frequently complicated by intradialytic hypotension and cramps (as suggested in Guideline 16: Strategies to Minimize Hypotensive Symptoms).

RECOMMENDATIONS FOR RESEARCH

The Work Group suggests that efforts be undertaken to develop accurate, but practical methods

* For the purpose of this guideline, EDW is the target postdialysis weight at which the patient has intravascular euvoolemia.

of measuring intravascular volume during hemodialysis and of relating these changes to blood pressure measurements.

GUIDELINE 16

Strategies to Minimize Hypotensive Symptoms (Evidence)

Without compromising the delivered dose of hemodialysis, efforts should be undertaken to minimize intradialytic symptoms that compromise the delivery of adequate hemodialysis, such as hypotension and cramps. These efforts may include one or more of the following:

1. Avoid excessive ultrafiltration.
2. Slow the ultrafiltration rate.
3. Perform isolated ultrafiltration.
4. Increase the dialysate sodium concentration.
5. Switch from acetate to bicarbonate-buffered dialysate.
6. Reduce the dialysate temperature.
7. Administer midodrine predialysis.
8. Correction of anemia to the range recommended by NKF-K/DOQI Anemia Guidelines.
9. Administer supplemental oxygen.

Rationale Clinicians have an obligation to minimize discomfort associated with hemodialysis treatments without compromising the efficacy of the treatment. Symptomatic hypotension and cramps during hemodialysis are well-documented causes of patient discomfort as well as of early termination of dialysis therapy.^{77,114} Therefore, efforts should be made to minimize the occurrence of hypotension and cramps by modification of the hemodialysis prescription. The HD Adequacy Work Group reviewed several relatively simple strategies that can be implemented in most hemodialysis units to attenuate these intradialytic complications.

Ultrafiltration changes. Severe recurrent hypotension and cramps should prompt a review of the current EDW. As stated earlier, hypotension cannot be used to define intravascular volume.^{192,212-215} Therefore, the dialysis care team should reevaluate the current EDW.^{214,216} A clue that the EDW may be too low is a history of an increased dietary intake accompanied by biochemical signs of improving nutrition (increasing serum albumin and/or creatinine concentra-

tion, and/or NPCR) in the presence of hypotension.

Both the ultrafiltration volume and the rate of ultrafiltration greatly affect blood pressure.^{213,215,216} Patients with excessive weight gain should be encouraged to decrease their fluid intake. Alternatively, if the large fluid intake is a consequence of robust food intake,²²⁴ the duration of the hemodialysis treatment should be extended so that the hourly ultrafiltration rate is lower. Lastly, ultrafiltration can be segregated temporally from diffusive clearance by performing sequential ultrafiltration/clearance.²²⁵⁻²²⁹ Ultrafiltration alone results in a prompt and appropriate increase in stroke index, cardiac index, pulmonary artery wedge pressure, and mean arterial pressure.²²⁵ However, if this strategy is used to attenuate intradialytic hypotension and cramps, the total duration of hemodialysis must be extended so that compensation is made for the time lost for diffusive clearance.

Dialysate modifications. The dialysate solute concentration can also be manipulated to attenuate the likelihood of intradialytic hypotension and cramps. Increasing the dialysate sodium concentration (≥ 148 mEq/L), especially early in the dialysis session, followed by a continuous or stepwise decrease later in the treatment ("sodium ramping") is a simple and effective means of ameliorating intradialytic hypotension and cramps.²³⁰⁻²³⁵ These interventions may be associated with increased weight gain and variable increase in interdialytic blood pressure.²³⁵

Conversion from an acetate-containing dialysate to a bicarbonate-containing dialysate will also minimize hypotension and cramps.^{215,237-240} In addition to a beneficial effect on blood pressure, the use of bicarbonate results in fewer headaches and less nausea and vomiting.²³⁹ Acetate contributes to the occurrence of hypotension by inappropriately decreasing total vascular resistance and increasing venous pooling and myocardial oxygen consumption.²³⁷

Reducing the dialysate temperature from 37°C to 34-35°C increases peripheral vasoconstriction and cardiac output, thereby reducing the occurrence of hypotension and accompanying symptoms.²⁴¹⁻²⁴⁶ This benefit is achieved secondary to increased sympathetic tone.²⁴⁷ In one study, decreasing the dialysate temperature to 35°C de-

creased the incidence of symptomatic hypotension from 44% to 34%.²⁴⁸ The benefit was greatest for patients with frequent episodes of hypotension²⁴⁹ and those with baseline mild hypothermia (tympanic membrane temperature $<36^{\circ}\text{C}$).²⁴⁹ This intervention is beneficial even in patients who have excessive weight gains.²⁴⁷ Cold dialysis does not compromise urea clearance or increase urea rebound,^{242,246} but does induce mild to intolerable symptomatic hypothermia in some patients.^{244,248,249}

Alternative strategies. Ingestion of the oral, selective α_1 -adrenergic agonist, midodrine, has been demonstrated to minimize intradialytic hypotensive events, raise the lowest intradialytic blood pressure, decrease interventions for hypotension, and reduce intradialytic hypotensive symptoms.²⁵⁰⁻²⁵³ When administered within 30 minutes of the initiation of hemodialysis, midodrine raises blood pressure by increasing peripheral vascular resistance (arteriolar vasoconstriction) and enhancing venous return and cardiac output (venular constriction).²⁵⁴ The drug is well tolerated and associated with few side-effects. The hemodynamic benefits of hypothermic dialysis alone or in combination with midodrine, were comparable across interventions.²⁵⁰

Finally, the experience of some members of the Work Group suggests that raising the hemoglobin to ≥ 11 g/L and/or administering supple-

mental inhaled oxygen also reduces the incidence of intradialytic hypotension, especially for patients with cardiovascular or respiratory disease.

Optimizing patient behavior. Patient behavior may also influence the likelihood of intradialytic cramps and hypotension. As stated earlier, appropriately limiting fluid intake is beneficial. In addition, food intake immediately prior to or during hemodialysis causes a decrease in peripheral vascular resistance and hence may result in hypotension.²⁵⁵⁻²⁵⁷

The Work Group found the literature characterizing the impact of antihypertensive medications on the occurrence of intradialytic hypotension and cramps to be contradictory. Some studies have observed a strong correlation between the use of antihypertensive medications and hypotension,²⁵⁸ but the correlation has not been observed by other investigators.²⁵⁹ This issue should be evaluated individually for problematic patients.

The Work Group emphasizes the need to engage the patient in the process of hemodialysis care, especially regarding the issue of adherence with the hemodialysis prescription. Failure of the hemodialysis care team to properly educate patients about the value of complying with a proper hemodialysis regimen compromises the success of all the aforementioned strategies.

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VIII. Appendices

APPENDIX A: RPA GUIDELINE ORDERING INFORMATION

Copies of the RPA's *Clinical Practice Guideline on Adequacy of Hemodialysis* may be obtained by contacting:

Renal Physicians Association
4701 Randolph Road
Suite 102
Rockville, MD 20852
(301) 468-3515; (800) RPA-7525;
FAX (301) 468-3511
E-mail rpa@renalmd.org

APPENDIX B: KINETIC DETERMINATION OF THE UREA DISTRIBUTION VOLUME¹

In formal UKM, the volume of distribution of urea (V) is calculated using computational software. The kinetic determination of V is based on the assumption of a single pool of urea that is coextensive with total body water and that expands during the interdialytic interval from fluid retention and contracts during hemodialysis by ultrafiltration. Assuming a thrice weekly hemodialysis schedule, the computational software reiterates the following two formulae until unique values are found to satisfy both expressions.

$V_t =$

$$Q_f \times t \left[1 - \left[\frac{G - C_t(K + K_r - Q_f)}{G - C_0(K + K_r - Q_f)} \right]^{\frac{Q_f}{K + K_r - Q_f}} - 1 \right] \quad (1)$$

$$G = \frac{(K_r + \alpha) \left[C_0 - C_t \left(\frac{V_t + \alpha \theta}{V_t} \right)^{-\frac{K_r + \alpha}{\alpha}} \right]}{\left(1 - \left(\frac{V_t + \alpha \theta}{V_t} \right) \right)^{-\frac{K_r + \alpha}{\alpha}}} \quad (2)$$

In Formula 1, V_t is the end dialysis volume; Q_f is the rate of volume contraction during dialysis that is calculated from total weight loss during dialysis divided by the length of dialysis, t ; G is the interdialytic urea generation rate; K and K_r are the dialyzer and kidney urea clearances, respectively; and C_t and C_0 are the BUN concentrations at the end and beginning of a dialysis treatment. In Formula 2, α is the rate of interdialytic volume expansion and is calculated by the total interdialytic weight gain divided by the length of the interdialytic interval, θ .

APPENDIX B REFERENCE

1. Gotch FA: Kinetic modeling in hemodialysis, in Nissenson AR, Fine RN, Gentile DE (eds): *Clinical Dialysis* (ed 3). Englewood Cliffs, NJ, Prentice Hall, 1995, pp 156-189

APPENDIX C: ANTHROPOMETRIC DETERMINATION OF THE UREA DISTRIBUTION VOLUME

The anthropometric volume of distribution of urea may be calculated by one of several formulae derived from stature, age, and gender-specific estimates of total body water (TBW) in healthy subjects.^{1,2}

The Watson formulae are:

$$\begin{aligned} \text{[Males]: } TBW = & 2.447 + (0.09156 \times \text{age}) \\ & + (0.1074 \times \text{height}) + (0.3362 \times \text{weight}) \end{aligned} \quad (3)$$

$$\begin{aligned} \text{[Females]: } TBW = & - 2.097 \\ & + (0.1069 \times \text{height}) + 0.2466 \times \text{weight} \end{aligned} \quad (4)$$

The Hume-Weyer formulae are:

$$\begin{aligned} \text{[Males]: } TBW = & (0.194786 \times \text{height}) \\ & + (0.296785 \times \text{weight}) - 14.012934 \end{aligned} \quad (5)$$

$$\begin{aligned} \text{[Females]: } TBW = & (0.34454 \times \text{height}) \\ & + (0.183809 \times \text{weight}) - 35.270121, \end{aligned} \quad (6)$$

where TBW is total body water.

Because these formulae were derived from analyses performed in healthy adults, their general applicability to ESRD patients has been questioned. Based on measurements of total body water using bioelectrical impedance (BEI) in ESRD patients, a population-specific equation for calculating total body water was derived.³ In comparison to the Watson and the Hume-Weyers formulae, the BEI-derived formula for ESRD patients (Formula 7) correlated better with TBW as measured by BEI. Both the Watson and the Hume-Weyers formulae underestimated TBW (~7.5%), so may overestimate the delivered dose of hemodialysis.

$$\begin{aligned} TBW = & - 0.07493713 \times \text{age} \\ & - 1.01767992 \times \text{male} + 0.12703384 \times \text{ht} \\ & - 0.04012056 \times \text{wt} + 0.57894981 \end{aligned}$$

$$\begin{aligned}
& \times \text{diabetes} - 0.00067247 \times \text{wt}^2 \\
& - 0.0348146 \times (\text{age} \times \text{male}) \\
& + 0.11262857 \times (\text{male} \times \text{wt}) \\
& + 0.00104135 \times (\text{age} \times \text{wt}) + 0.0186104 \\
& \times (\text{ht} \times \text{wt}), \quad (7)
\end{aligned}$$

where Wt and ht are the patients weight and height, respectively. Males and diabetics are assigned input values of 1.0. For pediatric patients, the Mellits-Cheek formulae are⁴:

$$\begin{aligned}
\text{[Males] TBW} &= -0.927 \\
&+ (0.465 \times \text{weight}) + (0.045 \times \text{height}), \\
&\text{when height} \leq 132.7 \text{ cm.} \quad (8)
\end{aligned}$$

$$\begin{aligned}
\text{TBW} &= -21.993 + (0.406 \times \text{weight}) \\
&+ (0.209 \times \text{height}), \\
&\text{when height} > 132.7 \text{ cm.} \quad (9)
\end{aligned}$$

$$\begin{aligned}
\text{[Females] TBW} &= 0.076 \\
&+ (0.507 \times \text{weight}) + (0.013 \times \text{height}), \\
&\text{when height} \leq 110.8 \text{ cm.} \quad (10)
\end{aligned}$$

$$\begin{aligned}
\text{TBW} &= -10.313 + (0.252 \times \text{weight}) \\
&+ (0.154 \times \text{height}), \\
&\text{when height} > 110.8 \text{ cm.} \quad (11)
\end{aligned}$$

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APPENDIX D: CONTRIBUTION OF RESIDUAL KIDNEY FUNCTION ON CLEARANCE WITH THRICE WEEKLY DIALYSIS THERAPY^{1,2}

Because of the short duration of impact, urea clearance provided by residual kidney function

(Kr) contributes little to the intradialytic drop in BUN concentration (K [dialyzer clearance] $>$ K_r). However, the long interdialytic interval more fully reveals the impact of K_r , which is manifest in the predialysis BUN concentration and the normalized protein catabolic rate (NPCR). The predialysis BUN concentration is lowered, and the NPCR is reduced. When K_r is zero, the interdialytic rise in the BUN concentration is linear; if $K_r > 0$, the rise in BUN will be more shallow and curvilinear resulting from continuous kidney urea excretion. Because K_r is continuous, whereas urea clearance by hemodialysis is intermittent, the basic relationships between the components of the dialysis treatment will not be modified. Thus, when the $K_r > 0$, the interdialytic rise in BUN is more shallow; less hemodialysis is required to achieve the same predialysis BUN concentration in comparison to when $K_r = 0$.

Quantitative relationships between K_r , and the decrease in the hemodialysis dose required to achieve identical predialysis BUN concentrations in the absence and presence of residual kidney function can be developed in a simplified form for hemodialysis prescription calculations by the formula:

$$kK_r = K_t - K't$$

K and K' are the dialyzer urea clearances in the absence and presence of residual kidney urea clearance, respectively, and t is the duration of hemodialysis. In this formula, k relates K_r to the difference between K and K' , or the decrease in dialysis that is possible while still achieving the same predialysis BUN concentration that would be expected when there is no residual kidney urea clearance. k has units of L/mL/min and permits direct expression of K_r in equivalent liters of urea clearance provided by the dialyzer that can be spared. Thus, the relationship between the total dialysis dose (K_t), the dose provided by the dialyzer (K_t), and the contribution of residual kidney urea clearance (kK_r), are expressed by

$$K_t/V_t \times K_t/V_t + kK_r/V_t.$$

Routinely solving these equations requires the use of computational software.

APPENDIX D REFERENCES

1. Gotch FA: Kinetic modeling in hemodialysis, in Nissenson AR, Fine RN, Gentile DE (eds): Clinical Dialysis (ed 3). Englewood Cliffs, NJ, Prentice Hall, 1995, pp 156-189
2. Yeun JY, Depner T: Principles of hemodialysis, in Owen WF, Pereira BJG, Sayegh M (eds): Dialysis and Transplantation (ed 1). Philadelphia, PA, Saunders, 1999, pp 1-21

APPENDIX E: DETAILED ERROR ANALYSIS FOR DEFICIENCIES IN DELIVERED KT/V OR URR

Dialyzer Clearance (K) < Prescribed

Elements include: Dialyzer permeability (KoA), effective dialyzer surface area, effective blood flow, and effective dialysate flow.

Effective Dialyzer Clearance

1. Fistula/Graft Recirculation
If suspected:
 Perform hydraulic compression test during dialysis.
If positive:
 Perform Fistula/Graft Recirculation Study with low flow or stop flow technique.
If recirculation is present:
 Revise graft/fistula.
 Needle placement and orientation of needle
 Needles placed in same direction and close proximity?
If true:
 Orient staff about different needle orientation.
 Document needle placement with each dialysis.
 Verify graft flow direction.
If current knowledge is incorrect:
 Document arterial and venous limbs in chart/Kardex.
 Document A/V needle placement on flow sheet.
2. Dialyzer clearance overestimated (dialyzer permeability KoA is less than manufacturer's specifications)
If suspected:
 Check kinetic modeling results on other patients using dialyzer, specifically the kinetic volume of distribution.
If consistent finding:
 Check with manufacturer for current data.
If KoA is different:

Correct KoA in prescription and calculate new Rx with new dialyzer clearance.

3. Dialyzer effective surface area reduced

If suspected:

Check for correlation of total cell volume (TCV) with kinetic modeling results, specifically the kinetic volume of distribution.

If there is a correlation:

Document results of visual inspection of the dialyzer after dialysis.

Review and correct anticoagulation.

Review reuse procedures.

If there is an obvious problem:

Correct reuse procedures.

Add heparin to post dialysis flush and recirculation after patient is disconnected from circuit.

Errors in Blood Flow Rate (Qb)

1. Inaccurate blood pump calibration
If suspected:
 Review last record/date/data from pump calibration.
 Check kinetic results on patients using the same piece of equipment.
If calibration is inaccurate:
 Recalibrate blood pump.
2. Inadequate blood pump occlusion
If suspected:
 Review last record/date/data from pump calibration and occlusion.
 Review documented extracorporeal pressures for the dialysis.
 Review pressure specifications for occlusion of the blood pump.
 Check kinetic results on patients using the same piece of equipment.
If there appears to be a pump occlusion problem:
 Recheck/correct pump occlusion.
3. Reduced blood pump stroke volume
If suspected:
 Measure volumetric "blood" flow rates on the equipment at the extremes of extracorporeal pressures seen in the patient/unit.
 Check variability in blood tubing specifications for cross-sectional area and wall thickness.
If problem exists:
 Correct dialysis prescription for lower Qb.
 Check for prepump tubing segment collapse

with negative prepump arterial pressure.

Review documented extracorporeal pressures, especially the prepump pressures.

If problem is seen:

Correct the dialysis prescription for lower Qb.
Check blood tubing wall thickness requirements with manufacturer.

4. Error in blood pump setting—reduced or lower setting than Rx

If suspected:

Check dialysis log sheet for clinical problems/symptoms.

If present:

Reorient patient and staff to need to maintain Qb as prescribed if possible.

Check for extracorporeal pressure problems.

If present:

Consider the use of different needle gauge.

Review needle placement and orientation.

Check hematocrit and ultrafiltration requirements.

If high:

Consider larger needle gauge.

If any problems present:

Correct the dialysis prescription for a lower Qb.

Error in Dialysate Flow Rate (Qd)

1. Inaccurate dialysate flow calibration

If suspected:

Review last record/date/data on machine calibrations.

If problem:

Recalibrate.

2. Error in dialysate flow setting

If present:

Standardize documentation of Qd.

Treatment Time (t) < Rx

Effective treatment time is the actual dialysis time at the prescribed blood and dialysate flow rates.

1. Inadequate measurement method

- Automated with equipment

If problem:

Document time from equipment on dialysis log sheet.

- Manual method

If problem:

Review time measurement with staff.

Standardize measurement method and record-

ing method and form for recording.

2. Numerous treatment interruptions

If suspected:

Review dialysis log sheets for events (and duration) such as dialyzer blood leaks, needle problems, and pressure problems. *If*

problem:

Standardize documentation of events.

Standardize documentation of the amount of time lost.

Reorient patients and staff to the importance of delivering the prescribed dialysis time.

3. Early termination of treatment

If suspected:

Check for documentation and reasons of early termination.

Check for documentation of the amount of time lost.

If problem:

Review frequency of early termination with patients and staff.

Review reasons for early termination with patients and staff.

Attempt to correct depending on findings.

Unit policy.

If frequent problem:

Review unit policy and reformulate as necessary.

4. Elective shortening of treatment

If suspected:

Check for persistent late arrival of patient.

If problem:

Review data with patient and problems with shortening treatments.

Discuss risks with patient.

Evaluate transportation needs of patient.

Staff/unit convenience.

If problem:

Review data with staff and problems with shortening treatments.

Discuss risks with staff.

Review Rx importance.

Errors in BUN Concentration Predialysis BUN Sample Concentration Low

1. Saline-filled needles used

If problem:

Use dry needles for sample.

Withdraw 10 mL from fistula needle before drawing sample.

2. Sample drawn after dialysis has started

If problem:

Review proper sample procedure with staff.

3. Laboratory procedure—high BUN value extrapolated from standards (BUN values of 99 or 98 mg/dL are seen often)

If problem:

Request dilution of samples with BUN >90 mg/dL.

Postdialysis BUN Sample Concentration High

1. Sample drawn late (>5 minutes after end of treatment—urea rebound)

If suspected:

Review sampling procedure relative to unit-approved procedure.

Standardize sampling time and technique.

2. Laboratory error

If suspected:

Check calibration range on equipment.

Pre/post samples analyzed on the different equipment or apparatus run.

If problem:

Request that pre/post dialysis samples be analyzed with same equipment and on the same analytic run.

3. Bloodlines/needles reversed

If suspected:

Check graft configuration.

Check for needle placement.

If problem:

Document graft configuration for staff.

Review needle placement and orientation with staff.

Postdialysis BUN Sample Concentration Low

1. Fistula recirculation

If suspected:

Reduce Q_b to 50 to 100 mL/min before sampling.

Clear arterial bloodline/fistula needle tubing with syringe before drawing sample.

2. Sample diluted with saline from reinfusion

If suspected:

Review sampling procedure with staff.

Standardize sampling procedure.

3. Sample drawn from venous bloodline port

If suspected:

Employ methods/techniques to reduce the incidence, eg, educate patient to observe sampling period.

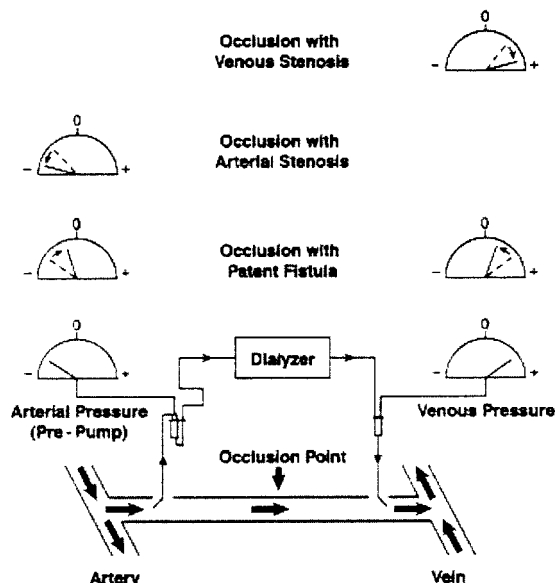


Fig 1-3. Illustration of the hydraulic pressure tests for graft assessment and the potential outcomes. During hemodialysis, prepump and postdialyzer pressures are noted and recorded. The central body of the graft is then manually occluded between the two needles. Pressure changes may be indicative of a problem. However, the absence of pressure changes does not eliminate the possibility of a problem. Reprinted with permission of American Nephrology Nurses Association.

APPENDIX F: PERFORMANCE OF HYDRAULIC COMPRESSION TEST DURING HEMODIALYSIS¹

Prepump and postdialyzer pressure changes observed with manual graft occlusion between the two needles during dialysis has been useful in identifying stenotic lesions in grafts. Prerequisites to use the hydraulic test of the graft are that: (1) the needles are oriented toward the respective vascular anastomoses; (2) the main channel of the access is cannulated; (3) prepump arterial pressure is monitored; (3) there is enough space between the needles to place 1 or 2 fingers for access occlusion; and (4) no compression of the feeder artery occurs during the occlusion. The hydraulic pressure test is performed as described.

1. During dialysis at the desired blood flow rate, extracorporeal pressures are noted and recorded.

2. The central body of the graft (between needles) is completely occluded for sufficient time to observe for any pressure changes.

3. The pressures changes are recorded.
4. If the graft is fully patent, the pressures will move towards zero with occlusion will move toward zero (arterial pressure less negative and venous pressure less positive). If an arterial stenosis is present, graft occlusion results in a significant increase in the prepump arterial pressure (becomes more negative). If no prepump arterial pressure monitor is available, observe the arterial bloodline to detect any increase in rhyth-

mic motion from the pump rotations. If a venous stenosis is present, an increase in the postdialyzer venous pressure is observed (becomes more positive). These changes are illustrated in Fig I-3.

APPENDIX F REFERENCE

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IX. Biographical Sketches of the NKF-K/DOQI Hemodialysis 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.

William Owen, Jr., MD (Work Group Chair), is the Director of Duke Institute of Renal Outcomes Research and Health Policy at the Duke University Medical Center in Durham, North Carolina, and an Associate Professor of Medicine with tenure at Duke University School of Medicine. Dr. Owen's professional career has focused on developing process measures of outcome for patients with end-stage renal disease (ESRD) and on broadening the tools for dialysis care teams to monitor relevant processes of patient care. Dr. Owen is the President-Elect of the Renal Physicians Association (RPA), a Scientific Councilor for the Warren Magnuson Clinical Center of the National Institutes of Health, a Director of the RPA/ Renal Education Foundation, a member of the Health Care Financing Administration's ESRD Clinical Performance Measure Advisory Panel, a panelist for the American Kidney Fund's African-American Early Kidney Disease Program, and a member of the Medical Advisory Board of the American Association of Kidney Patients. Dr. Owen is the recipient of several local and national awards for patient advocacy and care. As the recipient of several research grants from the National Institute of Diabetes, Digestive, and Kidney Disease, and the Agency for Health Care Policy Research, Dr. Owen is an active clinical and translational science investigator and has authored numerous original reports, chapters, and editorials.

Jimmy Roberts, MD, FACP (Work Group Vice-Chair), is a nephrologist working in private practice in Chico, California. Dr. Roberts served as Chairman of the Renal Physicians Association Working Committee on Clinical Practice Guidelines and editor of the *Clinical Practice Guideline on Adequacy of Hemodialysis*, published in 1993. He is Past President of the Renal Physicians Association and served on the RPA Board

of Directors from 1986-1998. Dr. Roberts is an Adjunct Professor of Biology at California State University in Chico, Medical Director of the Chico Dialysis Center in Chico, and an attending physician at Enloe Medical Center. Dr. Roberts is past chairman of the Board of Directors of the Transpacific ESRD Network (#17). He is actively involved in CQI programs for ESRD dialysis and transplant patients. During his career, Dr. Roberts has written more than 75 research articles, book chapters, abstracts, and letters to the editor, and has made kidney-related presentations at more than 40 scientific meetings.

Steven Alexander, MD, FAAP, is Professor of Pediatrics/Chief, Pediatric Nephrology at Stanford University Medical Center and Director of Dialysis Department/ Medical Director of Kidney Transplantation at Lucile Packard Children's Hospital. He has worked with ESRD patients for over 20 years. Dr. Alexander also serves as a Pediatric Nephrology Representative for the Health Care Financing Administrations ESRD Medical Review Criteria Expert Panel, and is a former member of the Board of Directors for the American Kidney Fund and the Renal Physicians Association. He has written more than 100 publications and is on the Editorial Board for *Peritoneal Dialysis International* and *Advances in Renal Replacement Therapy*.

David Cohen, MD, PhD, is Chief of the Renal Section at the West Palm Beach VA. In addition to his dialysis-related duties, Dr. Cohen is Chair of the Ethics Committee at the West Palm Beach VA. He is an active member of the American College of Physicians, American Society of Nephrology, and American Society of Transplant Physicians. Dr. Cohen has performed home hemodialysis on himself since 1984.

William Harmon, MD, is Chief, Division of Nephrology at the Childrens Hospital and an Associate Professor of Pediatrics at Harvard Medical School. Dr. Harmon has been involved in multiple studies designed to provide optimal treatment for children with end-stage renal disease, including both dialysis and renal transplantation. He is an active member of the North American Pediatric Renal Transplant Cooperative Study (NAPRTCS) and has been

instrumental in developing the dialysis component of that registry. He has been active in several professional societies; he is the past chairman of the NKF Pediatric Nephrology/Urology Council, served on the Board of Directors of UNOS, and is a member of the council of the American Society of Transplant Physicians.

Todd Ing, MB, FRCP(C), FRCP, FACP, joined the Hines Veterans Affairs Hospital as a nephrologist and the Loyola University Chicago Stritch School of Medicine as a faculty member in 1976, after a number of years in private practice. Committed to medical education, he is an editor of the *Handbook of Dialysis*. Topics of special interest to him include the formulation of dialysates, bicarbonate-buffered peritoneal dialysis, the first-use syndrome, peritoneal sclerosis, peritoneal fluid eosinophilia, dialysis ascites, and dialysis-associated pericarditis.

Judith Kari, MSW, LICSW, works for the Health Care Financing Administration. Ms. Kari has been working for more than 25 years to improve outcomes for ESRD patients. Her experience includes direct clinical work, research and evaluation, and work for the government and an ESRD Network. She has served as a consultant to industry and has also worked with the Egyptian government on ESRD program issues. Ms. Kari has been active in many professional societies and has served on the Board of Directors for the National Kidney Foundation.

Marcia Keen, PhD, MS, RN, is Senior Manager, Nephrology professional Services at Amgen Inc. She has been actively involved in dialysis patient care and clinical research for a number of years. Her research interests have included quantification techniques for hemodialysis and peritoneal dialysis therapy, anticoagulation control in hemodialysis, and vascular access. Her published work includes book chapters and research reports in a number of professional journals. She is a member of the Steering Committee for the National Institutes of Health-sponsored HEMO trial. She was a member of the writing committee for the RPA *Clinical Practice Guideline on Adequacy of Hemodialysis*. She completed her doctorate at

the University of California, San Francisco, in volume and osmolality control in hemodialysis patients.

Karren King, MSW, ACSW, LCSW, is a nephrology social work consultant. Previously, she was Program coordinator for the Missouri Kidney Program, where she was responsible for directing its patient education program for western Missouri for 9 years. Prior to this, she worked as a nephrology social worker for 11 years in both dialysis and kidney transplantation. Ms. King has published articles on various psycho-social aspects of kidney disease, including adherence, patient education, and rehabilitation. She is co-author of the National Kidney Foundation's Initiation or Withdrawal of Dialysis in End Stage Renal Disease: Guidelines for the Health Care Team. She also was a member of the working group that developed the Renal Physicians Association and American Society of Nephrology's Clinical Practice Guidelines on Shared Decision-Making in the Appropriate Initiation of and Withdrawal from Dialysis. Ms. King is a past national President of the Council of Nephrology Social Workers and previously served on the Board of Directors and Executive Committee of the National Kidney Foundation. She also chaired its Patients Services Committee.

Joseph Letteri, MD, is Professor of Clinical Medicine, Health Sciences Center, School of Medicine, for the State University of New York at Stony Brook in Stony Brook, New York. Dr. Letteri is also President of South Shore Renal Physicians, P.C., in Syosset, New York. He has treated ESRD patients for over 30 years and received multiple awards from the National Kidney Foundation for his work in the field, including the Presidents Award (1993), Distinguished Service Award (1990), and Hoenig Award (1987). Dr. Letteri has written more than 60 nephrology articles, and is on the editorial board of *Mineral and Electrolyte Metabolism*, *American Journal of Nephrology*, *Advances in Renal Replacement Therapy*, and *Journal of Nephrology*.

A. Peter Lundin, MD, FACP, is Medical Director of the Kings County Hospital Center Ambulatory Hemodialysis Unit and Professor of Clinical Medicine at the State University of New

York, Health Science Center at Brooklyn, New York. Dr. Lundin was a hemodialysis patient for 25 years, had been a transplant patient for 5 years, and is back on hemodialysis for the past 4 years. He served as President of the American Association of Kidney Patients. He has worked with the Health Care Financing Administration on quality assurance projects. He is involved in the teaching of medical students, residents and fellows. Dr. Lundin's current interests include quality of life and improvement of functional activity for dialysis and transplant patients. He reported an affiliation with Brooklyn Home Dialysis Training Center.

Anthony Messana, BSc, has been active within the kidney community since 1978 in the clinical, technical, and administrative areas. Mr. Messana served as President of the National Renal Administrators Association in 1991 and has worked with many other kidney community groups and associations. He has written and spoken extensively on reimbursement and operational issues for facilities and on policy and reimbursement issues related to the End-Stage Renal Disease Program.

Jean Nardini, MSN, is the Patient Care Director of the Hemodialysis Units for the Massachusetts General Hospital in Boston, Massachusetts. Ms. Nardini has been working to improve outcomes for ESRD patients for more than 25 years. She is involved with numerous professional groups. She is currently serving as President of the ANNA, is a member of the board of directors for the ESRD Network of New England, serving as its secretary since 1994, and has been an

active member of the Regional Council of Nurse Nephrology Administrators for nearly 20 years.

Keith Norris, MD, is the Vice Chair of the Department of Medicine and Director of the Clinical Research Center at the Charles R. Drew University of Medicine and Science in Los Angeles, California. He serves as a CQI and QA advisor to industry. He has over 50 publications and currently is active in research focusing on renal osteodystrophy, hypertensive kidney disease, and ESRD among minority populations. He is active in many professional societies and is the immediate Past President of the Association of Minority Nephrologists.

Gigi Politoski has more than 19 years of experience in non-profit public relations and program development. She is the current Director, Program Division of the National Kidney Foundation, Inc., in New York City. Ms. Politoski oversees the development and implementation of professional and patient education programs for the NKF in the areas of early intervention and prevention, end-stage renal disease, and organ donation and transplantation. Prior to her current position, Ms. Politoski was Communications/Marketing Director for the Foundation, a position she held since 1986. Active in many committees and boards in the kidney community, Ms. Politoski has written several articles and abstracts related to organ donation and the needs of donor families. She was also instrumental in overseeing the development of professional and patient implementation programs and resources for the NKF-K/DOQI guidelines.