K/DOQI™ Disclaimer

These guidelines are based on the best information available at the time of publication. They are designed to provide information and assist in decision making. They are not intended to define a standard of care, and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management. Variations in practice will inevitably and appropriately occur when clinicians take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every healthcare professional making use of these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation.

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FOREWORD

FROM ITS RUDIMENTARY beginnings in the 1960s, renal replacement therapy has become a lifesaving treatment that can provide end-stage renal disease (ESRD) patients with a good quality of life. As a result, the number of ESRD patients who receive renal replacement therapy has risen, and their survival has increased, but considerable geographic variability exists in practice patterns and patient outcomes. It was this realization, and the belief that substantial improvements in the quality and outcomes of renal replacement therapy were achievable with current technology, that prompted several organizations to seek to reduce variations in ESRD treatment with the goal of a more uniform delivery of the highest possible quality of care to dialysis patients. Notable among these efforts were the report on ''Measuring, Managing and Improving Quality in the ESRD Treatment Setting'' issued by the Institute of Medicine in September 1993; the ''Morbidity and Mortality of Dialysis'' report issued by the National Institute of Diabetes, Digestive and Kidney Diseases (NIDDK) in November 1993; the Core Indicator Project initiated by the ESRD Networks and the Health Care Financing Administration (HCFA) in 1993; the ''Clinical Practice Guidelines on the Adequacy of Hemodialysis'' issued by the Renal Physicians Association in December 1993; and the Dialysis Outcomes Quality Initiative (DOQI) initiated by the National Kidney Foundation (NKF) in 1995.

In keeping with its longstanding commitment to the quality of care delivered to all patients with kidney and urologic diseases, the NKF convened a Consensus Conference on Controversies in the Quality of Dialysis Care in March 1994. Following a series of nationwide town hall meetings held to obtain input into the recommendations made at the Consensus Conference, the NKF issued an ''Evolving Plan for the Continued Improvement of the Quality of Dialysis Care'' in November 1994. A central tenet of the plan was recognition of an essential need for rigorously developed clinical practice guidelines for the care of ESRD patients that would be viewed as an accurate and authoritative reflection of current scientific evidence. It was to this end that the NKF launched the ''Dialysis Outcomes Quality Initiative'' (DOQI) in March 1995, supported by an unrestricted grant from Amgen, Inc.

The objectives of DOQI were ambitious: to improve patient survival, reduce patient morbidity, improve the quality of life of dialysis patients, and increase efficiency of care. To achieve these objectives, it was decided to adhere to several guiding principles that were considered to be critical to that initiative's success. The first of these principles was that the process used to develop the DOQI guidelines should be scientifically rigorous and based on a critical appraisal of all available evidence. Such an approach was felt to be essential to the credibility of the guidelines. Second, it was decided that participants involved in the development of the DOQI guidelines should be multidisciplinary. A multidisciplinary guideline development process was considered to be crucial, not only to the clinical and scientific validity of the guidelines, but also to the need for multidisciplinary adoption of the guidelines following their dissemination, in order for them to have maximum effectiveness. Third, a decision was made to give the DOQI guideline develop-

ment Work Groups final authority over the content of the guidelines, subject to the requirement that guidelines be evidence-based whenever possible. By vesting decision-making authority in a group of individuals, from multiple disciplines and with diverse viewpoints, all of whom are experts with highly regarded professional reputations, the likelihood of developing sound guidelines was increased. Moreover, by insisting that the rationale and evidentiary basis of each DOQI guideline be made explicit, Work Group participants were forced to be clear and rigorous in formulating their recommendations. The final principle was that the guideline development process would be open to general review. Thus, the chain of reasoning underlying each guideline was subject to peer review and available for debate.

Based on the ''NKF Evolving Plan for the Continued Improvement of the Quality of Dialysis Care'' and criteria recommended by the Agency for Health Care Research and Quality (AHCRQ; formerly known as the Agency for Health Care Policy and Research [AHCPR]), four areas were selected for the initial set of clinical practice guidelines: hemodialysis adequacy, peritoneal dialysis adequacy, vascular access, and anemia. Each Work Group selected which topics were considered for guideline creation. During the DOQI guideline development process, nearly 11,000 potentially relevant published articles were subjected to evaluation, and both the content and methods of approximately 1,500 articles underwent formal, structured review. Although labor-intensive and costly, the process resulted in an intensive, disciplined, and credible analysis of all available peer-reviewed information. When no evidence existed, or the evidence was inadequate, guidelines were based on the considered opinion of the Work Group experts. In all cases the rationale and the evidentiary basis of each recommendation was stated explicitly.

Draft guidelines were then subjected to a three-stage review process. In the first stage, an Advisory Council, consisting of 25 experts and leaders in the field, provided comments on the initial draft of the guidelines. In the second stage, a variety of organizations (ESRD Networks, professional and patient associations, dialysis providers, government agencies, product manufacturers, and managed care groups) were invited to review and comment on a revised draft of the guidelines. After considering these comments and suggestions, the Work Groups produced a third draft of the Guidelines. In the final stage, this draft was made available for public review and comment by all interested individuals or parties. Following consideration of the comments submitted during this open review period, the guidelines were revised again and then published as supplements to the September and October 1997 issues of the *American Journal of Kidney Diseases* was made available on the Internet and widely distributed.

The four sets of DOQI guidelines published in 1997 addressed only part of the ''Evolving Plan for the Continued Improvement of the Quality of Dialysis Care'' adopted by the NKF in 1994. In that plan, as well as in the early DOQI prioritization process, nutrition was considered to be an important determinant of ESRD patient outcome. Consequently, a Nutrition Work Group was convened in 1997 to review the key clinical nutrition literature and to define topics for which guidelines related to the nutritional management of patients should be developed. Supported primarily by a grant from Sigma Tau Pharmaceuticals, Inc, the Nutrition Work Group began to work intensively on those topics in January 1998, and the Nutrition Guidelines that they have developed constitute this fifth set of the original DOQI guidelines.

NKF-DOQI achieved many, but not all of its goals. The guidelines have been well received and are considered by many to reflect the ''state of the art'' of medical practice in their fields. The frequency with which the DOQI guidelines have been cited in the literature and have served as the focus of local, national, and international scientific and educational symposia is one measure of their influence. The guidelines also have been translated into more than 10 languages and have been adopted in countries across the globe. In addition, DOQI has spawned numerous educational and quality improvement projects in virtually all relevant disciplines, as well as in dialysis treatment corporations and individual dialysis centers. Furthermore, the Health Care Financing Administration has responded to a Congressional mandate to develop a system for evaluation of the quality of care delivered in dialysis centers by developing a series of Clinical Perfor-

mance Measures (CPMs) based on selected DOQI guidelines.

It is encouraging that two of the ESRD Networks have developed a guideline prioritization tool and embarked on a Prioritization and Implementation Project that would link selected DOQI guidelines into the Health Care Quality Improvement Project proposed by HCFA in the ESRD Networks' most recent Scope of Work. This project would involve a collaborative effort of professional organizations, local practitioners, and patients. In fact, it is this collaborative spirit and total commitment to patient care that accounts for the success that DOQI has achieved heretofore.

As we begin the new millennium, the DOQI clinical practice guideline initiative will move forward into a completely new phase, in which its scope will be enlarged to encompass the spectrum of chronic kidney disease well before the need for dialysis, when early intervention and prevention measures can delay or prevent the need for dialysis and improve its outcomes. This enlarged scope increases the potential impact of improving outcomes of care from hundreds of thousands to millions of individuals with kidney disease. To reflect this expansion, the reference to ''Dialysis'' in DOQI will be changed to ''Disease'' and the new initiative will become known as Kidney Disease Outcomes Quality Initiative (K/DOQI).

The dissemination and implementation strategies that have proven so effective for NKF-DOQI have been adapted and expanded to reflect the new mission of K/DOQI and its multidisciplinary focus. Relevant material from the Nutrition Guidelines and future K/DOQI Guidelines will be developed into implementation tools appropriate not just for nephrology, but also the specialties most likely to encounter those at risk for chronic kidney disease early in the course of their illness, including cardiology, hypertension, diabetes, family practice, pediatrics, and internal medicine.

On behalf of the National Kidney Foundation, we would like to acknowledge the tremendous contributions of all the volunteers who gave so much of their time and effort to the success of DOQI in order to improve the quality of life and outcomes of dialysis patients. The Nutrition Guidelines extend the DOQI objectives even further into the new and broader K/DOQI goals. Since the effort that went into preparing the Nutrition Guidelines was under the aegis of the original DOQI Advisory Council and Steering Committee, these two bodies are acknowledged. The new K/DOQI Advisory Board now will assume the charge of disseminating and implementing the Nutrition Guidelines.

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Acronyms and Abbreviations List

Abbreviation	Term
a1-AG	a1-Acid Glycoprotein
aBW_{ef}	Adjusted Edema-Free Body Weight
AMA	Arm Muscle Area
APD	Automated Peritoneal Dialysis
BCG	Bromcresol Green
BCP	Bromcresol Purple
BIA	Bioelectrical Impedance Analysis
BMI	Body Mass Index, also called Quetelet's Index
BUN	Blood Urea Nitrogen
CAD	Coronary Artery Disease
CANUSA	Canada/United States Peritoneal Dialysis Study
CAPD	Continuous Ambulatory Peritoneal Dialysis
CCPD	Continuous Cyclic Peritoneal Dialysis
CoA	Coenzyme A
CPD	Chronic Peritoneal Dialysis
CrCl	Urinary Creatinine Clearance
CRF	Chronic Renal Failure (GFR less than 20 mL/min)
CRI	Chronic Renal Insufficiency (GFR less than normal but greater than 20 mL/min)
CRP	C-Reactive Protein
CVVHD	Continuous Venovenous Hemofiltration with Hemodialysis
DEI	Dietary Energy Intake
DPI	Dietary Protein Intake
DRI	Dietary Reference Intake
DXA	Dual Energy X-Ray Absorptiometry
ESRD	End-Stage Renal Disease
GH	Growth Hormone
GFR	Glomerular Filtration Rate
HD	Hemodialysis
hGH	Human Growth Hormone
IDWG	Interdialytic Weight Gain
IDPN	Intradialytic Parenteral Nutrition
IGF-I	Insulin-Like Growth Factor-I
IPAA	Intraperitoneal Amino Acids
Kt/V_{urea}	A measure of dialysis where K is the dialyzing membrane clearance, t is the time of dialysis delivered in minutes, and V_{urea} is the volume of distribution of urea
MAC	Mid-Arm Circumference
MAMA	Mid-Arm Muscle Area
MAMC	Mid-Arm Muscle Circumference
MD	Maintenance Dialysis (ie, maintenance hemodialysis or chronic peritoneal dialysis)
MHD	Maintenance Hemodialysis
NHANES	National Health and Nutrition Evaluation Survey
nPCR	Protein Catabolic Rate normalized to body weight
nPNA	Protein Equivalent of Total Nitrogen Appearance normalized to body weight
PCR	Protein Catabolic Rate
PEM	Protein-Energy Malnutrition

PNA	Protein Equivalent of Total Nitrogen Appearance
Predialysis serum	Serum obtained from an individual immediately before the initiation of a hemodialysis or intermittent peritoneal dialysis treatment
PTH	Parathyroid Hormone
RD	Registered Dietitian
RDA	Recommended Dietary Allowance
REE	Resting Energy Expenditure
RTA	Renal Tubular Acidosis
SBW	Standard Body Weight
SDS	Standard Deviation Score
SGA	Subjective Global Assessment
Stabilized serum	Serum obtained for performance of a specific measurement after the measurement has stabilized on a given dose of CAPD
SUN	Serum Urea Nitrogen
TBW	Total Body Water
TNA	Total Nitrogen Appearance
TPN	Total Parenteral Nutrition
TSF	Triceps Skinfold Thickness
UBW	Usual Body Weight
UNA	Urea Nitrogen Appearance
USRDS	United States Renal Data System
V	Volume of Distribution

Introduction

PROTEIN-ENERGY malnutrition (PEM) is very common among patients with advanced chronic renal failure (CRF) and those undergoing maintenance dialysis (MD) therapy worldwide. Different reports suggest that the prevalence of this condition varies from roughly 18% to 70% of adult MD patients. In adults, the presence of PEM is one of the strongest predictors of morbidity and mortality. However, in the poorly nourished pediatric patient, mortality is less common, and growth retardation is an additional and greater concern. Impaired linear growth persists despite ongoing renal replacement therapy with either hemodialysis (HD) or peritoneal dialysis, and improvements in linear growth after successful renal transplantation usually fail to fully correct pre-existing growth retardation unless growth hormone (GH) is administered. Although several factors contribute to the impaired skeletal growth in pediatric patients with chronic renal disease, protein and energy malnutrition play a critical role, particularly during the first few years of life. Additional factors that contribute to impaired growth in pediatric patients include anemia, acidemia, calcitriol deficiency, renal osteodystrophy, and tissue resistance to the actions of GH and insulin-like growth factor-I (IGF-I).

There are many causes of PEM in patients with advanced CRF. These include:

(a) inadequate food intake secondary to:
- anorexia caused by the uremic state
- altered taste sensation
- intercurrent illness
- emotional distress or illness
- impaired ability to procure, prepare, or mechanically ingest foods
- unpalatable prescribed diets

(b) the catabolic response to superimposed illnesses

(c) the dialysis procedure itself, which may promote wasting by removing such nutrients as amino acids, peptides, protein, glucose, water-soluble vitamins, and other bioactive compounds, and may promote protein catabolism, due to bioincompatibility

(d) conditions associated with chronic renal failure that may induce a chronic inflammatory state and may promote hypercatabolism and anorexia

(e) loss of blood due to:
- gastrointestinal bleeding
- frequent blood sampling
- blood sequestered in the hemodialyzer and tubing

(f) endocrine disorders of uremia (resistance to the actions of insulin and IGF-I, hyperglucagonemia, and hyperparathyroidism)

(g) possibly the accumulation of endogenously formed uremic toxins or the ingestion of exogenous toxins.

Notwithstanding the many causes of PEM in patients with CRF, provision of adequate nutrition is a key component of the prevention and treatment of PEM in adults and children receiving MD. These K/DOQI Nutrition Clinical Practice Guidelines provide recommendations regarding the nutritional assessment of protein-energy nutritional status and the desirable dietary energy and protein intake for adults and children undergoing MD. Guidelines were developed for children treated with MD concerning their nutritional needs for vitamins, zinc, and copper and for their treatment with recombinant human GH. Guidelines are also provided regarding the nutritional intake of L-carnitine for adult MD patients, the nutritional management of the nondialyzed adult patient with advanced CRF, and the management of the acutely ill pediatric and adult patient. For logistical reasons, recommendations for the nutritional management of nondialyzed pediatric patients with advanced CRF were not developed. The decision was made to not address vitamin and mineral needs or the use of anabolic agents in the adult MD patient, because the scope of the subject matter and the volume of scientific literature was considered to be too large for inclusion in this set of guidelines.

The guidelines are based on a structured review of the medical literature and, where insufficient evidence exists, on the expert opinion of the Work Group members. In each case, the

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guidelines are intended to serve as starting points for clinical decision making, and it is emphasized that the clinical judgment of the health care practitioner must always be included in the decision making process and the application of these guidelines. The guidelines are not to be considered as rules or standards of clinical practice. At the end of each guideline, recommendations are made for research studies that may enhance the scientific evidence base concerning the subject matter of that guideline. In keeping with the K/DOQI objectives, it is hoped that the information provided in these guidelines and the research recommendations will improve the quality of care provided to children and adults who have chronic kidney disease or are receiving chronic dialysis therapy and will stimulate additional research that will augment and refine these guidelines in the future.

The K/DOQI Nutrition Work Group expresses its indebtedness and appreciation to Thomas Golper, MD, and John Burkhart, MD, for their contributions to Guideline 27; to Tom Greene, PhD, and Thomas Depner, MD, for their assistance with the development of Appendix V; to Paul Shekelle, MD, and Erin Stone, MD, for the structured review and guidance in the guideline development process; and to Donna Fingerhut, MSEd, for the innumerable hours she devoted to the overall administration of the project. The efforts and expertise of these individuals were invaluable.

METHODS

The Guideline Development Process

CLINICAL PRACTICE GUIDELINES DEFINED

THE INSTITUTE OF Medicine has defined practice guidelines as ''systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances.'' The American Medical Association endorsed this definition by describing practice guidelines as ''systematically developed statements, based on current professional knowledge, that assist practitioners and patients to make decisions about appropriate health care for specific clinical circumstances.'' Put simply, practice guidelines constitute an effort to advise health-care providers and patients as to what constitutes optimal clinical practice, based on the best information available. As a result, practice guidelines can not only improve both quality and cost-effectiveness of care, but can also facilitate continuous improvement in clinical practice as new information becomes available.

K/DOQI GUIDING PRINCIPLES

Four principles guided decision-making in the conduct of the NKF-DOQI and will be retained for the K/DOQI guidelines:

1. K/DOQI practice guidelines will be developed using a scientifically rigorous process, and the rationale and evidentiary basis for each guideline will be clearly explained.
2. K/DOQI guidelines will be developed by multidisciplinary Work Groups with expertise in the topic of interest.
3. The Work Group members will work independently of any organizational affiliations and would have final responsibility for determining guideline content.
4. K/DOQI guidelines will undergo widespread critical review before being finalized.

EVIDENTIARY BASIS FOR GUIDELINES

The guidelines were developed using an evidence-based approach similar to the one used by The Federal Agency for Health Care Research and Quality (AHCRQ). That is, before formulating recommendations, the Work Groups reviewed all published evidence pertinent to the topics being considered and critically appraised the quality and strength of that evidence. For many issues that the Work Groups chose to address, there either was no pertinent literature available or available evidence was flawed or weak. As a result, in many instances the Work Groups formulated their recommendations based on the opinions of the Work Group members and comments received from the peer reviewers. In all instances, the Work Groups have documented the rationale for their recommendations. That is, they have articulated each link in the chain of logic they used as the evidentiary or opinion-related basis for their recommendation. This approach helps readers of the guidelines determine the quantity and quality of evidence underlying each recommendation.

Although some of the DOQI guidelines are clearly based entirely on evidence or entirely on opinion, many are based in part on evidence and in part on opinion. Such ''hybrid'' guidelines arise when some (or even most) of the links in the chain of logic underlying a guideline are based on empirical evidence, but some (ie, at least one) are based on opinion. The opinion of the Work Group members can enter the chain of logic that supports a guideline either to fill in a gap in available evidence on some scientific or clinical issue, or in the form of a value judgment regarding what they feel is appropriate clinical practice based on available evidence. Thus, many opinion-based guidelines may have substantial empirical evidence underlying them. These guidelines were developed using a seven-stage process.

Phase I: Work Group Member Selection

The DOQI Steering Committee selected a Chair to lead the Adult and Pediatric Nutrition Work Group and suggested names of individuals with particular expertise to serve on the Work Group. Final decisions on the membership of the

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Work Group were made by the Work Group Chair. In recognition of the different bodies of literature and expertise for nutrition issues in adult and pediatric ESRD and MD patients, the Work Group Chairs appointed separate nutrition Work Groups for adult and pediatric patients. Two Vice Chairs, for protein-energy nutrition and for carnitine, were appointed for the Adult Work Group, and one Vice Chair was appointed for the Pediatric Work Group.

Support for the Work Groups in coordinating and performing the systematic literature review, synthesizing data abstracted from the literature into evidence tables, facilitation of the guideline development process, conducting meetings of the Work Groups, and analyzing results of the guideline development meetings was provided by personnel from the RAND Corporation and Cedars-Sinai Medical Center. Both of these institutions are associated with the Southern California Evidence-Based Practice Center.

Phase II: Targeting

The Work Groups defined the specific topics on which guidelines would focus and the specific questions on which the systematic literature would focus. The following clinical questions were formulated:

Question 1. Which of the following measures of nutritional status best predicts patient morbidity/mortality (and growth rate in children) in MD patients?

Serum albumin, serum prealbumin, anthropometric measures (height, weight, skinfold thickness, body mass index [BMI], percent of normal body weight, percent of desirable body weight, postdialysis body weight), bioelectrical impedance (BIA), urea nitrogen appearance, serum creatinine and creatinine index, subjective global nutritional assessment (SGA), dietary diaries and interviews, serum cholesterol, serum transferrin, serum IGF in pediatric patients, protein equivalent of total nitrogen appearance (PNA/PCR), prognostic nutrition index, serum acute-phase proteins (C-reactive protein), serum alpha-1 glycoprotein, dual energy x-ray absorptiometry (DXA), a combination of more than one of these measures.

Question 2. Which of the following measures is the best diagnostic test for protein/energy nutritional status in MD patients?

Serum albumin, serum prealbumin, anthropometric measures (height, weight, skinfold thickness, BMI, percent of normal body weight, percent of ideal body weight, postdialysis body weight), BIA, urea nitrogen appearance, serum creatinine and creatinine index, SGA, dietary diaries and interviews, serum cholesterol, serum transferrin, serum IGF, PNA, prognostic nutrition index, serum acute phase proteins (C-reactive protein), serum alpha-1 glycoprotein, DXA, a combination of more than one of these measures.

Question 3. What is the effect of acid/base status on nutritional measures in MD patients?

Question 4. Which levels of intake of protein and energy in MD patients produce the following:

The lowest morbidity/mortality, the most optimum changes in nutritional status using measures from Question 1 above, positive nitrogen balance, the most optimal growth in children?

Question 5. Which levels of protein and energy intake in predialysis patients produce the lowest morbidity at the initiation of dialysis? (This question was included because of evidence that nutritional status at the onset of MD therapy is a strong predictor of nutritional status and mortality during the course of MD therapy.)

Question 6. What is the energy expenditure of MD patients during resting and other activities, and how does it compare with energy expenditure in normal individuals?

Question 7. Is interdialytic weight gain a good measure for dietary compliance or a good prognostic indicator?

Question 8. Does carnitine supplementation in adult MD patients improve morbidity or mortality?

Question 9. What are the toxic/adverse effects of L-carnitine, if any, in adult MD patients?

Question 10. Which nutritional interventions produce the lowest morbidity/mortality (and best growth in children) or the most optimum changes in nutritional status in MD patients using measures from Question 1 above?

Question 11. Does GH therapy improve growth or morbidity/mortality in pediatric MD patients?

Question 12. Does vitamin or mineral supplementation (exclusive of calcium, magnesium, and vitamin D) improve morbidity/mortality in pediatric MD patients?

Phase III: Literature Review, Selection, and Abstraction

A structured database search of two computerized bibliographic databases (MEDLINE and EMBASE) was performed with the following

specifications: *language*: English and non-English articles; *dates*: 1966 through 1997; *subjects*: human; *article types*: letters, editorials, reviews, case reports, and abstracts of meeting proceedings were excluded. The literature search was performed in collaboration with a librarian experienced in searching computerized bibliographic databases and performing ''evidence-based'' systematic reviews. *The Journal of Renal Nutrition* was hand-searched, because, at the time, it was not indexed in the bibliographic databases listed above. Additionally, referrals from DOQI Work Group members through August 1999 were reviewed.

After loading articles from MEDLINE, EMBASE, Work Group referrals, and the Sigma Tau bibliography into an electronic database, one reviewer performed an initial title review of these articles. Two independent reviewers then reviewed the abstracts of articles whose titles were selected. Selection disagreements were resolved by consensus. English language articles for which the abstracts were selected were then obtained and categorized based on the clinical question the article addressed. Two independent reviewers then reviewed these articles. Information was abstracted from the articles (see below) by one abstracter and verified by a second. Disagreements were resolved by consensus. Articles that were rejected at this stage were coded using the following codes:

R1: Editorial, letter, review, case report, article published as abstracts
R2: Article does not answer clinical question of interest
R3: Article does not have study design of interest
R4: Pediatric article (if adult section)
R5: Not human
R6: Adult article (if pediatric section)

In order to increase precision and reduce systematic errors, the language of manuscripts was not limited to English.[1,2] The English titles and English abstracts of foreign language articles, when available, were sent to all Work Group members for review. The abstracts of foreign language manuscripts were translated into English if any Work Group member thought that the paper might contribute positively to the evidence base. Selections were further based on study design. For prognostic articles, only those with prospective cohort or historical prospective cohort designs were included for further analysis. For assessment of nutritional status, only manuscripts in which a nutritional parameter was compared to a recognized standard nutritional measure or to a clinical outcome were included for further analysis. For manuscripts examining nutritional treatment, only those with a prospective design with concurrent controls were analyzed further. Because there were smaller numbers of these types of studies for carnitine treatment or pediatric renal nutrition, these requirements were not as rigidly applied for this literature.

After article abstraction (see below), evidence tables were produced from a subset of abstracted data elements and evaluated by the Work Group during meetings in Los Angeles in August 1998 (Adult Work Group), in October 1998 (Pediatric Work Group), and during a series of subsequent conference calls. The Work Group accepted or rejected articles based on the study design and methods and the adequacy with which it addressed the clinical questions. The final selected articles are indicated by an asterisk in the reference section. Other citations, that are not asterisked, were not used for guideline development, but were used to more fully explain the background or rationale for a guideline.

Critical Appraisal Method for Articles Concerning Prognosis. For each prognostic article, the following characteristics were ascertained[3]: (1) the study type; (2) the three main co-morbid conditions; (3) whether there was a representative and well-defined sample of patients at a similar phase in the course of disease; (4) the characteristics of the study population and dialysis procedures that might have affected the study results; (5) the duration of the follow-up period; (6) whether the outcomes were objective and the interpretation of the outcomes was unbiased; (7) whether adjustment was made for important known prognostic factors; and (8) the results of the study.

Critical Appraisal Methods for Articles Concerning Nutritional Assessment. For each article concerning nutritional assessment, the following information was obtained[4,5]: (1) the type of study; (2) the three main co-morbid conditions; (3) whether there was an independent blinded comparison with a reference (gold) standard; (4) the characteristics of the study population and the dialysis procedures that might have

affected the study results; (5) whether the results of the nutritional measure that was studied influenced the decision to measure the reference standard; (6) whether characteristics and variety of the patients' standard is similar to those found in dialysis centers; (7) whether the test methodology are described well enough to be reproducible; and (8) the results of the study.

Critical Appraisal Methods for Articles Concerning Nutritional Treatment. For each treatment article, the following information was obtained[6,7]: (1) the type of study; (2) the three main co-morbid conditions; (3) the Jadad quality scores[8]; (4) the randomization score; (5) the double blind score; (6) the score for whether all patients were accounted for; (7) an intention-to-treat score; (8) whether the treatment groups were similar at baseline; (9) the characteristics of the study population, dialysis procedure, and other ancillary treatment that might have affected the study results; (10) whether the treatment groups were treated similarly except for the study intervention; and (11) the results of the study.

The Jadad quality scores address issues most important in demonstrating the validity of randomized clinical trials and have been demonstrated to reflect methodological quality. Empirical evidence demonstrates that when these quality features are not met in clinical trials, bias and an exaggeration of the effect sizes often result.[8-12]

Results of the Systematic Review. The initial literature search identified 19,272 MEDLINE and 4,943 EMBASE articles. In addition, the Work Groups referred 134 articles for review, and the Sigma Tau Pharmaceutical Corporation submitted a bibliography that contained 138 additional references that were included in the analysis. Of these 24,487 references, 22,362 titles were rejected as not meeting the inclusion criteria, leaving 2,125 titles. Abstracts of these articles were reviewed and 1,021 were rejected as not meeting the inclusion criteria, thus leaving 1,104 articles. One hundred and seventy of these were foreign language articles whose titles and abstracts were sent to the Adult or Pediatric Work Groups. Of these, 102 were not selected for further evaluation. Two were selected but could not be translated, and 66 were further evaluated. Of the remaining 1,000 manuscripts (including the 66 mentioned above), 29 were unobtainable, leaving 971 to be abstracted. Of these, 640 were rejected because they were classified as an editorial, letter, review, case report, or abstract, did not answer a clinical question of relevance, did not have a valid study design, or did not involve humans. The remaining 331 articles were sent to the Adult or Pediatric Work Groups along with evidence tables for these articles created from the abstraction forms. The Work Groups rejected 81 additional articles for one or more of the same reasons indicated above, leaving 250 accepted articles.

Phase IV: Formulation of Guidelines

The group process used to develop the guidelines is a modification of the RAND/UCLA Appropriateness Method. This group process method has the following essential features: multidisciplinary, iterative, quantitative, and each panelist has equal weight in determining the final result.[13]

In conjunction with the Work Groups, RAND and Cedars-Sinai staff developed draft guidelines based on the results of the systematic review. The draft guidelines corresponded to the key questions developed by each Work Group. The draft guidelines included all possible topics articulated by the Work Groups during the targeting phase and at the Work Group meetings to discuss the evidence. These draft guidelines were then transmitted to the Work Group members, who used the evidence tables and their expert judgment to rate each guideline statement for validity on a 1-to-9 scale. The RAND staff then compiled summaries for the face-to-face meetings of the Work Groups. At these meetings, Work Group members were provided with the summaries of these first round ratings of validity. These summary ratings were used to key a point-by-point discussion of the evidence and opinion surrounding each potential guideline statement. After each discussion, the Work Group members privately re-rated each guideline statement for validity. These votes form the basis for the final guidelines. Statements were accepted as valid if the median panel rating on validity was 7 or greater on the 1-to-9 scale. ''Complete agreement'' was defined as occurring when all Work Group members rated a guideline statement within the same three-point range of the scale (for example, all members' ratings were in the range of 7, 8, or 9). After determining the final

guideline statements, Work Group members went through a similar two-step rating process to assess the level of evidence. A rating of ''*Evidence*'' was defined as ''mainly convincing scientific evidence, limited added opinion''; ''*Opinion*'' was defined as ''mainly opinion, limited scientific evidence''; and ''*Evidence plus Opinion*'' was defined as ''about equal mixtures of scientific evidence and opinion.''

Phase V: Draft Report With Supporting Rationale

Following the development of the guidelines, the Work Group drafted a report that included the supporting rationale for each guideline. While writing the rationale for each guideline, Work Group members cited additional references that had either not been identified previously in the literature search efforts, or had been identified but rejected. These citations contained information that was felt to be important either as background material, or to further explain the rationales. However, these additional references were not part of the evidence base that was used to either formulate the guideline statements or the votes on the validity or the rating of evidence versus opinion for each guideline.

Phase VI: Peer Review

The purpose of the peer review process was to identify:

- unclear wording in the draft guidlines
- substantive concerns regarding the content of specific guidelines
- important but uncited data relevant to specific draft guidelines
- guidelines that may be difficult to implement or that would benefit from specific strategies to facilitate compliance such as educational programs, tools, etc.

The nutrition guidelines were subjected to a three-stage peer review process:

Stage One: Primary Review. NKF-DOQI's multidisciplinary Steering Committee was assigned to review the draft report. Drafts were distributed to the committee in August 1999 and members had the opportunity to offer oral comments at a face-to-face meeting in mid-September. The draft report was also sent to the NKF-DOQI Advisory Council, the NKF Scientific Advisory Board, and selected experts in the field. Many substantive comments were received, and this resulted in substantive changes in the organization and content of some of the guidelines and rationales. Given the large volume of comments received, the Work Group vice-chairs reviewed the comments first and entered them into a computer database separating these according to whether they had a potential minor or substantive impact. Comments were sorted by guideline topic and then provided to the Work Groups for analysis and response.

Stage Two: Organizational Review. Close to 200 individuals representing nearly 50 end-stage renal disease (ESRD)-related organizations reviewed the second draft of the guidelines in December 1999. Organizations that were invited to participate in the second round of peer review were selected by the Steering Committee based on suggestions from the Advisory Council and the Work Groups. Organizations included various nephrology professional societies (eg, Renal Physicians Association, American Society of Nephrology, American Nephrology Nurses Association, and American Renal Administrators Association), the American Association of Kidney Patients, the ESRD Networks, NKF Councils, dialysis chains, managed care organizations, and private industry organizations selected their own reviewers.

Stage Three: Open Review. In the final round of review, in December 1999, approximately 400 individuals received copies of the revised draft guidelines. Within 3 weeks, 30% of these reviewers provided comments. The Work Group vice-chairs sorted and organized these comments and the Work Group analyzed the responses.

Phase VII: Issue Final Guidelines

The Work Group and staff performed several tasks to complete the guidelines. The guidelines were edited to ensure clarity and consistency. The Work Group carefully reviewed the final draft and made the indicated changes. Accuracy of the literature citations for each guideline document were also verified.

K/DOQI IMPLEMENTATION PLANNING

The NKF plans to undertake three types of activities to promote implementation of these recommendations.

1. Translating recommendations into practice. K/DOQI will develop core patient and

professional education programs and tools to facilitate the adoption of their recommendations.

2. Building commitment to reducing practice variations. K/DOQI will work with providers and insurers to clarify the need for and the benefits of changes in practice patterns and to encourage the adoption of the guidelines.
3. Evaluation. K/DOQI, in collaboration with other relevant organizations, will participate in the development of performance measures that can be used to assess compliance with the K/DOQI practice guidelines. In addition, the association between compliance with the K/DOQI guidelines and patient outcomes will be evaluated in an effort to validate and improve the guidelines over time.

The development of the K/DOQI practice guidelines is a cooperative, rewarding, and unifying effort for the participants and the community of health care workers who are involved in the care of the individual with kidney disease. We hope this spirit of cooperation and commitment to improvement of dialysis patient outcomes will help the K/DOQI in efforts to put its quality improvements into practice.

I. ADULT GUIDELINES

A. MAINTENANCE DIALYSIS

1. Evaluation of Protein-Energy Nutritional Status

GUIDELINE 1

Use of Panels of Nutritional Measures

Nutritional status in maintenance dialysis patients should be assessed with a combination of valid, complementary measures rather than any single measure alone. ***(Opinion)***

- There is no single measure that provides a comprehensive indication of protein-energy nutritional status.
- Measures of energy and protein intake, visceral protein pools, muscle mass, other dimensions of body composition, and functional status identify different aspects of protein-energy nutritional status.
- Malnutrition may be identified with greater sensitivity and specificity using a combination of factors.

RATIONALE

Optimal monitoring of protein-energy nutritional status for maintenance dialysis (MD) patients requires the collective evaluation of multiple parameters, particularly using measures that assess different aspects of protein-energy nutritional status. No single measure provides a complete overview of protein-energy nutritional status. Each of the valid indicators described in Guidelines 2 and 23 has a role in the overall nutritional assessment of dialysis patients.

There are ample data suggesting that complementary indicators of nutritional status exhibit independent associations with mortality and morbidity in maintenance hemodialysis (MHD) and chronic peritoneal dialysis (CPD) patients. For example, the serum albumin, serum creatinine, and body weight-for-height are independently associated with survival.[14] Data from the USRDS confirm these findings, using the serum albumin and body mass index (BMI; kg/m^2).[15] In the CANUSA study, both the serum albumin and SGA were independent predictors of death or treatment failure.[16] A discussion of why serum transferrin concentrations and bioelectrical impedance studies are not recommended for the nutritional assessment of MD patients in clinical practice is given in Appendix VIII.

RECOMMENDATIONS FOR RESEARCH

1. Studies are needed to determine the most effective combination of measures of nutritional status for evaluating protein-energy malnutrition.

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GUIDELINE 2

Panels of Nutritional Measures for Maintenance Dialysis Patients

For maintenance dialysis patients, nutritional status should be routinely assessed by predialysis or stabilized* serum albumin, percent of usual body weight, percent of standard (NHANES II) body weight, subjective global assessment, dietary interviews and diaries, and nPNA. ***(Opinion)***

• These parameters should be measured routinely (as indicated in Table 1) because they provide a valid and clinically useful characterization of the protein-energy nutritional status of maintenance dialysis patients

RATIONALE

The advantages to using these individual nutritional measures are discussed in Guidelines 3 and 8 through 10 and in Appendices III, V, and VII. The combination of these measurements provides an assessment of visceral and somatic protein pools, body weight and hence fat mass, and nutrient intake.

Serum albumin is recommended for routine measurement because there is a large body of literature that defines the normal serum albumin values, characterizes the nutritional and clinical factors affecting serum albumin concentrations, and demonstrates the relationship between serum albumin concentrations and outcome. Body weight, adjusted for height, is proposed because of the clear association between body weight and body fat mass and because body weight is correlated with clinical outcome. SGA is recommended because it gives a comprehensive overview of nutritional intake and body composition, including a rough assessment of both muscle mass and fat mass, and because it is correlated with mortality rates. Assessment of nutrient intake is essential for assessing the probability that a patient will develop PEM, for evaluating the contribution of inadequate nutrient intake to existing PEM, and for developing strategies to improve protein-energy nutritional status. Also, nutrient intake is correlated with clinical outcome. nPNA provides an independent and less time consuming assessment of dietary protein intake (DPI). Dietary interviews and diaries can be used to assess intake not only of protein and energy but also of a variety of other nutrients as well as the pattern and frequency of meals (information that may aid in identifying the cause of inadequate nutrient intake). A low predialysis or stabilized serum urea level may indicate a low intake of protein or amino acids.

*A predialysis serum measurement is obtained from an individual immediately before the initiation of a hemodialysis or intermittent peritoneal dialysis treatment. A stabilized serum measurement is obtained after the patient has stabilized on a given dose of CAPD.

RECOMMENDATIONS FOR RESEARCH

1. Research is necessary to identify and validate the following:

(a) The optimal panel of measures to screen for disorders in nutritional status.

Table 1. Recommended Measures for Monitoring Nutritional Status of Maintenance Dialysis Patients

Category	Measure	Minimum Frequency of Measurement
I. Measurements that should be performed routinely in all patients	• Predialysis or stabilized serum albumin	• Monthly
	• % of usual postdialysis (MHD) or post-drain (CPD) body weight	• Monthly
	• % of standard (NHANES II) body weight	• Every 4 months
	• Subjective global assessment (SGA)	• Every 6 months
	• Dietary interview and/or diary	• Every 6 months
	• nPNA	• Monthly MHD; every 3-4 months CPD
II. Measures that can be useful to confirm or extend the data obtained from the measures in Category I	• Predialysis or stabilized serum pre-albumin	• As needed
	• Skinfold thickness	• As needed
	• Mid-arm muscle area, circumference, or diameter	• As needed
	• Dual energy x-ray absorptiometry	• As needed
III. Clinically useful measures, which, if low, might suggest the need for a more rigorous examination of protein-energy nutritional status	• Predialysis or stabilized serum —Creatinine —Urea nitrogen —Cholesterol	 • As needed • As needed • As needed
	• Creatinine index	

(b) The optimal panel of measures for a comprehensive assessment of nutritional status.

(c) The optimal frequency with which these nutritional measures should be employed.

2. More information is needed concerning the appropriate parameters to be used for assessment of body composition (eg, for expressing dual energy x-ray absorptiometry [DXA] measurements, anthropometry, and the creatinine index).

3. Patient subgroups should be identified (eg, elderly, obese, severely malnourished, or physically very inactive individuals) for whom the use of specialized combinations of body composition measures are beneficial.

GUIDELINE 3

Serum Albumin

Serum albumin is a valid and clinically useful measure of protein-energy nutritional status in maintenance dialysis (MD) patients. *(Evidence)*

- The predialysis or stabilized serum albumin is a measure of visceral protein pool size.
- The serum albumin at the time of initiation of chronic dialysis therapy or during the course of maintenance dialysis is an indicator of future mortality risk.
- A predialysis or stabilized serum albumin equal to or greater than the lower limit of the normal range (approximately 4.0 g/dL for the bromcresol green method) is the outcome goal.
- Individuals with a predialysis or stabilized serum albumin that is low should be evaluated for protein-energy malnutrition.
- The presence of acute or chronic inflammation limits the specificity of serum albumin as a nutritional marker.

RATIONALE

Serum albumin levels have been used extensively to assess the nutritional status of individuals with and without chronic renal failure (CRF).[17] Malnutrition is common in the end-stage renal disease (ESRD) population,[18] and hypoalbuminemia is highly predictive of future mortality risk when present at the time of initiation of chronic dialysis as well as during the course of maintenance dialysis (MD).[14,19-27] It follows that nutritional interventions that maintain or increase serum albumin concentrations may be associated with improved long-term survival, although this has not been proven in randomized, prospective clinical trials. Serum albumin levels may fall modestly with a sustained decrease in dietary protein and energy intake and may rise with increased protein or energy intake.[28] Conversely, serum albumin levels may fall acutely with inflammation or acute or chronic stress and increase following resolution or recovery.

Despite their clinical utility, serum protein (eg, albumin, transferrin, and prealbumin) levels may be insensitive to changes in nutritional status, do not necessarily correlate with changes in other nutritional parameters, and can be influenced by non-nutritional factors.[29-32] Some of these non-nutritional factors, which are frequently present in this population, include infection or inflammation, hydration status, peritoneal or urinary albumin losses, and acidemia.[33-36] Hence, hypoalbuminemia in MD patients does not necessarily indicate protein-energy malnutrition (PEM). The patient's clinical status (eg, comorbid conditions, dialysis modality, acid-base status, degree of proteinuria) must be examined when evaluating changes in the serum albumin level. Serum albumin concentrations are inversely correlated with serum levels of positive acute-phase pro-

teins.[33,34,37] An elevated C-reactive protein has been reported to negate the positive relationship between serum albumin and nPNA.[34] However, some studies suggest that serum albumin is independently affected by both inflammation and nutritional intake.[34]

As indicated above, positive acute-phase proteins (eg, C-reactive protein [CRP], alpha-1 acid glycoprotein [a1-AG], ferritin, and ceruloplasmin) are not nutritional parameters but may be used to identify the presence of inflammation[38] in individuals with low serum albumin or prealbumin (Guideline 4) levels and possibly for predicting outcome. a1-AG may be more specific than CRP for detecting inflammation in MD patients.[37] Serial monitoring of serum concentrations of positive acute-phase proteins (CRP, a1-AG) during episodes of inflammation in MD patients indicate that serum levels follow patterns similar to those found in acutely ill individuals who do not have CRF.[39]

Although no single ideal measure of nutritional status exists, the serum albumin concentration is considered to be a useful indicator of protein-energy nutritional status in MD patients. The extensive literature, in individuals with or without renal failure, relating serum albumin to nutritional status, and the powerful association between hypoalbuminemia and mortality risk in the MD population, strongly support this contention. In addition, the measurement of serum albumin levels is inexpensive, easy to perform, and widely available. Methods for measuring serum albumin are discussed in Appendix I.

RECOMMENDATIONS FOR RESEARCH

1. More information is needed concerning the relative contributions of nutritional intake and inflammatory processes to serum albumin concentrations.

2. There is a need for a better understanding of the mechanisms by which hypoalbuminemia or the factors causing hypoalbuminemia lead to increased morbidity and mortality in MD patients.

3. Studies are needed to assess whether and under what conditions nutritional intervention increases serum albumin concentrations in hypoalbuminemic MD patients.

4. Will an increase in serum albumin levels induced by nutritional support reduce morbidity and mortality in persons undergoing MD?

GUIDELINE 4

Serum Prealbumin

Serum prealbumin is a valid and clinically useful measure of protein-energy nutritional status in maintenance dialysis (MD) patients. ***(Evidence and Opinion)***

- The predialysis or stabilized serum prealbumin is a measure of visceral protein pool size.
- The serum prealbumin level at the time of initiation of dialysis or during maintenance dialysis is an indicator of future mortality risk.
- An individual with predialysis or stabilized serum prealbumin less than 30 mg/dL should be evaluated for protein-energy malnutrition.
- The presence of acute or chronic inflammation limits the specificity of serum prealbumin as a nutritional marker.
- There is insufficient evidence to conclude that prealbumin is a more sensitive index of nutritional status than albumin.

RATIONALE

Serum prealbumin (transthyretin) has been used in individuals with or without CRF as a marker of protein-energy nutritional status.[40] It has been suggested that serum prealbumin may be more sensitive than albumin as an indicator of nutritional status, since it has a shorter half-life than albumin (~2 to 3 days versus ~20 days, respectively).[25,41] However, prealbumin is limited by many of the same factors described for albumin. Prealbumin may not correlate with changes in other nutritional parameters[31,32] and it is a negative acute-phase reactant (ie, serum levels decline in response to inflammation or infection[43]). In addition, recommendations for the routine use of serum prealbumin levels as a marker are tempered by the fact that prealbumin levels are increased in renal failure, presumably due to impaired degradation by the kidney.[17,42] Although fewer studies have been published relating prealbumin levels to outcomes in MD patients than have been published regarding albumin levels, several studies have demonstrated that prealbumin levels less than 30 mg/dL are associated with increased mortality risk and correlate with other indices of PEM.[25,41,42a,44]

Based on available evidence, serum prealbumin is considered to be a valid measure of protein-energy nutritional status in individuals undergoing MD. There is insufficient evidence to conclude that prealbumin is a more sensitive or accurate index of malnutrition than is serum albumin. If the predialysis or stabilized serum prealbumin level is used to monitor nutritional status, it is recommended that the outcome goal for prealbumin is a value greater than or equal to 30 mg/dL.

RECOMMENDATIONS FOR RESEARCH

1. What range of serum prealbumin concentrations is associated with optimal outcome?
2. More information is needed concerning the relative contributions of nutritional intake and inflammatory processes to serum prealbumin levels.
3. Data are needed concerning the mechanisms by which low serum levels of prealbumin lead to increased mortality in MD patients.
4. Will nutritional intervention in malnourished hypoprealbuminemic MD patients increase serum prealbumin concentrations?
5. Will an increase in serum prealbumin levels induced by nutritional support reduce morbidity and mortality in individuals undergoing MD?

GUIDELINE 5

Serum Creatinine and the Creatinine Index

The serum creatinine and creatinine index are valid and clinically useful markers of protein-energy nutritional status in maintenance dialysis (MD) patients. *(Evidence and Opinion)*

- The predialysis or stabilized serum creatinine and the creatinine index reflect the sum of dietary intake of foods rich in creatine and creatinine (eg, skeletal muscle) and endogenous (skeletal muscle) creatinine production minus the urinary excretion, dialytic removal, and endogenous degradation of creatinine.
- Individuals with low predialysis or stabilized serum creatinine (less than approximately 10 mg/dL) should be evaluated for protein-energy malnutrition and wasting of skeletal muscle.
- A low creatinine index and, in the absence of substantial endogenous urinary creatinine clearance, a low serum creatinine concentration suggest low dietary protein intake (DPI) and/or diminished skeletal muscle mass and are associated with increased mortality rates.

RATIONALE

In MHD patients with little or no renal function who are receiving a constant dose of dialysis, the predialysis serum creatinine level will be proportional to dietary protein (muscle) intake and the somatic (skeletal muscle) mass.[17,45,46] In chronic peritoneal dialysis (CPD) patients with little or no residual renal function, the stabilized serum creatinine level with a given dialysis dose will be proportional to skeletal muscle mass and dietary muscle intake. Thus, a low predialysis or stabilized serum creatinine level in an MD patient with negligible renal function suggests decreased skeletal muscle mass and/or a low dietary protein intake (DPI).[17] Among nonanuric individuals, this relationship persists, but the magnitude of the urinary creatinine excretion must be considered when interpreting the predialysis or stabilized serum creatinine as a nutritional parameter. This is particularly relevant to CPD patients, who are more likely to maintain residual renal function for longer periods.

The creatinine index is used to assess creatinine production and, therefore, dietary skeletal muscle protein intake and muscle mass. The creatinine index estimates fat-free body mass rather accurately in individuals with ESRD.[46,48] Appendix II discusses creatinine metabolism in greater detail and describes methods for calculating the creatinine index and, from this value, the fat-free body mass.

In individuals in whom loss of skeletal muscle mass is suspected on the basis of low or declining serum creatinine levels, this observation may be confirmed using the creatinine index. Direct relationships between serum creatinine and the serum albumin[29,33,42a] and prealbumin concentrations[42a] are reported. Among individuals undergoing CPD, the creatinine index is lower in individuals with protein-energy malnutrition as determined by a composite nutritional index.[30]

Serum creatinine and the creatinine index are predictors of clinical outcome. In individuals undergoing maintenance HD (MHD), predialysis serum creatinine[14,25,42,44,45,49-52] and the molar ratio of serum urea to creatinine are both predictive of and inversely related to survival. This relationship persists even after adjusting for patient characteristics (age, sex, diagnosis, and diabetic status) and dialytic variables.[14,25,44,45,50,52] The serum creatinine at the onset of MHD distinguishes between short-term ($<$ 12 months) and long-term ($>$ 48 months) survival in incident patients.[25] In longitudinal studies of PD patients, initial serum creatinine levels are inversely related to mortality.[25,44,52] The creatinine index is directly related to the normalized protein equivalent of total nitrogen appearance (nPNA) and independent of the dialysis dose (Kt/V_{urea}).[53] A low or declining creatinine index correlates with mortality independently of the cause of death, although people with catabolic diseases may have larger and faster declines in the creatinine index before death.[53] Some research has not shown a clear association between the serum creatinine concentration and outcome.[23,42,54]

The serum creatinine concentration that indicates malnutrition has not been well defined. The mortality risk associated with low serum creatinine increases at levels below 9 to 11 mg/dL in individuals on MHD or PD.[14,25,30,44,51] In individuals with negligible urinary creatinine clearance (CrCl), the nutritional status of individuals undergoing MHD or CPD who have a predialysis or stabilized serum creatinine of less than approximately 10 mg/dL should be evaluated.

RECOMMENDATIONS FOR RESEARCH

1. The degree of correlation of the serum creatinine and creatinine index with skeletal muscle mass and DPI, and the sensitivity to change in these parameters of creatinine metabolism, need to be better defined.
2. The relationship between the creatinine index and the edema-free lean body mass or skeletal muscle protein mass needs to be defined for ESRD patients.
3. The rate of creatinine degradation in ESRD patients needs to be defined more precisely.
4. The level of serum creatinine and the creatinine index associated with optimal nutritional status and lowest morbidity and mortality rates need to be defined.
5. The relationships between other markers of protein-energy nutritional status (eg, serum albumin, prealbumin, or anthropometry) and serum creatinine or creatinine index are limited, somewhat contradictory, and need to be further examined.
6. Whether nutritional interventions that increase serum creatinine or creatinine index will improve morbidity or mortality in malnourished MD patients should be tested.
7. The effects of age, gender, race, and size of skeletal muscle mass on the relationship between the serum creatinine and the creatinine index on morbidity and mortality need to be examined.

GUIDELINE 6

Serum Cholesterol

Serum cholesterol is a valid and clinically useful marker of protein-energy nutritional status in maintenance hemodialysis patients. *(Evidence and Opinion)*

- Low or declining serum cholesterol concentrations are predictive of increased mortality risk.
- Hypocholesterolemia is associated with chronic protein-energy deficits and/or the presence of comorbid conditions, including inflammation.
- Individuals with low, low-normal (less than approximately 150 to 180 mg/dL), or declining serum cholesterol levels should be investigated for possible nutritional deficits.

RATIONALE

The predialysis or stabilized serum cholesterol concentration may be a useful screening tool for detecting chronically inadequate protein-energy intakes. Individuals undergoing MHD who have a low-normal (less than approximately 150 to 180 mg/dL) nonfasting serum cholesterol have higher mortality than do those with higher cholesterol levels.[14,25,47,50,55] As an indicator of protein-energy nutritional status, the serum cholesterol concentration is too insensitive and nonspecific to be used for purposes other than for nutritional screening, and MD patients with serum cholesterol concentrations less than approximately 150 to 180 mg/dL should be evaluated for nutritional deficits as well as for other comorbid conditions.

Serum cholesterol is an independent predictor of mortality in MHD patients.[14,19,47,55] The relationship between serum cholesterol and mortality has been described as either ''U-shaped'' or ''J-shaped,'' with increasing risk for mortality as the serum cholesterol rises above the 200 to 300 mg/dL range[14] or falls below approximately 200 mg/dL.[19,25,47,50] The mortality risk in most studies appears to increase progressively as the serum cholesterol decreases to, or below, the normal range for healthy adults ($\leq$200 mg/dL).[14,19,25,50,55] Not all studies of MHD patients show that serum cholesterol levels predict mortality, however.[19,23,42] The relationship between low serum cholesterol and increased mortality is not observed in the CPD population,[14,25,42,44,52] possibly because sample sizes in studies of individuals undergoing CPD are smaller and possibly due to confounding by greater energy (glucose intake) and/or hypertriglyceridemia. In one study, higher serum cholesterol concentrations ($>$250 mg/dL) were associated with increased mortality in CPD patients.[56]

Predialysis serum cholesterol is generally reported to exhibit a high degree of collinearity with other nutritional markers such as albumin,[42] prealbumin,[42] and creatinine,[44] as well as age.[44] In MHD patients, the predialysis serum cholesterol level measured may be affected by nonnutritional factors. Cholesterol may be influenced by the same comorbid conditions, such as inflammation, that affect other nutritional markers (eg, serum albumin).[42] In one study there was

no difference in serum cholesterol in CAPD patients whose serum albumin level was less than 3.5 g/dL as compared with those with levels ≥3.5 g/dL.[33]

RECOMMENDATIONS FOR RESEARCH

1. What are the conditions under which serum cholesterol is a reliable marker of protein-energy nutrition? What can be done to increase the sensitivity and specificity of the serum cholesterol as an indicator of protein-energy nutritional status?

2. The relationships between other markers of protein-energy nutritional status (eg, serum albumin or anthropometry) and serum cholesterol are limited, somewhat contradictory, and need to be better defined.

3. How does nutritional intervention in malnourished MD patients affect their serum cholesterol concentrations?

4. Recent data suggest that serum cholesterol exhibits a negative acute-phase response to inflammation.[42] The relationship among serum cholesterol, nutritional status, and inflammation needs to be further investigated.

5. Why does mortality increase when the serum cholesterol falls outside the 200 to 250 mg/dL range?

6. More information is needed about the patterns of morbidity and mortality associated with abnormal serum cholesterol concentrations in MD patients. For example, in these individuals, is cardiovascular mortality directly related to the serum cholesterol level and are malnutrition and mortality from infection inversely related to the serum cholesterol level?

7. Additional data investigating the relationships among serum cholesterol, protein-energy nutritional status, morbidity, and mortality are needed for persons undergoing CPD.

GUIDELINE 7

Dietary Interviews and Diaries

Dietary interviews and/or diaries are valid and clinically useful for measuring dietary protein and dietary energy intake in maintenance dialysis patients. *(Evidence and Opinion)*

RATIONALE

Patients undergoing MHD or CPD frequently have low protein and energy intake. Evidence indicates that for patients ingesting low protein or energy intakes, increasing dietary protein or energy intake improves nutritional status.[57-60] It is important, therefore, to monitor the dietary protein and energy intake of MHD and CPD patients. A number of studies in individuals without renal disease indicate that dietary diaries and interviews provide quantitative information concerning intake of protein, energy, and other nutrients.[61,62] It is recommended, therefore, that individuals undergoing MHD or CPD periodically maintain 3-day dietary records followed by dietary interviews conducted by an individual trained in conducting accurate dietary interviews and calculating nutrient intake from the diaries and interviews, eg, a registered dietitian, preferably with experience in renal disease (see Appendices III and IV). When staffing conditions limit the time available to conduct more formal assessments of nutritional intake, a 24-hour dietary recall may be substituted for dietary interviews and/or diaries in nutritionally stable patients.

RECOMMENDATIONS FOR RESEARCH

1. Techniques to improve the reliability and precision of dietary interviews or diaries for MD patients are needed.
2. Other less laborious and more reliable methods to estimate nutrient intake, particularly energy intake, are needed.

GUIDELINE 8

Protein Equivalent of Total Nitrogen Appearance (PNA)

PNA or PCR is a valid and clinically useful measure of net protein degradation and protein intake in maintenance dialysis (MD) patients. ***(Evidence)***

- When nitrogen balance is zero in the steady state, the difference between nitrogen intake and total nitrogen losses is zero or only slightly positive (ie, up to about 0.5 g nitrogen/d because of unmeasured nitrogen losses). Hence, in the clinically stable patient, PNA provides a valid estimate of protein intake.
- The protein equivalent of total nitrogen appearance (PNA) can be estimated from interdialytic changes in urea nitrogen concentration in serum and the urea nitrogen content of urine and dialysate.
- Because both net protein breakdown under fasting conditions and dietary protein requirements are strongly influenced by body mass, PNA (or PCR) is often normalized to a function of body weight (Guideline 12).

RATIONALE

During steady-state conditions, nitrogen intake is equal to or slightly greater than nitrogen assessed as total nitrogen appearance (TNA).[63] TNA is equal to the sum of dialysate, urine, fecal nitrogen losses, and the postdialysis increment in body urea-nitrogen content. Because the nitrogen content of protein is relatively constant at 16%, the protein equivalent of total nitrogen appearance (PNA) can be estimated by multiplying TNA by 6.25 (PNA is mathematically identical to the protein catabolic rate or PCR). In the clinically stable patient, PNA can be used to estimate protein intake. Because protein requirements are determined primarily by fat-free, edema-free body mass, PNA is usually normalized (nPNA) to some function of body weight (eg, actual, adjusted, or standardized [NHANES II] body weight [SBW] or body weight derived from the urea distribution space [V_{urea}/0.58]).[63] Because urea nitrogen appearance (UNA; ie, the sum of urea nitrogen in urine and dialysate and the change in body urea nitrogen) is highly correlated with TNA and measurement of total nitrogen losses in urine, dialysate, and stool is inconvenient and laborious, regression equations to estimate PNA from measurements of urea nitrogen in serum, urine, and dialysate have been developed. The estimation of PNA from measurements of urea nitrogen is readily performed from the routine urea kinetic modeling session in HD patients and, at least in theory, should be subject to less measurement error than dietary diaries and recall. The equations used to estimate PNA are discussed in Appendix V.

There are several important limitations to PNA as an estimate of DPI. First, PNA approximates protein intake only when the patient is in nitrogen equilibrium (steady-state).[63] In the catabolic patient, PNA will exceed protein intake to the extent that there is net degradation and metabolism of endogenous protein pools to form urea. Conversely, when the patient is anabolic (eg, growth in children, recovering from an intercur-

rent illness, or during the last trimester of pregnancy) dietary protein is utilized for accrual of new body protein pools, and PNA will underestimate actual protein intake. Second, UNA (and hence PNA) changes rapidly following variations in protein intake. Hence, PNA may fluctuate from day to day as a function of protein intake, and a single PNA measurement may not reflect usual protein intakes. Third, when DPI is high, TNA underestimates protein intake (ie, nitrogen balance is unrealistically positive).[64,65] This is probably caused by increased nitrogen losses through unmeasured pathways of excretion (eg, respiration and skin).[66] Fourth, PNA may overestimate DPI when the protein intake is less than 1 g/kg/d (possibly due to endogenous protein catabolism).[67-69] Finally, normalizing PNA to body weight can be misleading in obese, malnourished, and edematous patients. Therefore, it is recommended that for individuals who are less than 90% or greater than 115% of SBW, the adjusted edema-free body weight (aBW_{ef}) be used when normalizing PNA to body weight (Guideline 12).

Notwithstanding these limitations, when consideration is given to the caveats discussed above, the nPNA is a valid and useful method for estimating protein intake. However, PNA should not be used to evaluate nutritional status in isolation, but rather as one of several independent measures when evaluating nutritional status.

RECOMMENDATIONS FOR RESEARCH

1. There are still a number of technical problems with measuring PNA in individuals undergoing HD or peritoneal dialysis that engender errors and increase the costs of measurement. Research to decrease these sources of error would be useful.

2. The mathematical relationship between PNA and protein intake in MHD patients has not been well defined. A larger database to examine these relationships more precisely would be useful.

3. More research into optimal methods for normalizing PNA to body mass would be valuable.

GUIDELINE 9

Subjective Global Nutritional Assessment (SGA)

SGA is a valid and clinically useful measure of protein-energy nutritional status in maintenance dialysis patients. *(Evidence)*

RATIONALE

Subjective global assessment (SGA) is a reproducible and useful instrument for assessing the nutritional status of MD patients.[16,29,70-72] It is a simple technique that is based on subjective and objective aspects of the medical history and physical examination. SGA was initially developed to determine the nutritional status of patients undergoing gastrointestinal surgery[73,74] and subsequently was applied to other populations.[16,29,70-72,74-77]

Among the benefits of using the SGA are that it is inexpensive, can be performed rapidly, requires only brief training, and gives a global score or summation of protein-energy nutritional status. Disadvantages to the SGA include the fact that visceral protein levels are not included in the assessment. SGA is focused on nutrient intake and body composition. It is subjective, and its sensitivity, precision, and reproducibility over time have not been extensively studied in MHD patients.

Many cross-sectional studies have used the SGA to assess nutritional status in individuals undergoing CPD.[16,29,71,75,78] Correlations among SGA and other measures of protein-energy nutritional status are well described.[29,71] SGA has been less well studied in MHD patients.[72] In the Canada-USA (CANUSA) study, a prospective cohort study of 680 continuous ambulatory peritoneal dialysis (CAPD) patients, SGA was modified to four items (weight loss, anorexia, subcutaneous fat, and muscle mass). Subjective weightings were assigned to each of the four items representing nutritional status (eg, 1 to 2 represented severe malnutrition; 3 to 5, moderate to mild malnutrition; and 6 to 7, normal nutrition).[16]

It is recommended that SGA be determined by the 4-item, 7-point scale used in the CANUSA Study,[16] because this method may provide greater sensitivity when assessing nutritional status and more predictive power in MD patients than the original 3-point ordinal scale.[73,74] The CANUSA study, using the 7-point scale, showed with multivariable analysis that a higher SGA score was associated with a lower relative risk of death and fewer hospitalized days per year.[16] Also, small

changes in the SGA score correlated with clinical outcomes.[79] Methods for performing SGA are discussed in Appendix VI.

RECOMMENDATIONS FOR RESEARCH

1. The most effective technique for performing SGA needs to be identified. Is the currently recommended 4-item scale optimal? Should visceral proteins (eg, serum albumin, transferrin, and/or prealbumin) be added to the SGA? Should a standard reference of body mass be included (eg, BMI or %SBW)?

2. The technique of SGA needs greater validation with regard to sensitivity, specificity, accuracy, intraobserver and interobserver variability, correlation with other nutritional measures, and predictability of morbidity, mortality, or other clinical outcomes.

GUIDELINE 10

Anthropometry

Anthropometric measurements are valid and clinically useful indicators of protein-energy nutritional status in maintenance dialysis patients. ***(Evidence and Opinion)***

- These measures include percent usual body weight, percent standard body weight, body mass index (BMI), skinfold thickness, estimated percent body fat, and mid-arm muscle area, circumference, or diameter.

RATIONALE

Anthropometry quantifies body mass, provides a semiquantitative estimate of the components of body mass, particularly the bone, muscle, and fat compartments, and gives information concerning nutritional status.[31,80-83] The anthropometric parameters that are generally assessed include body weight, height, skeletal frame size, skinfold thickness (an indicator of body fat), mid-arm muscle circumference (MAMC; an indicator of muscle mass), area, or diameter, or percent of the body mass that is fat, percent of usual body weight (%UBW), percent of standard (NHANES II) body weight (%SBW), and BMI. The various anthropometric measures provide different information concerning body composition; therefore, there are advantages to measuring all of the parameters indicated above. Hence, the emphasis given to different anthropometric parameters and their relative precision should be taken into consideration. Anthropometry requires precise techniques of measurement and the use of proper equipment to give accurate, reproducible data; otherwise, the measurements may give quite variable results.[82] Some measures of anthropometry are more precise, such as %UBW, %SBW, and BMI, than are skinfold thickness and MAMC. Methods for performing anthropometry and calculating body composition from these measurements and reference tables are presented in Appendix VII.

In adult MD patients, height is not a valid method for measuring protein or energy nutritional status. However, it must be measured because it is used in height-adjusted reference tables for weight (including SBW and BMI). Because height may decrease with aging, particularly in MD patients who have bone disease, height should be measured annually. Skeletal frame size must also be determined to calculate an individual's %SBW (see Appendix VII).

Muscle area, diameter, or circumference is used to estimate muscle mass and, by inference, the fat-free mass and somatic protein pool. Significant changes in these measurements reflect changes in body muscle and somatic protein mass and may indicate a nutritionally compromised state. Anthropometry has been used to assess nutritional status in MHD and CPD patients.[29,31,32,71,75,84] These studies indicate that

muscle mass is decreased, often markedly, in many, if not the majority, of MD patients.

Anthropometric monitoring of the same patient longitudinally may provide valuable information concerning changes in nutritional status for that individual. The desirable or optimal anthropometric measures for MD patients have not been defined. There is evidence that MHD patients who have larger body-weight-for-height (eg, BMI) measurements are more likely to survive, at least for the subsequent 12 months.[15,50,85,86] Patients in the lower 50th percentile of weight-for-height clearly have a reduced survival rate.[15,85-87] One study indicates that MHD patients who are in the upper 10th percentile of body weight-for-height have the greatest 12-month survival rate.[85]

In contrast to these findings, virtually all studies of normal populations indicate that low weight-for-height measures are associated with greater survival, especially if the analyses are adjusted for the incidence of cigarette smoking in individuals with low BMI.[88] Interpretation of these disparate findings among individuals undergoing MD and the normal population is also confounded by the lack of interventional trials in which a change in anthropometric measurements is correlated with clinical outcome.

Anthropometric measurements in MD patients can be compared with normal values obtained from the NHANES II data[89] or with values from normal individuals who have the greatest longevity.[88,90-97] Anthropometric norms for patients treated with HD are published and generally are similar to the values available for the general population.[98] Differences in anthropometric measurements among MD patients and normal individuals may indicate a nutritional disorder or other clinical abnormality (eg, edema or amputation). The use of currently available anthropometric norms obtained from MD patients is of questionable value since age-, sex-, and race- or ethnicity-specific reference data are not available for this population. Furthermore, it has not been shown that the norms for MHD patients are desirable or healthy values.

RECOMMENDATIONS FOR RESEARCH

1. Age-, sex-, and race- or ethnic-specific desirable reference values for anthropometry obtained in large numbers of MD patients are needed.
2. The risk of morbidity and mortality associated with different anthropometric measurements in MD patients should be determined.
3. To determine whether anthropometry might be an acceptable intermediate outcome in nutrition intervention trials.
4. Will improvement in anthropometric values through nutritional intervention be associated with decreased morbidity and mortality and enhanced quality of life in individuals undergoing MD?

GUIDELINE 11

Dual Energy X-Ray Absorptiometry (DXA)

DXA is a valid and clinically useful technique for assessing protein-energy nutritional status. ***(Evidence and Opinion)***

- Accurate data on body composition are helpful to assess long-term adequacy of protein-energy nutritional status.
- Whole body DXA provides an accurate method to assess body composition which is less influenced by the abnormalities in hydration status common in maintenance dialysis patients.

RATIONALE

Assessment of body composition, particularly with serial evaluation, can provide information concerning the long-term adequacy of protein-energy nutritional intake.[58,99] Most clinically useful techniques for measuring body composition are not very precise unless obtained by trained anthropometrists using standardized methods, such as in Guideline 10. Whole body dual energy x-ray absorptiometry (DXA) is a reliable, noninvasive method to assess the three main components of body composition (fat mass, fat-free mass, and bone mineral mass and density). The accuracy of DXA is less influenced by the variations in hydration that commonly occur in ESRD patients.[100-102] In vivo precision and accuracy of fat mass estimates by DXA are approximately 2% to 3% and 3%, respectively, in MHD[101] and CPD patients. Studies of DXA in CRF, MHD, and CPD patients have demonstrated the superior precision and accuracy of DXA as compared with anthropometry, total body potassium counting, creatinine index, and bioelectrical impedance (BIA).[80,100-102]

DXA scanning utilizes an x-ray source that produces a stable, dual-energy photon beam.[80,100-102] These beams are projected through the body by scanning in a rectilinear raster pattern. Various tissues (fat, fat-free mass, and bone) attenuate the x-ray beams to different extents. Body composition is computed from the ratios of the natural logarithms of the attenuated and unattenuated beams.

The main limitations to DXA are the substantial cost of acquiring the instrument, the requirement for dedicated space to house it, the costs for the DXA measurement, and the fact that individuals may need to travel to the DXA facility for the measurements. DXA also does not distinguish well between intracellular and extracellular water compartments. However, DXA scanners are becoming increasingly common in metropolitan settings. Where precise estimates of body composition and bone mineral density are required, use of DXA is preferred over traditional anthropometric techniques or BIA. However, the routine use of DXA is not recommended.

RECOMMENDATIONS FOR RESEARCH

1. The sensitivity and specificity of DXA as a marker of protein-energy nutritional status, and

specifically body composition, need to be defined more precisely.

2. Careful studies of the relationships between changes in more traditional markers of protein-energy nutritional status (eg, albumin, prealbumin, or anthropometry) and changes in body composition by DXA are needed.

3. Whether DXA assessment of body composition might be an acceptable intermediate outcome in nutrition intervention trials needs to be determined.

4. Whether DXA measurements correlate with morbidity and mortality in MD patients needs to be determined.

GUIDELINE 12

Adjusted Edema-Free Body Weight (aBW_{ef})

The body weight to be used for assessing or prescribing protein or energy intake is the aBW_{ef}. For hemodialysis patients, this should be obtained postdialysis. For peritoneal dialysis patients, this should be obtained after drainage of dialysate. ***(Opinion)***

- The adjusted edema-free body weight should be used for maintenance dialysis patients who have an edema-free body weight less than 95% or greater than 115% of the median standard weight, as determined from the NHANES II data.
- For individuals whose edema-free body weight is between 95% and 115% of the median standard weight, the actual edema-free body weight may be used.
- For DXA measurements of total body fat and fat-free mass, the actual edema-free body weight obtained at the time of the DXA measurement should be used.
- For anthropometric calculations, the postdialysis (for MHD) or post-drain (for CPD) actual edema-free body weight should be used.

RATIONALE

The wide range in body weight and body composition observed among dialysis patients seriously limits the use of the *actual* body weight for assessment or prescription of nutritional intake. The use of the actual or unadjusted body weight to assess the actual nutrient intake or to prescribe the intake of energy and protein can be hazardous when individuals are very obese or very underweight. On the other hand, it may be hazardous to ignore the effects of the patient's body size on dietary needs and tolerance in individuals who are markedly underweight or overweight. It is recognized that the determination of the patient's edema-free body weight is often difficult and not precise. Clinical judgement based on physical examination and, if necessary, body composition measurements are used to estimate the presence or absence of edema.

The following equation can be used to calculate the edema-free *adjusted* body weight (aBW_{ef})[63]:

$$aBW_{ef} = BW_{ef} + [(SBW - BW_{ef}) \times 0.25]$$

Equation 1

where BW_{ef} is the actual edema-free body weight and SBW is the standard body weight as determined from the NHANES II data.[89] Since interdialytic weight gain (IDWG) can be as high as 6 to 7 kg in HD patients, and peritoneal dialysate plus intraperitoneal ultrafiltrate can reach 2 to 5 kg, the aBW_{ef} should be calculated based on postdialysis values for HD patients and post-dialysate drain measurements for peritoneal dialysis patients.

Equation 1 takes into account the fact that the metabolic needs and dietary protein and energy requirements of adipose tissue in obese individuals is less than that of edema-free lean body mass

and also that very underweight individuals are less likely to become metabolically overloaded if they are prescribed diets based on their aBW_{ef} as compared with the standard (normal) body weight for individuals of similar age, height, gender, and skeletal frame size. Since the volume of distribution of urea and other protein metabolites is reduced in smaller individuals, a reduced protein prescription based on the aBW_{ef}, as compared with the standard weight, should lead to a lesser rate of accumulation of these metabolites in the body. On the other hand, use of the aBW_{ef} instead of the actual body weight of an underweight individual may provide the additional nutrients necessary for nutrient repletion. The use of the aBW_{ef} for prescribing protein or energy intake should be considered as a starting point. As always, clinical judgment and longitudinal assessment of body weight and other nutritional measures should be used to assess the response to dietary therapy and for making further decisions concerning dietary management.

The use of the aBW_{ef} may not be required for all patients. Clinical experience suggests that the *actual* edema-free body weight may be used effectively for nutritional assessment and nutritional prescription when the BW_{ef} is between 95% and 115% of the SBW as determined from the median body weights obtained from the NHANES II data.[89]

RECOMMENDATIONS FOR RESEARCH

1. The use of the aBW_{ef} for assessment and prescription of nutritional intake must be validated.

2. More precise and practical methods are needed for assessing the size of body water compartments and, in particular, undesirable increases or reductions in total body water, intracellular water, or extracellular or intravascular water.

2. Management of Acid-Base Status

GUIDELINE 13	**Measurement of Serum Bicarbonate** **Serum bicarbonate should be measured in maintenance dialysis patients once monthly.** ***(Opinion)***

GUIDELINE 14	**Treatment of Low Serum Bicarbonate** **Predialysis or stabilized serum bicarbonate levels should be maintained at or above 22 mmol/L.** ***(Evidence and Opinion)***

RATIONALE

Acidemia refers to abnormally increased hydrogen ion concentrations in the blood. Acidosis refers to the existence of one or more conditions that promote acidemia. Acidemia, as measured by serum bicarbonate and/or blood pH, is common in individuals who have CRF or who are undergoing MD. Low serum bicarbonate concentrations in a MD patient almost always indicate metabolic acidosis. Questions concerning the presence or severity of acidemia can be resolved by measuring arterial blood pH and gases. Acidemia due to metabolic acidosis is associated with increased oxidation of branched chain amino acids (valine, leucine, and isoleucine),[103] increased protein degradation[104] and PNA,[105,106] and decreased albumin synthesis.[107] Levels of plasma branched chain amino acids have been described to be low in CRF, and a significant direct correlation between plasma bicarbonate levels and free valine concentrations in muscle has been reported in MD patients.[108] Similarly, a direct correlation between serum bicarbonate and albumin concentrations has been observed in MHD patients.[105,109] Acidemia may have detrimental effects on vitamin D synthesis and bone metabolism and may increase beta-2 microglobulin turnover.[110]

Normalization of the predialysis or stabilized serum bicarbonate concentration can be achieved by higher basic anion concentrations in the dialysate and/or by oral supplementation with bicarbonate salts. Higher concentrations of bicarbonate in hemodialysate (>38 mmol/L) has been shown to safely increase predialysis serum bicarbonate concentrations.[45,104,111-113] An oral dose of sodium bicarbonate, usually about 2 to 4 g/d or 25 to 50 mEq/d, can be used to effectively increase serum bicarbonate concentrations.[109,112,114-116] In individuals undergoing CPD, higher dialysate lactate or bicarbonate levels and oral sodium bicarbonate may each raise serum bicarbonate levels.[114,117,118]

Correction of acidemia due to metabolic acidosis has been associated with increased serum albumin,[119] decreased protein degradation rates,[113,114,120] and increased plasma concentrations of branched chain amino acids and total essential amino acids.[116,119,121] It has been proposed that eradication of acidemia increases cellular influx and decreases cellular efflux of branched chain amino acids.[121] An increase in plasma bicarbonate levels may promote greater body weight gain and increased mid-arm circumference[117]; a rise in triceps skinfold (TSF) thickness is also reported but is not a consistent finding.[113,117] In one long-term study of CPD patients, raising the serum bicarbonate level was associated with fewer hospitalizations and shorter hospital stays.[117] Rapid correction of acidemia by bicarbonate infusion has been associated with an increase in serum $1,25(OH)_2D_3$ concentrations[122] and a decrease in osteocalcin, suggesting an improvement in osteoblast function.[123]

A few studies have not found any detrimental effects of mild metabolic acidemia, and some investigators found that small increases in serum bicarbonate concentrations were not associated with significant improvements in nutritional or clinical status.[124-126] Indeed, some epidemiological studies report that a slightly increased anion gap, unadjusted for serum creatinine or albumin, is associated with a lower risk of mortality. This latter relationship may be due to greater appetites and protein intake in healthier people. However, most trials report that normalizing the predialysis or stabilized serum bicarbonate concentrations is beneficial for protein, amino acid and bone metabolism, and protein-energy nutritional status.[36] Thus, the serum bicarbonate should be monitored regularly at monthly intervals and correction of metabolic acidemia by maintaining serum bicarbonate at or above 22 mmol/L should be a goal of the management of individuals undergoing MD.

There are several technical problems with measuring bicarbonate. The techniques of blood collection and transportation and the assay methods can each influence the measured values. Serum bicarbonate (as total CO_2) was found to be significantly lower (about 4 mmol/L) in a reference laboratory when measured by enzymatic assay as compared with when it was measured directly by an electrode.[127] Introduction of air into the collecting tube, the technique of removal of blood for assay, and long delays in the measurement can each adversely affect the results. For more accurate values, blood should not be allowed to have contact with air, delays in processing of the sample should be avoided, and the same laboratory and methods of analysis should be used for serial measurements.

RECOMMENDATIONS FOR RESEARCH

1. The optimum serum bicarbonate and blood pH levels for MD patients need to be defined. There are data from individuals without renal insufficiency indicating that mid-normal or high normal blood pH range maintains better nutritional status than does the low-normal range.

2. More research is needed on the long-term effects of correcting acidemia on clinical outcomes and particularly on intermediate nutrition-related outcomes as well as morbidity and mortality.

3. The effect of correction of acidemia on muscle function and on beta-2 microglobulin metabolism needs more investigation.

3. Management of Protein and Energy Intake

GUIDELINE 15

Dietary Protein Intake (DPI) in Maintenance Hemodialysis (MHD)

The recommended DPI for clinically stable MHD patients is 1.2 g/kg body weight/d. ***(Evidence and Opinion)***

- At least 50% of the dietary protein should be of high biological value.

RATIONALE

The findings from many studies that MHD patients have a high incidence of PEM underscores the importance of maintaining an adequate nutrient intake.[128,129] Although there are numerous causes for malnutrition, decreased nutrient intake is probably the most important. Causes of poor nutrient intake include anorexia from uremia itself, the dialysis procedure, intercurrent illness, and acidemia. Inadequate intake is also caused by comorbid physical illnesses affecting gastrointestinal function, depression, other psychiatric illness, organic brain disease, or socioeconomic factors. Removal of amino acids (about 10 to 12 g per HD),[130-132] some peptides,[133] low amounts of protein ($\leq$1 to 3 g per dialysis, including blood loss), and small quantities of glucose (about 12 to 25 g per dialysis if glucose-free dialysate is used) may contribute to PEM. Hypercatabolism from a chronic inflammatory state, associated illnesses, the dialysis procedure itself, or acidemia may also induce malnutrition.[134-137]

DPI is often reported to be low in MHD patients. A number of publications have described the mean DPI of individuals treated with MHD to vary from about 0.94 to 1.0 g protein/kg/d.[57,138-140] Hence, approximately half of MHD patients ingest less than this quantity of protein. Few studies have directly assessed the dietary protein requirements for MHD patients. No prospective long-term clinical trials have been conducted in which patients are randomly allocated to different dietary protein levels and the effects of protein intake on morbidity, mortality, or quality of life have been assessed.

Several prospective nutritional-metabolic studies have compared the effects of different levels of DPI on nutritional status. Most of these latter studies have been carried out in in-hospital clinical research centers, and hence, the numbers of patients studied have been small.[57,58,137,139] Taken together, these studies suggest that a DPI of about 1.2 g/kg/d is necessary to ensure neutral or positive nitrogen balance in most clinically stable MHD patients. At least 50% of the protein in-

gested should be of high biological value. Protein of high biological value has an amino acid composition that is similar to human protein, is likely to be an animal protein, and tends to be utilized more efficiently by humans to conserve body proteins. The increased efficiency of utilization of high biological value protein is particularly likely to be observed in individuals with low protein intakes.

Retrospective studies analyzing the relationships between DPI and such outcomes as nutritional status[138] or morbidity and mortality have also been conducted.[141-143] Protein intake in these studies has been estimated from dietary histories obtained from patient recall or estimated from the protein equivalent of total nitrogen appearance (PNA or PCR; see Appendix V for discussion of these methods). In two retrospective studies of MHD patients, protein intakes of less than 1.2 g/kg/d were associated with lower serum albumin levels and higher morbidity.[140,141] On the other hand, not every epidemiological study found a significant relationship between morbidity or mortality and normalized PNA (nPNA or nPCR).[142,143]

In summary, a number of studies have shown a relationship between DPI and such measures of nutritional status as levels of serum albumin, prealbumin and transferrin, body weight, morbidity, and mortality. DPI also correlates with nitrogen balance. Protein intakes of less than 0.75 g/kg/d are inadequate for most MHD patients. Ingestion of 1.1 g of protein/kg/d (with at least 50% of the protein of high biological value) may maintain good protein nutrition in some MHD patients but is not sufficient to maintain good nutrition in the great majority of clinically stable patients ingesting 25 or 35 kcal/kg/d.[58] It is therefore recommended that a safe DPI that will maintain protein balance in almost all clinically stable MHD patients is 1.2 g protein/kg BW/d; at least 50% of the protein should be of high biological value.

It is difficult for some MHD patients to maintain this level of daily protein intake. Techniques must be developed to ensure this level of intake for all patients. Education and dietary counseling should be the first steps in attempting to maintain adequate protein intake. If this approach is unsuccessful, nutritional support, such as that outlined in Guideline 19, should be considered. These techniques include food supplements, tube feeding, and intravenous nutrition. It should be recognized that foods containing protein are major sources of phosphorus, hydrogen ions, cholesterol (in the case of animal protein), and dietary fats. When increasing dietary protein intake, adjustments in therapy (eg, dialysis dose, phosphate binders, bicarbonate supplementation, and cholesterol management) should be considered.

RECOMMENDATIONS FOR RESEARCH

1. More studies are needed on the relationship between the quantity and type of DPI and nutritional status, morbidity, mortality, and quality of life in MHD patients. Long-term, randomized, prospective clinical trials would be particularly helpful in addressing these questions. To reduce the large costs for such studies, innovative investigational tools are needed.

2. Information concerning dietary protein requirements of special subsets of MHD patients is needed. Such subsets include individuals with PEM or low dietary energy intake (DEI), obese individuals, and the elderly.

GUIDELINE 16

Dietary Protein Intake (DPI) for Chronic Peritoneal Dialysis (CPD)

The recommended DPI for clinically stable CPD patients is 1.2 to 1.3 g/kg body weight/d. *(Evidence)*

- Dietary protein intake should be no less than 1.2 g/kg/d.
- Unless a patient has demonstrated adequate protein nutritional status on a 1.2 g protein/kg/d diet, 1.3 g protein/kg/d should be prescribed.
- At least 50% of the dietary protein should be of high biological value.

RATIONALE

The fact that patients with ESRD treated with CPD often have PEM emphasizes the importance of maintaining an adequate intake of protein.[29,30,33] Many of the causes of malnutrition in CPD patients are similar to those in MHD patients. However, protein losses into peritoneal dialysate are almost invariably higher than are protein losses into hemodialysate. Peritoneal protein losses average about 5 to 15 g/24 hours, and during episodes of peritonitis, dialysate protein may be considerably higher.[144] Peritoneal amino acid losses average about 3 g/d,[145] and some peptides are dialyzed. Anorexia due to glucose absorption from dialysate may also contribute to reduced dietary intake and malnutrition. These factors result in a requirement for dietary protein that is higher than in the normal population. Compounding these factors and predisposing to malnutrition is the finding that DPI is often rather low, less than 1.0 g/kg/d. As with MHD patients, malnutrition in peritoneal dialysis patients is associated with poor outcome.[16,19,44,145,147]

Several studies have examined nitrogen balances in CPD patients consuming various levels of dietary protein. These studies indicate that DPIs of 1.2 g/kg/d or greater are almost always associated with neutral or positive nitrogen balance.[59,60,148] A number of studies show a relationship between DPI and such nutritional parameters as serum albumin, total body protein and nitrogen balance in patients undergoing CPD.[59,60,148] Based on these considerations, it is recommended that a safe DPI that will maintain protein balance in almost all clinically stable CPD patients is at least 1.2 g protein/kg body weight/d. A DPI of 1.3 g/kg/d probably increases the likelihood that adequate protein nutrition will be maintained in almost all clinically stable individuals. At least 50% of the protein should be of high biological value. The nPNA for a 70-kg man ingesting 1.2 g and 1.3 g protein/kg body weight/d, based on the Bergstrom and Blumenkrantz data, is estimated to be 1.02 and 1.14 g protein/kg/d.[149,150] It is recognized that some CPD patients will maintain good protein nutritional status with somewhat lower

dietary protein intakes. The current guideline is recommended to provide assurance that almost all clinically stable CPD patients will have good protein nutrition.

Patients who do not have an adequate DPI should first receive dietary counseling and education. If DPI remains inadequate, oral supplements should be prescribed. If the oral supplements are not tolerated or effective and protein malnutrition is present, consideration should be given to use of tube feedings to increase protein intake. Amino acids may be added to dialysate to increase amino acid intake and to replace amino acid losses in dialysate.[151,152]

RECOMMENDATIONS FOR RESEARCH

1. The research recommendations for management of DPI for patients treated with maintenance peritoneal dialysis are similar to those for patients treated with MHD.

2. Studies to determine the optimum protein intake should be undertaken in subsets of CPD patients, including those who are elderly, malnourished, obese, or who have a low energy intake or catabolic illness such as peritonitis.

GUIDELINE 17

Daily Energy Intake for Maintenance Dialysis Patients

The recommended daily energy intake for maintenance hemodialysis or chronic peritoneal dialysis patients is 35 kcal/kg body weight/d for those who are less than 60 years of age and 30 to 35 kcal/kg body weight/d for individuals 60 years or older. (*Evidence and Opinion)*

- Energy expenditure of patients undergoing maintenance hemodialysis or continuous ambulatory peritoneal dialysis is similar to that of normal, healthy individuals.
- Metabolic balance studies of people undergoing maintenance hemodialysis indicate that a total daily energy intake of about 35 kcal/kg/d induces neutral nitrogen balance and is adequate to maintain serum albumin and anthropometric indices.
- Because individuals more than 60 years of age tend to be more sedentary, a total energy intake of 30 to 35 kcal/kg is acceptable.

RATIONALE

Longitudinal and cross-sectional data indicate that MD patients frequently have low energy intake and are underweight, often despite receiving apparently adequate dialysis therapy.[128,153] Low body weights (adjusted for height, age, and gender) are associated with increased mortality rates in MD patients.[15,50,85,86] Hence, it would seem important to aggressively attempt to maintain adequate energy intakes.

Dietary energy requirements have been studied in MHD patients under metabolic balance conditions. Dietary energy requirements were examined in six MHD patients while they ingested diets providing 25, 35, and 45 kcal/kg/d and a DPI of 1.13 g/kg/d for 21 days each. These studies indicated that the mean energy intake necessary to maintain both neutral nitrogen balance and unchanging body composition was about 35 kcal/kg/d.[58] The finding that energy expenditure in MHD and CPD patients appears to be normal corroborates the observations from the aforementioned nitrogen balance and body composition studies.[154-157]

Based on the aforementioned studies, it is recommended that MHD patients consume a diet with a total daily energy intake of 35 kcal/kg body weight/d. For CPD patients, the recommended total daily energy intake, including both diet and the energy intake derived from the glucose absorbed from peritoneal dialysate, should be 35 kcal/kg/d. Most of the patients who participated in these studies were younger than 50 years of age, and this recommendation is therefore made only for individuals less than 60 years of age. Because older age may be associated with reduced physical activity and lean body mass, a daily energy intake of 30 to 35 kcal/kg/d for older patients with more sedentary lifestyles is acceptable. These recommendations are approximately the same as those for normal adults of the same age who are engaged in mild daily physical activity as indicated in the Recommended Dietary Allowances (RDA).[158]

Many patients will be unable to attain these recommended energy intakes. For individuals who are unable to consume an adequate energy intake, intensive education and dietary counseling by a trained dietitian should be undertaken. If this strategy is unsuccessful, oral nutritional supplements that are high in energy are recommended. Tube feedings and parenteral nutrition may also be considered (Guideline 19). Obese patients may not require as much energy per kilogram of body weight as nonobese patients (Guideline 12).

RECOMMENDATIONS FOR RESEARCH

1. Few studies have examined energy requirements of persons undergoing MHD or CPD. Hence, there is a great need for more research in this area. It would be of particular value to conduct both carefully controlled metabolic studies, as well as long-term, randomized outpatient clinical trials, particularly in which patients are randomly assigned to different energy intakes. It would be helpful to relate daily energy intake to morbidity, mortality, and quality of life scales, as well as to nutritional measures. To reduce the high cost and length of time to collect such data, innovative investigative tools to address these issues are needed.

2. Studies are needed to assess the optimal energy requirements of subsets of MD patients (eg, individuals with PEM, patients with superimposed catabolic illnesses, obese individuals, and elderly patients).

3. Studies are needed to examine whether increasing energy intake of MD patients with protein or energy malnutrition would be beneficial to the patients.

4. Assessment of energy intake is laborious, time-consuming, and therefore expensive. Developmental studies to create accurate and less costly methods for assessing energy intake are greatly needed.

4. Nutritional Counseling and Follow-Up

GUIDELINE 18

Intensive Nutritional Counseling With Maintenance Dialysis (MD)

Every MD patient should receive intensive nutritional counseling based on an individualized plan of care developed before or at the time of commencement of MD therapy. ***(Opinion)***

- A plan of care for nutritional management should be developed before or during the early phase of MD care and modified frequently based on the patient's medical and social conditions.
- The plan of care should be updated at least every 3 to 4 months.
- Nutrition counseling should be intensive initially and provided thereafter every 1 or 2 months and more frequently if inadequate nutrient intake or malnutrition is present or if adverse events or illnesses occur that may cause deterioration in nutritional status.

RATIONALE

The high incidence of PEM and the strong association between measures of malnutrition and mortality rate in individuals undergoing MD suggests the need for careful nutritional monitoring and treatment of these individuals. Whether or not such intervention prevents or improves nutritional status has not been examined, but evidence clearly suggests that inadequate nutritional intake is an important contributor for PEM in these patients.[159] Moreover, evidence from large multicenter trials utilizing nutrition intervention indicates that frequent nutrition counseling results in compliance with the intervention and improved outcomes.[160-163] Although similar studies have not been performed in MD patients, it is reasonable to assume that similar results would occur with the ESRD patient population.

The dietitian-performed nutrition assessment includes the development of a plan of care that incorporates all aspects of the nutrition evaluation (nutritional status assessment, nutrition history, patient preferences, and the nutritional prescription). These are incorporated into an active plan that is then implemented by the medical team. This care plan should be updated on a quarterly basis. The nutrition care plan should be incorporated into a continuous quality improvement plan. This plan of care should be implemented and reviewed in a multidisciplinary fashion that includes the patient and/or caregiver (often the patient's spouse) and the physician, nurse, social worker, and dietitian.

Conditions in which the patient's nutritional status may deteriorate rapidly may dictate more frequent evaluation of the nutrition care plan. Examples of such conditions are unexplained reductions in energy or protein intake, depression, deterioration in other measures of protein-energy status, pregnancy, acute inflammatory or catabolic illnesses particularly in the elderly, hospitalization, diabetes mellitus, large or prolonged doses of glucocorticoid or other catabolic medications, and post-renal transplant allograft loss. Under these circumstances, monthly or weekly updates to the nutrition plan of care and more intensive nutrition counseling may be necessary.

RECOMMENDATIONS FOR RESEARCH

1. A better understanding of the effects of nutrition intervention counseling methods (including quality of life scales) on nutritional intake, nutritional status, morbidity, and mortality should be evaluated in MD patients.

GUIDELINE 19

Indications for Nutritional Support

Individuals undergoing maintenance dialysis who are unable to meet their protein and energy requirements with food intake for an extended period of time should receive nutrition support. (*Evidence and Opinion*)

- The period of inadequate intake after which nutritional support should be instituted ranges from days to 2 weeks, depending on the severity of the patient's clinical condition, degree of malnutrition (if any), and the degree of inadequacy of their nutritional intake.
- Before considering nutrition support, the patient should receive a complete nutritional assessment.
- Any potentially reversible or treatable condition or medication that might interfere with appetite or cause malnutrition should be eliminated or treated.
- For nutrition support, the oral diet may be fortified with energy and protein supplements.
- If oral nutrition (including nutritional supplements) is inadequate, tube feeding should be offered if medically appropriate.
- If tube feedings are not used, intradialytic parenteral nutrition (IDPN; for hemodialysis) or intraperitoneal amino acids (IPAA; for peritoneal dialysis) should be considered if either approach in conjunction with existing oral intake meets the protein and energy requirements.
- If the combination of oral intake and IDPN or IPAA does not meet protein and energy requirements, daily total or partial parenteral nutrition should be considered.
- The dialysis regimen should be regularly monitored and modified to treat any intensification of the patient's uremic state that is caused by superimposed illness or increased protein intake.

RATIONALE

Many apparently well-dialyzed patients consume approximately 80% or less of their recommended energy intake,[164] even when counseled by an experienced renal dietitian. Inadequate nutrient intake may have a variety of causes, including anorexia, inadequate nutritional training, inability to procure or prepare food, psychi-

atric illnesses, superimposed acute or chronic diseases, mechanical impairments to food intake (eg, lack of dentures), cultural food preferences, and the uremic state, sometimes intensified by underdialysis.[165] Hospitalized MD patients often ingest even lower amounts (eg, as low as 66% and 50%, respectively) of protein and energy,[138,150] even though protein and energy needs of patients often increase during acute illness. Even in individuals who consumed an adequate diet prior to an illness, food intake may fall to inadequate levels. In the acutely ill hospitalized patient, prescription of an oral diet is often unlikely to improve the intake to a level that maintains neutral or positive nitrogen balance.[138,150] These considerations underscore the need for nutrition support for MD patients who sustain inadequate nutrient intake for extended periods of time. There are no large-scale, randomized, prospective clinical trials evaluating the effects of nutrition support in MD patients. Recommendations are therefore based on the experience in nonrenal patients as well as current information regarding nutrition and metabolism of ESRD patients.

Published guidelines and available recommendations suggest that counseling to increase dietary protein and energy intake, nutritional supplements, and tube feeding should be considered before attempting forms of parenteral nutrition in MD patients.[166-169] If the intestinal tract is functional, enteral tube feeding is traditionally considered the first line of nutritional therapy in the hospitalized patient who is unable to eat adequately. It has been used successfully to provide nutritional support to infants and children who are receiving MD.[170-172] Adult MHD patients have been nourished exclusively with oral supplements.[173] There is no reason to suspect that malnourished adult MD patients would differ from infants or children or that acutely ill adult MD patients would differ from acutely ill nondialysis patients in their response to enteral feedings, except for a greater need to restrict the water, mineral, and possibly protein loads in these feedings.[173]

Advantages to enteral feeding include its ability to provide a patient's total nutritional needs chronically and on a daily basis, to provide balanced nutrients, to administer specialized formulas, to provide a smaller water load than intravenous feedings, to constitute a lower risk of infection than total parenteral nutrition (TPN), and to be less expensive than TPN or IDPN.[174,175] Risks of enteral feeding include pulmonary aspiration, fluid overload, reflux esophagitis, and other complications of enteral feeding devices.

MHD patients who satisfy each of the following three criteria may benefit from IDPN:

1. Evidence of protein or energy malnutrition and inadequate dietary protein and/or energy intake.[176]

2. Inability to administer or tolerate adequate oral nutrition, including food supplements or tube feeding.

3. The combination with oral or enteral intake which, when combined with IDPN, will meet the individual's nutritional needs.

Previously published studies support the use of IDPN for selected MHD patients who are malnourished and eating poorly.[169,175,177] Advantages of IDPN as compared to tube feeding or TPN include the following: no need for a dedicated enteral feeding tube or vascular access, ultrafiltration during dialysis (which reduces the risks of fluid overload), and no demands on the time or effort of the patient. Disadvantages to IDPN include provision of insufficient calories and protein to support longterm daily needs (ie, IDPN is given during dialysis for only 3 days out of 7), it does not change patients' food behavior or encourage them to eat more healthy meals, and it is expensive.[178]

IPAA may increase protein balance in clinically stable, malnourished CPD patients who have low protein intakes.[151,152,179-185] The net infusion of 2 L of peritoneal dialysate containing 1.1% amino acids with a peritoneal dwell time of 5 to 6 hours is associated with a retention of about 80% of the amino acids. The amount retained varies directly with peritoneal transport characteristics as determined by peritoneal equilibrium testing.[187] Hence, the administration of a single 2-L exchange of 1.1% amino acid dialysate for 5 to 6 hours provides a net uptake of about 17 to 18 g of amino acids, which is greater than the quantity of both protein (about 9 g) and amino acids (about 3 g) removed each day by peritoneal dialysis.[187]

IPAA may also reduce the infused daily carbohydrate load by about 20%, thereby reducing the risk of hyperglycemia and the tendency to hyper-

triglyceridemia.[188] Most studies of IPAA were not randomized or controlled and used an open (before-after) or crossover design. Intermediate nutrition-related outcome variables (eg, nitrogen-protein balance, serum proteins, and anthropometry) were used in all studies. No study of IPAA has evaluated patient survival, hospitalization, or other clinical outcomes (eg, health-related quality of life). The long-term effects of IPAA on nutritional status and clinical outcomes are unknown. In some patients given IPAA, a mild metabolic acidosis may occur that is readily treatable.

CPD patients who satisfy each of the following three criteria may benefit from IPAA:

1. Evidence of protein malnutrition and an inadequate DPI.

2. Inability to administer or tolerate adequate oral protein nutrition, including food supplements, or enteral tube feeding.

3. The combination of some oral or enteral intake which, when combined with IPAA, will meet the individual's nutritional goals.

Also, in some patients who have difficulty with control of hyperglycemia, hypercholesterolemia, or hypertriglyceridemia that is related to the extensive carbohydrate absorption from peritoneal dialysate, IPAA might reduce serum glucose and lipid levels.

RECOMMENDATIONS FOR RESEARCH

1. Conduct a randomized clinical trial comparing oral nutritional supplements, tube feeding, and IDPN in malnourished MD patients. Outcomes should include survival, morbidity, and quality of life as well as nutritional status.

2. Research is needed to define the optimal composition of oral supplements, enteral nutrition, and IDPN formulas for MD patients.

3. Conduct studies of the indications for nutritional support in MD patients.

4. Determine the optimal timing for IPAA administration (eg, daytime CAPD versus nighttime with cycler).

5. Evaluate the effects of IPAA on physical function, hospitalization, and other clinical outcomes.

6. Examine the clinical value and cost-effectiveness of nutritional support through hemodialysate.[130]

GUIDELINE 20

Protein Intake During Acute Illness

The optimum protein intake for a maintenance dialysis patient who is acutely ill is at least 1.2 to 1.3 g/kg/d. ***(Opinion)***

- Acutely ill maintenance hemodialysis patients should receive at least 1.2 g protein/kg/d.
- Acutely ill chronic peritoneal dialysis patients should receive at least 1.3 g protein/kg/d.

GUIDELINE 21

Energy Intake During Acute Illness

The recommended energy intake for a maintenance dialysis patient who is acutely ill is at least 35 kcal/kg/d for those who are less than 60 years of age and at least 30 to 35 kcal/kg/d for those who are 60 years of age or older. ***(Evidence and Opinion)***

RATIONALE

For the purposes of this guideline, acutely ill refers to an acute medical or surgical illness associated with a state of increased catabolism. Such events would be expected to increase the protein and energy requirements. Hospitalization is not a prerequisite for this definition.

Few data exist on the protein requirements of acutely ill MD patients.[138,150,189,190] There are no published data of the energy requirements of acutely ill MD patients. Septic patients with acute renal failure have an increased resting energy expenditure (REE).[155] There is no reason to assume that the protein requirements of the acutely ill MD patient is less than that needed by the clinically stable MD patient.[60,138,148,150,190,191] The recommended safe protein intake for MHD and CPD patients is considered to be 1.2 g/kg/d and 1.3 g/kg/d, respectively (Guidelines 15 and 16). The recommended daily energy intake for both MHD and CPD patients with light to moderate physical activity is 35 kcal/kg/d for those less than 60 years of age and 30 to 35 kcal/kg/d for those 60 years of age or older (Guideline 17).

Acutely ill, hospitalized MD patients often ingest less than 1.2 or 1.3 g protein/kg/d and are usually in negative nitrogen balance.[138,150] On the other hand, hospitalized dialysis patients who were given a mean protein intake of 1.3 g/kg/d or greater, with a non-protein energy intake of 34 $\pm$ 6 kcal/kg/d, were able to improve biochemical markers of nutritional status.[189] A protein intake of 0.79 g/kg/d or less and an energy intake of 18 $\pm$ 8 kcal/d or less is associated with neutral or negative nitrogen balance in hospitalized MHD patients.[138] In CAPD patients, hypoalbuminemia is more likely to occur when the protein intake is less than 1.3 g/kg/d and is significantly associated with an increased incidence of peritonitis and more prolonged hospital stays.[190] Protein intakes of 1.5 g/kg/d or greater appear to be well tolerated in CPD patients.[60,192]

Hospitalized MD patients frequently have a decreased energy intake that, in one study, averaged 50% of recommended levels, and this was associated with negative nitrogen balance.[138] Hospitalized infected MD patients displayed an increase in serum proteins when their energy intake was 34 kcal/kg/d, and the increase in their serum prealbumin concentrations was directly correlated with the cumulative non-protein energy intake ($r = 0.37$, $P < 0.01$).[189]

For acutely ill individuals without renal disease, greater DPIs, as high as 1.5 to 2.5 g/kg/d, are often recommended.[166] It is proposed that these higher protein intakes may preserve or even replete body protein more effectively than lower protein intakes.[166,167] These considerations raise the possibility that protein intakes greater than 1.2 or 1.3 g/kg/d may also benefit the catabolic, acutely ill MHD or CPD patient. However, there are no data as to whether these benefits will occur in acutely ill MD patients. Moreover, DPIs in this range, and the attendant increase in water and mineral intake, often will not be well tolerated by MD patients unless they are undergoing more intensive HD with increased dialysis dose (ie, more than three times per week or continuous venovenous hemofiltration with HD [CVVHD]).[193,194] Thus, MD patients who receive more intensive dialysis treatment may tolerate protein intakes greater than 1.2 to 1.3 g protein/kg/d. Amino acid losses and, hence, amino acid requirements may increase with more intensive HD (about 10 to 12 g of amino acids removed with each HD)[130-132] or with CVVHD (an average of about 5 to 12 g of amino acids per day removed with CVVHD in patients receiving nutritional support).[194]

Because acutely ill MD patients are generally very inactive physically, their energy needs will be diminished by the extent to which their physical activity has been decreased. In rather sedentary individuals, however, physical activity accounts for only roughly 3% of total daily energy expenditure. In acutely ill nonrenal patients, REE may increase modestly, and daily energy requirements are not increased over normal. Thus, energy intakes of 30 to 35 kcal/kg/d are recommended for acutely ill MHD and CPD patients. The energy provided by the uptake of dextrose or other energy sources from dialysate should be included when calculating energy intake.

It is emphasized that many acutely ill individuals are not able to ingest this quantity of protein or energy,[138,150] and tube feeding, IDPN, or TPN may be necessary (Guideline 19). Hospitalized dialysis patients who have evidence of malnutrition at the time of admission may require more

immediate nutrition support depending on the adequacy of their nutrient intake. For some patients in whom an extended period of inadequate nutrient intake can be projected, nutritional support should be instituted immediately. These recommendations refer to the acutely ill MD patient. The appropriate nutritional management of the acutely ill patient with acute renal failure may be quite different.[195]

RECOMMENDATIONS FOR RESEARCH

1. Studies to define the optimal protein intake for the MD patients who are acutely ill are needed.

2. The effects of different levels of protein intake on patient outcome and on nutritional markers are needed. Because increasing protein intake may alter dialysis requirements, the effect of higher levels of protein intake on the optimal dose of dialysis should be defined.

3. The energy needs of acutely ill MD patients should be better defined. It would be particularly valuable to define how energy needs may vary with different protein and amino acid intakes.

4. The development of simple and inexpensive methods for determining the energy expenditure in individual acutely ill patients would be very helpful.

5. The optimal mixes of energy sources (ie, protein, amino acids, carbohydrates, and fat) for acutely ill MD patients should be defined.

6. Studies are needed that examine which energy intakes are associated with the most optimal clinical outcomes.

5. Carnitine

GUIDELINE 22

L-Carnitine for Maintenance Dialysis Patients

There are insufficient data to support the routine use of L-carnitine for maintenance dialysis patients. (*Evidence and Opinion)*

- Although the administration of L-carnitine may improve subjective symptoms such as malaise, muscle weakness, intradialytic cramps and hypotension, and quality of life in selected maintenance dialysis patients, the totality of evidence is insufficient to recommend its routine provision for any proposed clinical disorder without prior evaluation and attempts at standard therapy
- The most promising of proposed applications is treatment of erythropoietin-resistant anemia

RATIONALE

The use of L-carnitine in MD patients is attractive on the theoretical level, because it is well known that patients undergoing MD usually have low serum free L-carnitine concentrations and that skeletal muscle carnitine is sometimes decreased. Because L-carnitine is known to be an essential co-factor in fatty acid and energy metabolism, and patients on dialysis tend to be malnourished, it might follow that repletion of L-carnitine by the intravenous or oral route could improve nutritional status, particularly among patients with low dietary L-carnitine intakes. L-carnitine has been proposed as a treatment for a variety of metabolic abnormalities in ESRD, including hypertriglyceridemia, hypercholesterolemia, and anemia. It has also been proposed as a treatment for several symptoms or complications of dialysis, including intradialytic arrhythmias and hypotension, low cardiac output, interdialytic and post-dialytic symptoms of malaise or asthenia, general weakness or fatigue, skeletal muscle cramps, and decreased exercise capacity or low peak oxygen consumption. Studies using L-carnitine for each of these potential indications were reviewed. Randomized clinical trials were given particular consideration, although the evidence was not restricted to these studies, many of which are summarized in Appendix X.

There was complete agreement that there is insufficient evidence to support the routine use of L-carnitine for MD patients. In selected individuals who manifest the above symptoms or disorders and who have not responded adequately to standard therapies, a trial of L-carnitine may be considered. In reaching these conclusions, we considered the strength of available evidence as well as the alternative therapies available for each potential indication.

RECOMMENDATIONS FOR RESEARCH

1. Additional clinical trials in the area of erythropoietin-resistant anemia, carefully ac-

counting for anticipated differences in response based on factors such as iron stores and the level of inflammatory mediators.

2. Further definition of the L-carnitine response by taking an ''outcomes'' approach to patients treated with L-carnitine. Can patient subgroups be identified who are likely to respond to L-carnitine for one or more of its proposed indications? Are certain individuals uniform ''responders'' across indications (a ''carnitine-deficient'' phenotype) or do certain patient characteristics predict specific responses?

3. A randomized clinical trial of L-carnitine in MD patients with cardiomyopathy and reduced ejection fraction.

4. A randomized clinical trial of L-carnitine for the treatment of hyperlipidemia, restricted to patients with preexisting hyperlipidemia.

B. ADVANCED CHRONIC RENAL FAILURE WITHOUT DIALYSIS

GUIDELINE 23

Panels of Nutritional Measures for Nondialyzed Patients

For individuals with CRF (GFR <20 mL/min) protein-energy nutritional status should be evaluated by serial measurements of a panel of markers including at least one value from each of the following clusters: (1) serum albumin; (2) edema-free actual body weight, percent standard (NHANES II) body weight, or subjective global assessment (SGA); and (3) normalized protein nitrogen appearance (nPNA) or dietary interviews and diaries. ***(Evidence and Opinion)***

- It is recommended that serum albumin and actual or percent standard body weight and/or SGA be measured every 1 to 3 months.
- Dietary interviews and diaries and/or nPNA should be performed every 3 to 4 months.
- For patients with more advanced CRF (ie, GFR ≤15 mL/min), concomitant illness, inadequate nutrient intake, deteriorating nutritional status, or frank malnutrition, more frequent monitoring may be necessary.

RATIONALE

Deterioration of nutritional status often begins early in the course of CRI, when the GFR is as high as 28 to 35 mL/min/1.73 m^2 or greater.[196-198] As a result, frank PEM is frequently present at the time that individuals commence MD therapy.[16,23,128] Malnutrition in patients commencing MD is a strong predictor of poor clinical outcome.[22,23,79,199] Thus, it is important to prevent or correct PEM in patients with progressive CRF, although randomized prospective clinical trials to test this hypothesis are not available. Methods for estimating or measuring GFR are discussed in Appendix IX.

The use of effective techniques to monitor nutritional status is an essential component of protocols to prevent or treat malnutrition in individuals with progressive CRI or CRF. Serum albumin, a measure of body weight-for-height (eg, %SBW), SGA, and assessment of dietary intake are all recommended because of the extensive experience with these indices and each is predictive of future morbidity and mortality in individuals with CRI or CRF or patients on MD. Serum albumin and prealbumin are indicators of visceral protein mass as well as inflammatory status and have been used extensively in persons with or without renal disease to assess nutritional status.[17,42] Moreover, hypoalbuminemia and low serum prealbumin at the initiation of dialysis are predictive of increased mortality risk.[19,42,44,145,199]

For the nondialyzed patient with chronic renal failure, there are much more data relating serum albumin rather than serum prealbumin concentrations to outcome. Also, since serum prealbumin levels are affected by the GFR,[17] variations in renal function may confound the results. There-

fore, although either measurement could be used to assess the nutritional or inflammatory status of the CRI or CRF patient, the serum albumin may be the preferred measurement.

Reduction in body weight below reference values correlates with the loss of somatic protein, as well as increased risk of hospitalization, postoperative complications, and mortality.[15,85] In MD patients, evidence of moderate to severe malnutrition as determined by SGA is associated with increased mortality.[16,79,200,201] Measurements of dietary interviews/diaries and nPNA are recommended because these measures can detect inadequate nutrient intake, which predicts poor outcome and is also a key cause of PEM (see Appendices III, V, and VI).

RECOMMENDATIONS FOR RESEARCH

1. More sensitive and specific measures of protein-energy nutritional status in CRI/CRF patients need to be developed.

2. Studies are needed to test whether monitoring nutritional status in individuals with progressive CRI/CRF by a combination of measures is beneficial for detecting and preventing malnutrition.

3. Additional research is needed to define more accurately the combination of measures that provides the most useful information concerning the nutritional status of individuals with CRI/CRF.

GUIDELINE 24

Dietary Protein Intake for Nondialyzed Patients

For individuals with chronic renal failure (GFR <25 mL/min) who are not undergoing maintenance dialysis, the institution of a planned low-protein diet providing 0.60 g protein/kg/d should be considered. For individuals who will not accept such a diet or who are unable to maintain adequate DEI with such a diet, an intake of up to 0.75 g protein/kg/d may be prescribed. *(Evidence and Opinion)*

- When properly implemented and monitored, low-protein, high-energy diets maintain nutritional status while limiting the generation of potentially toxic nitrogenous metabolites, the development of uremic symptoms, and the occurrence of other metabolic complications.
- Evidence suggests that low protein diets may retard the progression of renal failure or delay the need for dialysis therapy.
- At least 50% of the dietary protein should be of high biologic value.
- When patients with CRF consume uncontrolled diets, a decline in protein intake and in indices of nutritional status is often observed.

RATIONALE

There are several potential advantages to prescribing a carefully designed low-protein diet (eg, about 0.60 g protein/kg/d) for the treatment of individuals with progressive CRF. Low-protein diets reduce the generation of nitrogenous wastes and inorganic ions, which cause many of the clinical and metabolic disturbances characteristic of uremia. Moreover, low-protein diets can diminish the ill effects of hyperphosphatemia, metabolic acidosis, hyperkalemia, and other electrolyte disorders. Although the main hypothesis of the Modification of Diet in Renal Disease Study was not proven,[202] post hoc analyses indicated that low protein diets retarded the progression of renal failure.[203,204] Three meta-analyses each indicate that such diets are associated with retardation of the progression of renal failure or a delay in the onset of renal replacement therapy.[205-207] It is also possible that in patients with higher levels of GFR, possibly as great as 50 mL/min/1.73 m^2, a planned low protein diet may retard progression of renal failure. There has been much confusion in the nephrology community regarding the collective results of these studies.

A decline in protein and energy intake and in indices of nutritional status have been documented in patients with a GFR below about 50 mL/min/1.73 m^2 who have been consuming uncontrolled diets.[196-198] Indeed, patients who are allowed to eat ad libitum diets may ingest inadequate energy and, occasionally, insufficient protein rather than too much. In contrast, both metabolic balance studies as well as clinical trials suggest that the preponderance of CRF patients ingesting a controlled low-protein diet providing 0.60 g protein/kg/d will maintain nutritional status,[57,99,208-210] particularly if they receive higher energy intakes (ie, 35 kcal/kg/d).[211]

DPIs providing somewhat larger quantities of protein have been recommended based on the findings that adherence is easier with such diets and actual protein intakes of 0.75 g/kg/d or lower were all associated with similar rates of progression of renal failure in patients with a GFR of 25 mL/min/1.73 m^2 or lower.[203] Thus, for individuals who are unwilling or unable to ingest 0.60 g protein/kg/d or are unable to maintain adequate energy intakes with this dietary regimen, a diet providing up to 0.75 g protein/kg/d may be prescribed. Such diets must be carefully implemented by personnel with expertise and experience in dietary management (Appendix IV), and individuals prescribed such a diet must be carefully monitored (Guidelines 1 and 26 and Appendix III). Methods for measuring or estimating GFR are discussed in Appendix IX.

RECOMMENDATIONS FOR RESEARCH

1. Which subpopulations of patients with progressive chronic renal disease are particularly likely or unlikely to display slowing in the decline of their GFR with dietary protein restriction?

2. Are there any additive benefits to prescribing both low protein diets and angiotensin converting enzyme inhibitors for patients with progressive chronic renal disease?

GUIDELINE 25

Dietary Energy Intake (DEI) for Nondialyzed Patients

The recommended DEI for individuals with chronic renal failure (CRF; GFR <25 mL/min) who are not undergoing maintenance dialysis is 35 kcal/kg/d for those who are younger than 60 years old and 30 to 35 kcal/kg/d for individuals who are 60 years of age or older. ***(Evidence and Opinion)***

- Energy expenditure of nondialyzed individuals with CRF is similar to that of healthy individuals.
- Metabolic balance studies of such individuals indicate that a diet providing about 35 kcal/kg/d engenders neutral nitrogen balance and maintains serum albumin and anthropometric indices.
- Because individuals more than 60 years of age tend to be more sedentary, a lower total energy intake of 30 to 35 kcal/kg/d is acceptable.

RATIONALE

In patients with CRF who are not receiving dialysis therapy, energy expenditure (and hence energy requirements) when measured at rest, while sitting quietly, during prescribed exercise, or after ingesting a meal of a defined composition is similar to that of healthy subjects.[154,155] Available evidence indicates that a diet providing about 35 kcal/kg/d is necessary to maintain neutral nitrogen balance, to promote higher serum albumin concentrations and more normal anthropometric parameters, and to reduce the UNA (ie, to improve protein utilization).[211] These energy needs are similar to those described in the USRDA for normal adults of similar age.[158] In CRF patients 60 years of age or older, who tend to be less physically active, an energy intake of 30 to 35 kcal/kg/d may be sufficient, although energy requirements of CRF patients in this age range have not been well studied. This latter recommendation is based, in part, on the recommended dietary allowances of older normal adults (US Recommended Dietary Allowances).[158]

The recommendation for this energy intake for individuals with GFR less than 25 mL/min is based on findings of low energy intakes in clinically stable individuals with this level of renal insufficiency and evidence that these patients often show signs of nutritional deterioration.[196] Methods for measuring or estimating GFR are discussed in Appendix IX.

It may be difficult (or impossible in some circumstances) for patients to achieve this energy goal with dietary counseling alone. However, inadequate energy intake is considered to be one of the principal reversible factors contributing to malnutrition in the ESRD population. To facilitate compliance with the energy prescription, creative menu planning is encouraged, taking into consideration the patient's food preferences. Foods, beverages, and nutritional supplements with high energy density may be used. If sufficient energy intake to maintain nutritional status cannot be attained by these techniques, supplemental tube feeding may be considered.

RECOMMENDATIONS FOR RESEARCH

1. Studies are needed to assess why spontaneous DEI is reduced in persons with CRF who are not undergoing MD.
2. More data are needed on the energy require-

ments of clinically stable patients with CRI. There are very few data in this area.

3. Data are also needed on the energy requirements of individuals with CRF who are obese or malnourished or who have associated catabolic illnesses.

4. What techniques can be used to increase energy intake in individuals with CRI and CRF?

GUIDELINE 26

Intensive Nutritional Counseling for Chronic Renal Failure (CRF)

The nutritional status of individuals with CRF should be monitored at regular intervals. ***(Evidence)***

- A spontaneous reduction in dietary protein intake (DPI) and a progressive decline in indices of nutritional status occur in many nondialyzed patients with CRF.
- The presence of protein-energy malnutrition at the initiation of maintenance dialysis is predictive of future mortality risk.
- Interventions that maintain or improve nutritional status during progressive renal failure are likely to be associated with improved long-term survival after commencement of maintenance dialysis.
- Because evidence of protein-energy malnutrition may develop before individuals require renal replacement therapy, regular monitoring (eg, at 1- to 3-month intervals) of the patient's nutritional status should be a routine component of the care for the patient with CRF.
- Nutritional status should be assessed more frequently if there is inadequate nutrient intake, frank protein-energy malnutrition, or the presence of an illness that may worsen nutritional status.

RATIONALE

PEM is common in people with ESRD and several studies indicate that it is often present at the time that MD therapy is initiated, indicating that deterioration in nutritional status often predates the onset of renal replacement therapy.[16,21,75,128,201] Indeed, research indicates that patients with CRI who are not receiving nutritional management often demonstrate evidence of deterioration in nutritional status before dialysis therapy is initiated.[196,198] Moreover, biochemical and anthropometric indicators of PEM present at the initiation of dialysis are predictive of future morbidity and mortality risk.[22,23,25,42,52,199,201,212] A progressive decline in dietary protein and energy intake, anthropometric values, and biochemical markers (eg, serum albumin, transferrin, cholesterol, and total creatinine excretion) of nutritional status has been documented in patients with progressive CRF consuming uncontrolled diets. The decline in spontaneous protein and energy intake, serum proteins, and anthropometric values is evident when the GFR falls below 50 mL/min and is particularly notable below a CrCl of about 25 mL/min.[196,197] In one prospective observational study, for each 10 mL/min decrease in CrCl, DPI decreased by 0.064 ± 0.007 g/kg/d, weight declined by 0.38% ± 0.13% of initial weight, and serum transferrin decreased by 16.7 ± 4.1 mg/dL.[196] A positive correlation between energy intake and GFR has also been

reported, independent of the prescribed protein intake.[197]

In summary, evidence of PEM may become apparent well before there is a requirement for renal replacement therapy. Interventions that maintain or improve nutritional status are likely to be associated with improved long-term survival, although this has not been proven in randomized, prospective clinical trials. Therefore, it is recommended that regular monitoring of the patient's nutritional status should be a routine component of predialysis care.

RECOMMENDATIONS FOR RESEARCH

1. Why do apparently clinically stable patients with creatinine clearances under 50 mL/min often have decreased dietary protein and energy intakes and evidence of deteriorating nutritional status?
2. What interventions are likely to prevent or reverse the developing PEM in these individuals?
3. Will interventions that improve nutritional status reduce morbidity and mortality in these individuals?

GUIDELINE 27

Indications for Renal Replacement Therapy

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

RATIONALE

It is well documented that mortality and morbidity are increased in individuals with ESRD who begin dialysis therapy with overt evidence of PEM. Accumulating evidence also indicates that initiation of dialysis more in line with current NKF-DOQI practice guidelines (ie, GFR ~10.5 mL/min) results in improved patient outcomes compared with when dialysis is delayed until the GFR is <5 mL/min and symptomatic uremia and associated medical complications are present.[213-215] Furthermore, there is evidence that initiating maintenance dialysis under these circumstances, and when there has been nutritional deterioration, results in an improvement in nutritional indices.[215-220] There is no evidence that earlier initiation of dialysis leads to improved nutritional status among patients without overt uremia. Moreover, it has not been established that improved nutritional status at the initiation of dialysis directly leads to improved survival or fewer dialysis-related complications. Despite the lack of evidence from controlled clinical trials, interventions that maintain or improve nutritional status before the requirement for renal replacement therapy are likely to result in improved long-term survival.

There is ample evidence that the survival of patients with ESRD is closely associated with their nutritional status (Guidelines 3 through 6, 8, 18, and 23). These findings have been demonstrated not only in large, diverse populations of prevalent MD patients, but also in patients commencing MD therapy.[23,79,221] Hypertension, preexisting cardiac disease, and low serum albumin concentrations were independently associated with diminished long-term survival in 683 ESRD patients who started dialysis during 1970 through 1989.[221] In 1,982 HD patients, a low serum albumin concentration at the initiation of dialysis was associated with a significant increase in the relative risk of death.[23] A direct relation between serum albumin and survival and an independent association between modified SGA and survival was observed in 680 incident CPD patients.[79] In contrast, in one study no significant associations were found between serum albumin, creatinine, and urea concentrations and survival in incident HD patients.[222] The sample size in the latter study was relatively small (n = 139), and 94% of

the study sample were Black (83%) or Hispanic (11%).[222] No studies have specifically examined the relations among other nutritional indicators (eg, %SBW, PNA, and DXA) and survival in incident HD or peritoneal dialysis patients.

Low-protein (eg, 0.60 g protein/kg/d), high-energy (35 kcal/kg/d) diets may retard the rate of progression of chronic renal disease[206-207] and should maintain patients with chronic renal disease in good nutritional status (Guidelines 24 and 25).[57,99,208,209,211] However, it is recognized that such low-protein diets may not maintain adequate nutritional status in all patients, particularly if an adequate energy intake is not maintained (Guideline 25).[99,211] Furthermore, there is evidence that the spontaneous intake of protein and energy, and other indicators of nutritional status, tend to diminish in patients with progressive CRI who are consuming unregulated diets.[196] Therefore, patients with CRI need to undergo nutritional assessment at frequent intervals so that any deterioration in nutritional status can be detected early (Guidelines 23 and 26 and Appendix IV). The plan of care and nutritional interventions outlined in Guideline 18 for the nutritional management of the dialysis patient is also appropriate for patients with progressive CRI.

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

RECOMMENDATIONS FOR RESEARCH

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

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

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

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

C. APPENDICES (ADULT GUIDELINES)

Appendix I. Methods for Measuring Serum Albumin

Most laboratories utilize a colorimetric method for the measurement of the serum albumin concentration and particularly the bromcresol green (BCG) assay. If another assay is utilized, the normal range specific to that assay should be used. Research that reports the serum albumin should specify the assay used and its normal range.

Nephelometry and the electrophoretic method[223] are very specific for the determination of the serum albumin concentration. However, these methods are time-consuming, expensive, and not generally used in clinical laboratories. The BCG colorimetric method is rapid, reproducible, and has been automated.[224] This method uses small aliquots of plasma, has a low coefficient of variation (5.9%), and is not affected by lipemia, salicylates, or bilirubin. With values in the normal electrophoretic range of 3.5 to 5.0 g/dL, the BCG method gives values that are comparable to the values obtained by electrophoresis. The normal range for the serum albumin by the BCG method is 3.8 to 5.1 g/dL.[224] The BCG method differs from the electrophoretic method by about 0.3 g/dL.[223] The BCG method underestimates albumin in the high normal range and overestimates albumin below the normal range with an overall mean overestimation of approximately 0.61 g/dL.[225]

Some laboratories use the bromcresol purple (BCP) colorimetric method to measure the serum albumin concentration.[223] Although this method is more specific for albumin and has specificity similar to electrophoretic methods, clinically it has proved to be less reliable than the BCG method. BCP has been shown to underestimate serum albumin in pediatric HD patients with a mean difference of 0.71 g/dL.[226] Maguire and Price[227] have demonstrated similar results in CRF patients.

Serum albumin concentrations obtained by the BCG method in HD patients were virtually identical to the values obtained using nephelometry. Values obtained by the BCP assay underestimated the nephelometric values by 19%. Agreement between BCG and BCP with the nephelometric values in CAPD patients showed less variation; however, the BCG values were not different from the nephelometric values.[228]

Chronic dialysis units often have little influence over the method used by their reference laboratories. If the BCG method is available, it should be requested. If the BCP method must be used, then the normal range for that laboratory should serve as the reference. Additionally, less clinical weight might be given to serum albumin concentrations measured by the BCP method and other markers of malnutrition in ESRD patients might be more heavily weighted.

Appendix II. Methods for Calculation and Use of the Creatinine Index

The creatinine index is defined as the creatinine synthesis rate. The creatinine index is used to assess the dietary skeletal muscle protein intake and skeletal muscle mass. The creatinine index is determined primarily by the size of the skeletal muscle mass and the quantity of skeletal (and cardiac) muscle ingested (ie, the intake of creatine and creatinine). Hence, creatinine production is approximately proportional to skeletal muscle mass in stable adults who are neither anabolic nor catabolic and who have a constant protein intake.[46,102,234] In normal individuals, dietary intake of creatine and creatinine from skeletal (and cardiac) muscle is associated with increased urinary excretion of creatinine.[53,229] In clinically stable individuals undergoing MD, creatinine is synthesized and levels rise in plasma at a rate that is approximately proportional to somatic protein (skeletal muscle) mass and dietary muscle (protein) intake.[17,46,102] In CPD patients, the stabilized serum creatinine and creatinine index are also proportional to skeletal muscle mass and dietary muscle intake.

The creatinine index is measured as the sum of creatinine removed from the body (measured from the creatinine removed in dialysate, ultrafiltrate, and/or urine), any increase in the body creatinine pool, and the creatinine degradation rate.[48]

The equation for calculating the creatinine index is as follows:

Creatinine index (mg/24 h)
= dialysate (or ultrafiltrate) creatinine (mg/24 h)
+ urine creatinine (mg/24 h)
+ change in body creatinine pool (mg/24 h)
+ creatinine degradation (mg/24 h)

Equation 2

The change in the body creatinine pool is calculated as follows:

Change in body creatinine pool (mg/24 h)
= [serum creatinine $(mg/L)_f$
− serum creatinine $(mg/L)_i$]
× [24/h/(time interval between the i and f measurements)]
× [body weight (kg) × (0.50 L/kg)]

Equation 3

where i and f are the initial and final serum creatinine measurements (usually separated by about 20 to 68 hours), body weight is the time averaged body weight between the initial and final serum creatinine measurements, and 0.50 L/kg is the estimated volume of distribution of creatinine in the body.[230,231]

The change in the body creatinine pool when body weight varies can be calculated from the following equation:

Change in creatinine pool (mg/24 h)
= [[serum creatinine $(mg/L)_f$
× (body weight $(kg)_f$ × 0.5 L/kg)]
− [serum creatinine $(mg/L)_i$
× (body weight $(kg)_i$ × 0.5 L/kg)]]
× (24 h/time interval between the i and f measurements)

Equation 4

The creatinine degradation rate is estimated as follows:

Creatinine degradation (mg/24 h)
= 0.38 dL/kg/24 h × serum creatinine (mg/dL)
× body weight (kg)[230]

Equation 5

The creatinine index can be used to estimate dietary skeletal muscle protein or mass and edema-free lean body mass.[232,233] The relation between the creatinine index and edema-free lean body mass may be estimated as follows:

Edema-free lean body mass (kg)
= (0.029 kg/mg/24 h)
× creatinine index (mg/24 h) + 7.38 kg[234]

Equation 6

The constant used in this last equation (0.029 kg/mg/24 h) was derived from individuals without renal disease[234] and should be reevaluated for ESRD patients; at least one study suggests that this constant is also applicable for MD patients.[232] Skeletal or cardiac muscle protein intake as well as total protein intake can affect the creatinine index,[235,236] and marked variations in these nutrients may therefore have major effects on the creatinine index. Thus, until the relationships between total protein intake and muscle intake and the creatinine index are well defined for ESRD patients, some caution must be exercised in interpreting the creatinine index, particularly if the diet of the individual in question is particularly high or low in these nutrients.

Appendix III. Dietary Interviews and Diaries

There are several methods for estimating dietary nutrient intake.[153,237] The most common methods are food intake records and dietary recalls. The dietary recall (usually obtained for the previous 24 hours) is a simple, rapid method of obtaining a crude assessment of dietary intake. It can be performed in approximately 30 minutes, does not require the patient to keep records, and relies on the patient's ability to remember how much food was eaten during the previous 24 hours. Accurate quantification of the amounts of foods eaten is critical for the 24-hour recall. Various models of foods and measuring devices are used to estimate portion sizes. Advantages to the recall method are that respondents usually will not be able to modify their eating behavior in anticipation of a dietary evaluation and they do not have to be literate. Disadvantages of the 24-hour recall include its reliance on memory (which may be particularly limiting in the elderly), that the responses may be less accurate or unrepresentative of typical intakes, and that it must be obtained by a trained and skilled dietitian.

Dietary diaries are written reports of foods eaten during a specified length of time. A food-intake record, lasting for several days (3 to 7 days), provides a more reliable estimate of an individual's nutrient intake than do single-day records. Records kept for more than 3 days increase the likelihood of inaccurate reporting because an individual's motivation has been shown to decrease with increasing number of days of dietary data collection, especially if the days are consecutive.[238] On the other hand, records maintained for shorter times may not provide accurate data on usual food and nutrient intakes. The actual number of days chosen to collect food records should depend on the degree of accuracy needed, the day-to-day variability in the intake of the nutrient being measured, and the cooperation of the patient. When food records are chosen to estimate dietary energy and DPI in MD patients, it is recommended that 3-day food records be obtained for accuracy and to minimize the burden on the patient and/or his family. Records should include at least one weekday and one weekend day, in addition to dialysis and nondialysis days for MHD patients, so that variability in food intake can be estimated more accurately.

The validity and reliability of the dietary interviews and diaries depend on the patient's ability to provide accurate data and the ability of the nutritionist to conduct detailed, probing interviews. The intake of nutrients is generally calculated using computer-based programs. Food records must be maintained meticulously to maximize the accuracy of the diary. Food intake should be recorded at the time the food is eaten to minimize reliance on memory. Special data collection forms and instructions are provided to assist the individual to record adequate detail. Recording error can be minimized if instructions and proper directions on how to approximate portion sizes and servings of fluid are provided.

Food models are also helpful for instruction. The food record should indicate the time of day of any intake (both meals and snacks), the names of foods eaten, the approximate amount ingested, the method of preparation, and special recipes or steps taken in the food preparation. The dietitian should carefully review the food record with the patient for accuracy and completeness shortly after it is completed.

Calculation and Expression of Protein and Energy Intake

DPI can be expressed in absolute units such as grams of protein per day (g/d) or as a function of the patient's actual or adjusted body weight (eg, g/kg/d; Guideline 12). Dietary energy intake (DEI) refers to the energy yielded from ingestion of protein, carbohydrates, fat, and alcohol. DEI can be expressed in absolute units such as kilocalories per day (kcal/d) or as a function of the patient's actual or adjusted body weight per day (kcal/kg/d). Consideration should be given to using the adjusted edema-free body weight (aBW_{ef}, Guideline 12) to express DPI or DEI in individuals who are less than 95% or greater than 115% of SBW.

In CPD patients with normal peritoneal transport capacity, approximately 60% of the daily dialysate glucose load is absorbed, resulting in a glucose absorption of about 100 to 200 g of glucose per 24 hours.[239,240] Another method of

estimating the quantity of glucose absorbed is the following formula[240]:

$$\text{Glucose absorbed (g/d)} = 0.89x\ \text{(g/d)} - 43 \qquad \text{Equation 7}$$

where x is the total amount of dialysate glucose instilled each day. Both of the methods described above are based on the observation that (anhydrous) glucose in dialysate is equal to about 90% of the glucose listed. For example, dialysate containing 1.5% glucose actually contains about 1.30 g/dL of glucose and 4.25% glucose in dialysate actually contains 3.76 g/dL of glucose.[240] It is probable that the relationship between dialysate glucose concentration and glucose absorbed may be different with automated peritoneal dialysis.

The net glucose absorption from dialysate should be taken into consideration when calculating total energy intake for PD patients.

Appendix IV. Role of the Renal Dietitian

Implicit in many of the guidelines in this document is the availability to the patient of an individual with expertise in renal dietetics. Implementation of many of the guidelines concerning nutritional assessment (anthropometry, subjective global assessment, dietary interviews and diaries, and integration of the results of nutritional measurements) and nutritional therapy (developing a plan for nutritional management, counseling the patient and his/her family on appropriate dietary protein and energy intake, monitoring nutrient intake, educational activities, and encouragement to maximize dietary compliance) is best performed by an individual who is trained and experienced in these tasks. Although occasionally a physician, nurse, or other individual may possess the expertise and time to conduct such activities, a registered dietitian, trained and experienced in renal nutrition, usually is best qualified to carry out these tasks. Such an individual not only has undergone all of the training required to become a registered dietitian, including, in many instances, a dietetic internship, but has also received formal or informal training in renal nutrition. Such a person, therefore, is particularly experienced in working with MD patients as well as individuals with CRF.

There appears to be a general sense among renal dietitians, based on experience, that an individual dietitian should be responsible for the care of approximately 100 MD patients but almost certainly no more than 150 patients to provide adequate nutritional services to these individuals.[241,242] Because, in many dialysis facilities, the responsibilities of the renal dietitian are expanded beyond the basic care described in these guidelines (eg, monitoring protocols and continuous quality improvement), these facilities should consider a higher ratio of dietitians to patients. Randomized prospective controlled clinical trials have not been conducted to examine whether this is the maximum number of patients at which dietitians are still highly effective.

Appendix V. Rationale and Methods for the Determination of the Protein Equivalent of Nitrogen Appearance (PNA)

The reader is referred to previously published guidelines and to the works of primary investigators in the field for a more in-depth explanation of urea modeling and kinetics. The DOQI Nutrition Work Group endorses the previous DOQI recommendations concerning Kt/V and offers new material concerning eKt/V and a new recommendation for the normalization of PNA (nPNA). The Work Group recognizes that dialysis units may use a variety of methods for determining Kt/V and nPNA. These may range from the use of previously published nomograms and simple, noniterative formulas to the use of iterative urea kinetic modeling. The Work Group does not propose that one method is superior to another, but only that the formulas listed in this Appendix are preferable for the uses indicated. The term nPNA will be substituted for normalized protein catabolic rate (nPCR) when the latter term was used in earlier equations and published reports.

RATIONALE

The results of the National Cooperative Dialysis Study (NCDS) led to a mechanistic analysis of dialysis adequacy based on solute clearance.[243] Two important concepts emerged from these analyses: urea clearance (a measure of dialysis dose not related to protein catabolism) and nPNA (a measure of protein nitrogen appearance unrelated to dialysis dose). Some have pointed out that Kt/V and nPNA may be mathematically interrelated, because they share some common parameters.[244] Potential causes of coupling including error coupling, calculation bias, and confounding variables.[244] Certain study designs are sensitive to specific errors due to these types of mathematical coupling. For example, cross-sectional studies may suffer from all three types of errors. Nonrandomized longitudinal studies may be affected by calculation bias and confounding variables; and randomized, prospective trials are subject to calculation bias. The prospective, randomized HEMO trial should help to determine the physiological relationship between Kt/V and nPNA.[244] Current data suggest that there is little relationship clinically between Kt/V and nPNA.[245] nPCR did not differ between the Kt/V = 1.0 and Kt/V = 1.4 groups, but did increase with a higher protein diet group (1.3 versus 0.9 g/kg/d). The presence of these three types of error in the determination and interpretation of Kt/V and nPNA must be recognized by the clinician if Kt/V and nPNA are to be correctly interpreted.

nPNA may be affected by protein intake, by anabolic and catabolic factors such as corticosteroids or anabolic hormones, and possibly by other factors that are currently unrecognized. nPNA is closely correlated with DPI only in the steady state; ie, when protein and energy intake are relatively constant ($< 10\%$ variance), when there are little or no internal or external stressors, when there is no recent onset or cessation of anabolic hormones, and, when calculated by the two-BUN method, the dose of dialysis is constant. In the individual patient who is in a stable steady-state and who has none of the previously mentioned conditions that would interfere with the interpretation of the nPNA, it may be reasonable to assume that nPNA reflects the DPI. As has been done in the HEMO study, it is advisable to independently check the DPI (derived from nPNA) by intermittently obtaining dietary histories.

The terminology for PCR has recently been questioned. It has been argued that, although it represented a useful concept, it was a misnomer, because intact proteins, peptides, and amino acids are lost in dialysate and urine and are not catabolized. Moreover, protein catabolism in nutrition and metabolic literature refers to the absolute rate of protein breakdown that commonly requires measurement of isotopically labeled amino acids. The absolute rate of protein breakdown is much greater than the net degradation of exogenous and endogenous proteins that result in urea excretion.[63] Instead of PCR, the term ''protein equivalent of total nitrogen appearance'' (PNA) has been suggested,[63] which is in keeping with the original definition suggested by Borah et al.[137] The DOQI Nutrition Work Group prefers the use of PNA instead of PCR and recommends its acceptance by the dialysis community, because it is more precise and is a term that better reflects the actual physiology.

PNA may be normalized (nPNA) to allow comparison among patients over a wide range of body sizes. The most convenient index of size is the urea distribution volume (V), because it is calculated from urea modeling, is equivalent to body water volume, and is highly correlated with fat free or lean body mass. Total body weight is a poor index of PNA because nitrogen appearance is not affected by body fat. However, because V is an index that is unfamiliar to clinicians and not readily available, it is customary to convert V to a normalized body weight by dividing by 0.58, its average fraction of total body weight. The resulting nPNA is expressed as the equivalent number of grams of protein per kilogram of body weight per day, but it is important to note that body weight in the denominator is not the patient's actual body weight but instead is an idealized or normalized weight calculated from V/0.58. For example, to calculate DPI (for a patient who satisfies the previously discussed criteria for steady state), one must not multiply nPNA by the patient's actual body weight but instead multiply by V/0.58.

The Work Group believes that ideal body weight (aBW_{ef}), which correlates very closely with body water volume, is a good denominator for normalizing PNA. Ideal weight may be more appropriate than V/0.58 in patients who are emaciated or edematous. Like many physiologic variables, PNA may correlate better with body surface area, but because water volume is highly correlated with surface area within the range of adult body sizes, urea volume is a reasonable substitute.

The methods used to determine the PNA (PCR) differ between maintenance hemodialysis and chronic peritoneal dialysis because of the differences in calculating total nitrogen appearance (TNA). TNA is the sum of all outputs of nitrogen from the body including skin, feces, urine, and dialysate. The technique for the measurement of TNA is expensive, labor intensive, and impractical for routine clinical use. In metabolically stable patients, the nitrogen output in feces (including flatus) and skin (including nails and hair) is constant and can be ignored for the sake of simplifying the calculation. The TNA is very strongly correlated with UNA.[137,150,246-248] Although this correlation is strong, the 95% confidence limits are ±20% of the mean.[249] The regression equations used to estimate TNA from UNA may not be accurate if a patient has unusually large protein losses into dialysate, has high urinary ammonium excretion, or is in marked positive or negative nitrogen balance.[63]

The formulas used to calculate the single-pool Kt/V (spKt/V) and PNA (PCR) can be divided into two separate groupings: those that depend on a three-BUN measurement, single-pool, variable-volume kinetic model and those that depend on a two-BUN measurement, single-pool, variable-volume model.

The two-BUN method is more complex than the three-BUN method, because it requires computer iteration over an entire week of dialysis to arrive at G (urea generation rate). The three-BUN method calculates the urea generation rate (G) from the end of the first dialysis to the beginning of the second dialysis and is primarily determined by the difference between the two-BUN values (post- to pre-). It also requires iteration and a computer but only over the time span of a single dialysis and a single interdialysis interval. The two-BUN method calculates G from the absolute value of the predialysis BUN (C_0) and Kt/V. Because C_0 is determined both by G and by Kt/V, if Kt/V is known (calculated from the fall in BUN during dialysis), then G can be determined from the absolute value of C_0 (by the complicated iteration scheme over an entire week). Note that the absolute value of C_0 is not used to calculate Kt/V, which is determined by the log ratio of C_0/C. Comparing the two methods, although the three-BUN method is mathematically simpler, it is actually more difficult to do because it requires waiting 48 to 72 hours before the third BUN can be drawn. It is also a more narrow measure of G because it is constrained to the single interdialysis period and can be manipulated by the patient who becomes aware that the measurement will be done when the first two blood samples are drawn. Fortunately, graphical nomograms have been developed and validated that allow the calculation of PNA based on predialysis and postdialysis BUN samples from the same dialysis session.[250]

Equations for the Determination of spKt/V, V, and PNA (PCR) in HD and Peritoneal Dialysis Patients

Hemodialysis. Two-BUN, single-pool, variable-volume model:

$$\text{Beginning of week PNA (PCR)} = C_0/[36.3 + (5.48)(spKt/V) + ((53.5)/(spKt/V))] + 0.168 \quad \text{Equation 8}$$

Midweek PNA (PCR)
$= C_0/[25.8 + ((1.15)/(spKt/V)) + (56.4)/(spKt/V)] + 0.168$ Equation 9

End of week PNA (PCR)
$= C_0/[16.3 + (4.3)(spKt/V) + (56.6)/(spKt/V) + 0.168$ Equation 10

where C_0 is the predialysis BUN. C_0 is adjusted upward in patients who have significant remaining GFR according to the formula:

$$C_0' = C_0\,[1 + (0.79 + (3.08)/(Kt/V))Kr/V] \quad \text{Equation 11}$$

Kr is residual urinary urea clearance in mL/min, C_0' and C_0 are in mg/dL, and V is in L. Because these formulas introduce errors ranging from 3.7% (end of week) to 8.39% (beginning of week) and the *r* ranges from 0.9982 to 0.9930, the Work Group believes that they represent an excellent approach to the simplified measurement of PNA (PCR).

The DOQI Hemodialysis Adequacy Work Group has recommended the use of the natural log formula to calculate Kt/V:

$$spKt/V = -Ln(R - 0.008 \times t) + (4 - (3.5 \times R)) \times UF/W \quad \text{Equation 12}$$

where R is the postdialysis/predialysis BUN ratio, t is the dialysis session in hours, UF is the ultrafiltration volume in liters, and W is the postdialysis weight in kilograms.[251] Multiple errors can occur that will affect the calculated PCR, Kt/V, and UNA. To decrease errors in the timing of the collection of BUN and to standardize the measurement, the BUN should be drawn using the Stop Flow/Stop Pump technique recommended by the DOQI Hemodialysis Adequacy Work Group. A complete discussion of the sampling techniques, problems, and trouble shooting can be found in the Clinical Practice Guidelines.[252,253]

The DOQI Hemodialysis Adequacy Work Group has recommended the following formulas for UKM using a single pool, three-sample model. These should be determined using already available computer software and should be utilized by those dialysis units that have formal UKM available to them. These formulas assume thrice-weekly HD.

$$V_t = (QF)\,(t)\,[[1 - [(G - (C_t)(K + Kr - Qf))/(G - (C_0)(K + Kr - Qf))]^{((Qf)/(K+Kr-Qf))}]^{-1} - 1] \quad \text{Equation 13}$$

$$PNA\,(G) = (Kr + a) \times [C_0 - C_t((Vt + a(theta))/Vt)^{-(Kr + a)}] \quad \text{Equation 14}$$

where Vt is the postdialysis volume; Qf is the rate of volume contraction during dialysis (difference in pre and post weights divided by length of dialysis); G is the interdialytic urea generation rate (PNA); K and Kr are the dialyzer and renal urea clearances; C_t and C_0 are the BUN concentrations at the end and beginning of dialysis; a is the rate of interdialytic volume expansion and it is calculated by the total IDWG divided by the length of the interdialytic period (theta); and $C_{0'}$ is the predialysis BUN of the subsequent dialysis session. An initial estimate of Vt is obtained from the use of an anthropometric or regression formula found in the Clinical Practice Guidelines.[254]

It is important to recognize that spKt/V overestimates the actual delivered dose of dialysis because of urea disequilibrium. The spKt/V actually measures the dialyzer removal of urea, not the actual patient clearance of urea. As dialysis time is shortened and the intensity of dialysis increases, the error in the estimation of the delivered dose of dialysis increases, because the effects of urea equilibrium are accentuated. Urea disequilibrium may occur because of diffusion disequilibrium between body water compartments (membrane dependent), flow disequilibrium because of differences of blood flow in various tissues and organs, and disequilibrium caused by cardio-pulmonary recirculation of blood. The latter type of disequilibrium is only seen in patients undergoing arterio-venous hemodialysis and not those undergoing veno-venous HD. Membrane, flow, and recirculation disequilibrium errors are magnified as dialysis time is shortened and the intensity of the session increased (eg, increasing Qb). For these reasons, a more accurate description of the delivered dose of dialysis has been developed that uses the equilibrated postdialysis BUN and bypasses the necessity of keeping the patient in the dialysis unit for an hour to obtain the true equilibrated postdialysis BUN sample.[255] The work group recommends that this measurement of the effective patient clearance of urea (eKt/V) be utilized instead of spKt/V.

$$eKt/V = spKt/V - (0.6)(K/V) + 0.03 \quad \text{Equation 15}$$

where K/V is expressed in hours^{-1}.

$$K/V = (spKt/V)/t \quad \text{Equation 16}$$

Peritoneal dialysis. The formulas for calculation of PNA (PCR) in CPD patients have been validated for CAPD. However, they are generally applied to all CPD patients. In CPD patients the following formulas apply (yielding grams per 24 hours):

$$PNA\ (PCR) = 15.7 + (7.47 \times UNA)^{256} \quad \text{Equation 17}$$

$$PNA\ (PCR) = 34.6 + (5.86 \times UNA)^{60} \quad \text{Equation 18}$$

$$PNA\ (PCR) = 10.76 \times (0.69 \times UNA + 1.46)^{257} \quad \text{Equation 19}$$

$$PNA\ (PCR) = 20.1 + (7.50 \times UNA)^{149} \quad \text{Equation 20}$$

The UNA is calculated by measuring the 24-hour urea excretion by peritoneal dialysate and residual renal urea excretion and adding the change in total body urea nitrogen (calculated as BUN change over time):

$$UNA = (Vd \times DUN + Vu \times UUN)t + (d(\text{body urea nitrogen}))/t \quad \text{Equation 21}$$

where Vd and Vu are dialysate and urine volumes in L, t is the time of collection, and DUN and UUN are dialysate and urine concentrations of urea nitrogen. Because daily changes in daily BUN in CPD patients are negligible, the formula can be shortened to

$$UNA = ((Vd \times DUN) + (Vu \times UUN)/t)^{63} \quad \text{Equaion 22}$$

Normalization of PNA for HD and Peritoneal Dialysis Patients

The PNA should be normalized or adjusted to a specific body size. The most common normalization and the one recommended by the DOQI Hemodialysis Work Group is to normalize to V/0.58[251]:

$$nPNA\ (nPCR)\ (g/kg/d) = (PNA)/(V/0.58) \quad \text{Equation 23}$$

There are no data to support other normalization techniques, but normalization to edema-free aBW (aBW_{ef}) may be the preferred normalization technique.[63] The DOQI Nutrition Work Group recommends the use of the following normalization formula (Guideline 12):

$$nPNA = (PNA)/aBW_{ef} \quad \text{Equation 24}$$

where aBW_{ef} is the actual edema-free body weight.

Calculation of V[252]

Anthropometric determination of urea distribution volume.

Watson formula:

$$\text{Males: TBW} = 2.447 - (0.09156 \times \text{age}) + (0.1074 \times \text{height}) + (0.3362 \times \text{weight}) \quad \text{Equation 25}$$

$$\text{Females: TBW} = -2.097 + (0.1069 \times \text{height}) + (0.2466 \times \text{weight}) \quad \text{Equation 26}$$

Hume-Weyer formula:

$$\text{Males: TBW} = (0.194786 \times \text{height}) + (0.296785 \times \text{weight}) - 14.012934 \quad \text{Equation 27}$$

$$\text{Females: TBW} = (0.34454 \times \text{height}) + (0.183809 \times \text{weight}) - 35.270121 \quad \text{Equation 28}$$

where TBW = total body water (V).

The Watson and Hume-Weyer formulas were derived from analyses of healthy individuals and their applicability to ESRD patients has been questioned. When compared with TBW calculated by BIA, the TBWs calculated from these formulas underestimate TBW by about 7.5%.

TBW by BIA Formula

$$TBW = -0.07493713 \times age - 1.01767992 \times male + 0.12703384 \times ht - 0.04012056 \times wt + 0.57894981 \times diabetes - 0.00067247 \times wt^2 - 0.0348146 \times (age \times male) + 0.11262857 \times (male \times wt) + 0.00104135 \times (age \times wt) + 0.00186104\ (ht \times wt) \quad \text{Equation 29}$$

where wt and ht represent the patient's weight and height and male = 1 and diabetes = 1. If not male or not diabetic, then these values = 0.[258]

Appendix VI. Methods for Performing Subjective Global Assessment

Healthcare professionals (eg, physicians, dietitians, and nurses) should undergo a brief training period before using SGA. This training is recommended to increase precision and skill in using SGA. The four items currently used to assess nutritional status are weight change over the past 6 months, dietary intake and gastrointestinal symptoms, visual assessment of subcutaneous tissue, and muscle mass.

Weight change is assessed by evaluating the patient's weight during the past 6 months. A loss of 10% of body weight over the past 6 months is severe, 5% to 10% is moderate, and less than 5% is mild. This is a subjective rating on a scale from 1 to 7, where 1 or 2 is severe malnutrition, 3 to 5 is moderate to mild malnutrition, and 6 or 7 is mild malnutrition to normal nutritional status. If the weight change was intentional, the weight loss would be given less subjective weight. Edema might obscure greater weight loss. Dietary intake is evaluated and includes a comparison of the patient's usual and recommended intake to current intake. Duration and frequency of gastrointestinal symptoms (eg, nausea, vomiting, and diarrhea) are also assessed. The interviewer rates this component of SGA on the 7-point scale with higher scores indicative of better dietary intake, better appetite, and the absence of gastrointestinal symptoms.

The physical examination includes an evaluation of the patient's subcutaneous tissue (for fat and muscle wasting) and muscle mass. Subcutaneous fat can be assessed by examining the fat pads directly below the eyes and by gently pinching the skin above the triceps and biceps. The fat pads should appear as a slight bulge in a normally nourished person but are ''hollow'' in a malnourished person. When the skin above the triceps and biceps is gently pinched, the thickness of the fold between the examiner's fingers is indicative of the nutritional status. The examiner then scores the observations on a 7-point scale. Muscle mass and wasting can be assessed by examining the temporalis muscle, the prominence of the clavicles, the contour of the shoulders (rounded indicates well-nourished; squared indicates malnutrition), visibility of the scapula, the visibility of the ribs, and interosseous muscle mass between the thumb and forefinger, and the quadriceps muscle mass. These are also scored on a 7-point scale, with higher scores indicating better nutritional status. The scores from each of these items are summated to give the SGA rating. It is recommended that SGA be used to measure and monitor nutritional status periodically in both MHD and peritoneal dialysis patients.

Appendix VII. Methods for Performing Anthropometry and Calculating Body Measurements and Reference Tables

Anthropometry comprises a series of noninvasive, inexpensive, and easy-to-perform methods for estimating body composition. However, they are operator dependent and, to be useful clinically, must be performed in a precise, standardized, and reproducible manner. It is recommended that any individual who performs the measurements should first undergo training to increase precision and skill. Without such training, considerable variance will occur both within and between observers in obtaining and interpreting the measurements. Standardized methods for collecting anthropometric data are available and should be utilized.

The anthropometric measurements that are valid for assessing protein-energy nutritional status in MD patients include skinfold thickness, midarm muscle area or circumference, %UBW, and %SBW. An estimate of skeletal frame size is also necessary for evaluating an individual's anthropometric measurements. Therefore, a brief description of the methodology and reference tables for evaluating frame size in addition to other measures are provided.

Skeletal Frame Size

Measurement of elbow breadth is a rough estimate of an individual's skeletal frame size. Frame size estimates of small, medium, and large for males and females are available and presented in Table 2.[89]

Method for Estimating Skeletal Frame Size

Equipment. Sliding bicondylar caliper.

Method. Ask the patient to stand erect, with feet together facing the examiner. Ask the patient to extend either arm forward until it is perpendicular to the body. Flex the patient's arm so that the elbow forms a 90° angle with the fingers pointing up and the posterior part of the wrist is toward the examiner. Hold the small sliding caliper (bicondylar caliper) at a 45° angle to the plane of the long axis of the upper arm and find the greatest breadth across the epicondylis of the elbow. Measure to the nearest 0.1 cm twice with the calipers at a slight angle (this may be necessary because the medial condyle is more distal than the lateral condyle). An average of the two measurements is used (Table 2).[89]

Percent of Usual Body Weight (%UBW)

UBW is obtained by history or from previous measurements. A stable weight in adult dialysis patients may be an indicator of good nutritional status, because adults normally are expected to maintain their body weight. The formula below for percent of UBW is appropriate for patients whose weight has been stable for most of their lives.

$$\text{Percent of UBW} = ([\text{actual weight} \div \text{UBW}] \times 100) \quad \text{Equation 30}$$

Weight loss over time is a simple and useful longitudinal measure to monitor nutritional status because it is a risk factor for malnutrition. Even if the patient is overweight or obese, a significant weight loss in a short period of time may indicate malnutrition and predict increased morbidity and mortality.

Percent of Standard Body Weight (%SBW)

SBW is the patient's actual weight (postdialysis) expressed as a percentage of normal body weight for healthy Americans of similar sex, height, and age range and skeletal frame size.

$$\%\text{SBW} = (\text{actual weight} \div \text{SBW}) \times 100 \quad \text{Equation 31}$$

For individuals in the United States, these data are usually obtained from the National Health and Nutrition Evaluation Survey (NHANES). The third and most recent NHANES study indicates that the average American has gained about 7% in body weight.[97] This was considered a compelling argument for using the NHANES II data rather than data from NHANES III. However, individuals undergoing MHD who are in the upper 50th percentile or greater of body weight-for-height have an increased odds ratio for survival.[97] Patients who are less than 90% of normal body weight are considered to be mildly to moderately malnourished, and those who are less than 70% of normal body weight are consid-

Table 2. Frame Size by Elbow Breadth (cm) of US Male and Female Adults Derived From the Combined NHANES I and II Data Sets

	Frame Size		
Age (y)	Small	Medium	Large
Men			
18-24	≤6.6	>6.6 and <7.7	≥7.7
25-34	≤6.7	>6.7 and <7.9	≥7.9
35-44	≤6.7	>6.7 and <8.0	≥8.0
45-54	≤6.7	>6.7 and <8.1	≥8.1
55-64	≤6.7	>6.7 and <8.1	≥8.1
65-74	≤6.7	>6.7 and <8.1	≥8.1
Women			
18-24	≤5.6	>5.6 and <6.5	≥6.5
25-34	≤5.7	>5.7 and <6.8	≥6.8
35-44	≤5.7	>5.7 and <7.1	≥7.1
45-54	≤5.7	>5.7 and <7.2	≥7.2
55-64	≤5.8	>5.8 and <7.2	≥7.2
65-74	≤5.8	>5.8 and <7.2	≥7.2

The 10th and 90th percentiles, respectively, represent the predicted mean ± 1.282 times the SE. Similarly, the 15th and 85th percentiles are the predicted mean minus and plus, respectively, 1.036 times the SE of the regression equation. There were significant black-white population differences in weight and body composition when age and height were considered. However, when the comparisons were made with reference to age, height, and frame size, there were only minor interpopulation differences. For this reason, all races (white, black, and other) included in the NHANES I and II surveys were merged together for the purpose of calculating percentiles of anthropometric measurements.

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ered severely malnourished.[85] Individuals who are 115% to 130% of SBW are considered mildly obese, those between 130% and 150% are moderately obese, and those above 150% of SBW are considered to be severely obese.[259] Therefore, it is recommended that a target body weight for maintenance dialysis patients is between 90% and 110 % of SBW. At present, it is recommended that the NHANES II data be used for the reference source (Tables 3 through 8).[89]

Body Mass Index (BMI)

BMI is a useful and practical method for assessing the level of body fatness. BMI is calculated by dividing weight (in kilograms) by height squared (in meters). Based on epidemiological data,[85] it is recommended that the BMI of MD patients be maintained in the upper 50th percentile, which would be BMIs for men and women of at least approximately 23.6 and 24.0 kg/m^2, respectively. Notwithstanding the greater unadjusted survival data for men and women in the upper 10th percentile of body weight for height,[15,85] the large numbers of epidemiological data in normal individuals suggest that persons who are severely obese (eg, %SBW greater than 120 or BMI greater than 30 kg/m^2) should be placed on weight reduction diets. Shorter survival also suggests that obese MD patients should also be placed on weight reduction diets, but no studies have been performed in MD patients to determine the safety and efficacy of this theory.

Skinfold Thickness

Skinfold anthropometry is a well-established clinical method for measuring body fat.[260] Subcutaneous fat measurement is a rather reliable estimate of total body fat in nutritionally stable individuals. About one-half of the body's fat content is found in the subcutaneous layer.[83] Measurement of skinfold thickness at only one site is a relatively poor predictor of the absolute amount of body fat and the rate of change in total body fat because each skinfold site responds differently relative to changes in total body fat.[83] Measuring skinfold thickness at four sites (triceps, biceps, subscapular, and iliac crest) that quantify subcutaneous adipose tissue thickness on the limbs and trunk can make an accurate assessment of body fat.[86,261,262] Equations have been developed for estimating total body fat from these skinfold thicknesses,[260] although these equations have been developed from people without renal failure. Tables 2 through 7 give normal values for triceps and subscapular skinfold thicknesses.[89] Nonetheless, measuring skinfold thickness should be considered a semiquantitative measure of the amount or rate of change in total body fat.

In a study that measured four-site skinfold anthropometry, a reduction in percent total body fat was observed in a group of MHD patients when compared with controls.[261] Loss of fat from subcutaneous stores occurs proportionally. Therefore, repeated measures in the same patient over time may provide useful information on trends of fat stores.[83]

Table 3. Selected Percentiles of Weight, Triceps and Subscapular Skinfolds, and Bone-Free Upper Arm Muscle Area (AMA) for US Men and Women With Small Frames (25 to 54 Years Old)

Height			Weight (kg)							Triceps (mm)							Subscapular (mm)							Bone-Free AMA (cm^2)						
Inches	cm	n	5†	10	15	50	85	90	95	5†	10	15	50	85	90	95	5†	10	15	50	85	90	95	5†	10	15	50	85	90	95
Men																														
62	157	23	46*	50*	52*	64	71*	74*	77*				11							16							52			
63	160	43	48*	51*	53	61	70	75*	79*			6	10	17					8	12	20					32	48	54	
64	163	73	49*	53	55	66	76	76	80*		5	5	10	16	18			7	7	15	25	29			37	38	49	58	63	
65	165	112	52	53	58	66	77	81	84	4	5	6	11	17	19	21	7	8	9	14	25	28	35	31	35	37	47	60	63	71
66	168	129	56	57	59	67	78	83	84	5	6	6	11	18	18	20	7	8	8	14	26	26	32	31	36	38	49	60	62	71
67	170	132	56	60	62	71	82	83	88	5	6	6	11	18	20	22	6	7	9	15	23	25	30	35	39	41	49	58	60	62
68	173	107	56	59	62	71	79	82	85	5	6	6	10	15	16	20	7	8	9	13	24	30	40	33	37	40	49	59	62	69
69	175	97	57*	62	65	74	84	87	88*		6	6	11	17	20			7	7	13	24	26			36	40	58	61	63	
70	178	46	59*	62*	67	75	87	86*	90*			7	10	17					9	14	23					35	48	57		
71	180	49	60*	64*	70	76	79	88*	91*			7	10	16					8	13	22					39	47	52		
72	183	21	62*	65*	67*	74	87*	89*	93*				10							14							45			
73	185	9	63*	67*	69*	79*	89*	91*	94*																					
74	188	6	65*	68*	71*	80*	90*	92*	96*																					
Women																														
58	147	53	37*	43	43	52	58	62	66*		12	13	24	30	33			10	12	23	34	38			22	24	29	36	44	
59	150	108	42	43	44	53	63	69	72	8	11	14	21	29	36	37	6	9	10	17	29	32	34	17	20	22	28	38	39	43
60	152	142	42	44	45	53	63	65	70	8	11	12	21	28	29	33	6	7	8	18	27	32	39	19	21	22	28	36	40	44
61	155	218	44	46	47	54	64	66	72	11	12	14	21	28	31	34	7	8	9	16	28	32	36	20	21	23	28	38	39	42
62	157	255	44	47	48	55	63	64	70	10	12	14	20	28	31	34	6	7	8	14	22	27	32	20	21	21	27	33	35	37
63	160	239	46	48	49	55	65	68	79	10	11	13	20	27	30	36	6	7	7	14	27	29	31	20	21	22	27	33	35	38
64	163	146	49	50	51	57	67	68	74	10	13	13	20	28	30	34	6	7	8	13	24	27	34	22	23	23	28	34	38	42
65	165	113	50	52	53	60	70	72	80	12	13	14	22	29	31	34	7	8	8	15	26	30	33	21	22	23	28	37	39	47
66	168	47	46*	49*	54	58	65	71*	74*			12	19	30					9	12	25					23	27	35		
67	170	18	47*	50*	52*	59	70*	72*	76*				18							13							26			
68	173	18	48*	51*	53*	62	71*	73*	77*				20							15							25			
69	175	5	49*	52*	54*	63*	72*	74*	78*																					
70	178	1	50*	53*	55*	64*	73*	75*	79*																					

*Values estimated through linear regression equation.

†Numbers refer to percentiles of the normal population from the NHANES study. In general, the body weights of normal individuals at the 50th percentile who have the same height, gender, age range, and skeletal frame size as the patient in question are used as the standard.

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Methods for Performing Skinfold Thickness

Measuring Upper Arm Length

Equipment. Flexible, nonstretchable (eg, metal) tape measure.

Method. (1) Ask the patient to stand erect with his/her feet together. (2) Stand behind the patient. (3) Ask the patient to flex his/her right arm 90° at the elbow with the palm facing up. (4) Mark the uppermost edge of the posterior border of the acromion process of the scapula with a cosmetic pencil. (5) Hold the tape measure at this point and extend the tape down the posterior surface of the arm to the tip of the olecranon process (the bony part of the mid-elbow). (6) Keep the tape in position and find the distance halfway between the acromion and the olecranon process that is the midpoint of the upper arm. (7) Mark a (+) at the midpoint on the posterior surface (back) of the arm. (8) Mark another (+) at the same level on the anterior (front) of the arm.

Measuring Skinfold Thickness (Biceps, Triceps, Subscapular, and Iliac Crest)

Equipment. Skinfold calipers.

Method: triceps skinfold (TSF). (1) Ask the patient to stand with his/her feet together, shoulders relaxed, and arms hanging freely at the sides. (2) Stand to the patient's right side. (3) Locate the point on the posterior surface of the right upper arm in the same area as the marked

Table 4. Selected Percentiles of Weight, Triceps and Subscapular Skinfolds, and Bone-Free Upper Arm Muscle Area (AMA) for US Men and Women With Medium Frames (25 to 54 Years Old)

Height			Weight (kg)							Triceps (mm)							Subscapular (mm)							Bone-Free AMA (cm^2)						
Inches	cm	n	5†	10	15	50	85	90	95	5†	10	15	50	85	90	95	5†	10	15	50	85	90	95	5†	10	15	50	85	90	95
Men																														
62	157	10	51*	55*	58*	68	81*	83*	87*				15							13							58			
63	160	30	52*	56*	59*	71	82*	85*	89*				11							18							55			
64	163	71	54*	60	61	71	83	84	90*		6	6	12	18	20			7	9	17	30	32			43	47	56	67	71	
65	165	154	59	62	65	74	87	90	94	5	7	8	12	20	22	25	8	9	10	16	26	29	32	40	43	45	56	67	69	70
66	168	212	58	61	65	75	85	87	93	5	6	7	11	16	18	22	7	7	9	16	25	27	33	38	42	44	55	69	72	78
67	170	409	62	66	68	77	89	93	100	5	7	7	13	21	23	28	8	9	10	18	26	30	33	39	42	44	53	66	69	73
68	173	478	60	64	66	78	89	92	97	4	5	7	11	18	20	24	7	8	9	16	25	28	31	41	44	45	55	67	71	76
69	175	464	63	66	68	78	90	93	97	5	6	7	12	18	20	24	7	8	9	16	25	27	31	38	41	44	54	66	69	73
70	178	419	64	66	70	81	90	93	97	5	6	7	12	18	20	23	7	8	9	15	24	27	30	39	42	43	55	65	68	72
71	180	282	62	68	70	81	92	96	100	4	5	7	12	19	21	25	7	8	9	14	24	27	30	37	41	44	54	67	68	73
72	183	231	68	71	74	84	97	100	104	5	7	7	12	20	22	26	7	8	9	15	26	30	32	40	42	44	56	65	67	74
73	185	106	70	72	75	85	100	101	104	6	7	8	12	20	24	27	8	9	9	15	25	29	32	39	42	43	55	67	69	73
74	188	50	68*	76	77	88	100	100	104*		6	9	13	21	23			7	9	14	25	30			43	43	55	62	63	
Women																														
58	147	40	41*	46*	50	63	77	75*	79*			20	25	40					15	23	38					24	35	42		
59	150	104	47	50	52	66	76	79	85	15	19	21	30	37	40	40	10	12	13	29	38	39	43	23	24	26	33	43	45	49
60	152	208	47	50	52	60	77	79	85	14	15	17	26	35	37	41	8	10	11	22	35	37	41	22	25	25	32	42	45	49
61	155	465	47	49	51	61	73	78	86	11	14	15	25	34	36	42	7	9	10	19	32	36	42	21	24	25	31	42	45	51
62	157	644	49	50	52	61	73	77	83	12	14	16	24	34	36	40	7	9	10	18	33	37	40	21	23	25	31	40	43	48
63	160	685	49	51	53	62	77	80	88	12	13	15	24	33	35	38	7	8	10	18	31	34	38	22	23	25	32	41	43	50
64	163	722	50	52	54	62	76	82	87	11	14	15	23	33	36	40	7	7	8	16	31	35	38	21	23	24	31	40	43	48
65	165	628	52	54	55	63	75	80	89	12	14	15	22	31	34	38	7	8	8	15	29	33	38	21	23	24	31	40	43	49
66	168	428	52	54	55	63	75	78	83	11	13	14	22	31	33	37	7	8	9	14	28	30	35	21	23	24	30	39	41	44
67	170	257	54	56	57	65	79	82	88	12	13	15	21	29	30	35	7	8	8	15	28	32	37	22	24	25	30	40	43	48
68	173	119	58	59	60	67	77	85	87	10	14	15	22	31	32	36	8	8	9	15	29	33	35	22	24	25	30	37	38	39
69	175	59	49*	58	60	68	79	82	87*		11	12	19	29	31			8	8	12	25	29			23	24	30	36	39	
70	178	15	50*	54*	57*	70	80*	83*	87*				19							20							32			

*Values estimated through linear regression equation.

†Numbers refer to percentiles of the normal population from the NHANES study. In general, the body weights of normal individuals at the 50th percentile who have the same height, gender, age range, and skeletal frame size as the patient in question are used as the standard.

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midpoint for the upper arm circumference. (4) Grasp the fold of skin and subcutaneous adipose tissue gently with your thumb and forefingers, approximately 1.0 cm above the point at which the skin is marked, with the skinfold parallel to the long axis of the upper arm. (5) Place the jaws of the calipers at the level that has been marked on the skin with the marking pencil. The jaws should be perpendicular to the length of the fold. (6) Hold the skinfold gently and measure the skinfold thickness to the nearest 1 mm. (7) Record the measurement. If two measurements are within 4 mm of each other, record the mean. If the measurements are more than 4 mm apart, take four measurements and record the mean of all four.

Method: biceps skinfold. (1) Follow the same procedure as for the TSF, but with the measurement of the biceps skinfold at the front of the upper arm (instead of the back, as with the triceps). The level is the same as for the triceps and arm circumference, and the location is in the midline of the anterior part of the arm. (2) Ask the patient to stand with his/her feet together, shoulders relaxed, and arms hanging freely at the sides. (3) Stand behind the patient's right side. (4) Rotate the right arm so that the palm is facing forward. (5) Locate the point on the anterior surface of the right upper arm in the same area as the marked midpoint for the upper arm circumference. (6) Grasp the fold of skin and subcutaneous adipose tissue on the anterior surface of the

Table 5. Selected Percentiles of Weight, Triceps and Subscapular Skinfolds, and Bone-Free Upper Arm Muscle Area (AMA) for US Men and Women With Large Frames (25 to 54 Years Old)

Height			Weight (kg)							Triceps (mm)							Subscapular (mm)							Bone-Free AMA (cm^2)						
Inches	cm	n	5†	10	15	50	85	90	95	5†	10	15	50	85	90	95	5†	10	15	50	85	90	95	5†	10	15	50	85	90	95
Men																														
62	157	1	57*	62*	66*	82*	99*	103*	108*																					
63	160	1	58*	63*	67*	83*	100*	104*	109*																					
64	163	5	59*	64*	68*	84*	101*	105*	110*																					
65	165	15	60*	65*	69*	79	102*	106*	111*				14							21							62			
66	168	37	60*	65*	75	84	103	106*	112*			9	14	30					13	22	36					48	58	76		
67	170	54	62*	70	71	84	102	111	113*		7	7	11	23	27			8	11	20	36	40			50	52	61	73	78	
68	173	84	63*	74	76	86	101	104	114*		9	10	14	22	23			12	14	20	31	35			51	53	65	78	86	
69	175	126	68	71	74	89	103	105	114	6	7	8	15	25	29	31	9	10	11	18	31	32	38	46	48	49	61	73	78	83
70	178	150	68	72	74	87	106	112	114	7	7	7	14	23	25	30	7	10	11	17	31	35	38	43	47	50	61	75	77	86
71	180	123	73	78	82	91	113	116	123	6	8	10	15	25	27	31	9	11	11	20	35	40	46	47	48	50	62	75	81	83
72	183	114	73	76	78	91	109	112	121	5	6	7	12	20	22	25	8	9	9	19	28	30	36	45	48	50	61	77	80	86
73	185	109	72	77	79	93	106	107	116	5	6	7	13	19	22	31	7	9	9	18	27	28	30	47	49	51	66	79	83	86
74	188	37	69*	74*	82	92	105	115*	120*			8	12	19					9	18	32					53	66	78		
Women																														
58	147	6	56*	63*	67*	86*	105*	110*	117*																					
59	150	19	56*	62*	67*	78	105*	109*	116*				36							35							45			
60	152	32	55*	62*	66*	87	104*	109*	116*				38							42							44			
61	155	92	54*	64	66	81	105	117	115*		25	26	36	48	50			17	17	35	48	53			29	33	41	62	74	
62	157	135	59	61	65	81	103	107	113	16	19	22	34	48	48	50	13	16	18	32	48	51	55	26	28	31	44	56	63	72
63	160	162	58	63	67	83	105	109	119	18	20	22	34	46	48	51	11	14	16	32	44	48	50	27	30	32	43	60	65	77
64	163	196	59	62	63	79	102	104	112	16	20	21	32	43	45	49	10	12	15	28	42	46	50	26	28	29	39	50	55	63
65	165	242	59	61	63	81	103	109	114	17	20	21	31	43	46	48	10	12	14	29	42	48	52	27	28	29	39	56	59	67
66	168	166	55	58	62	75	95	100	107	13	17	18	27	40	43	45	8	9	11	25	36	40	45	23	24	27	35	49	53	69
67	170	144	58	60	65	80	100	108	114	13	16	17	30	41	43	49	7	10	11	25	41	46	55	25	28	30	37	50	53	55
68	173	81	51*	66	66	76	104	105	111*		16	20	29	37	40			10	12	21	45	48			28	30	38	51	54	
69	175	39	50*	57*	68	79	105	104*	111*			21	30	42					11	20	43					27	35	49		
70	178	17	50*	56*	61*	76	99*	104*	110*				20							16							37			

*Values estimated through linear regression equation.

†Numbers refer to percentiles of the normal population from the NHANES study. In general, the body weights of normal individuals at the 50th percentile who have the same height, gender, age range, and skeletal frame size as the patient in question are used as the standard.

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upper arm, in the midline of the upper arm, and about 1.0 cm above the marked line on the middle of the arm. (7) Measure the skinfold thickness to the nearest 1 mm while you continue to hold the skinfold with your fingers. (8) Record the measurement. If two measurements are within 4 mm of each other, record the mean. If the measurements are more than 4 mm apart, take four measurements and record the mean of all four.

Method: subscapular skinfold. (1) Ask the patient to stand erect, with relaxed shoulders and arms. (2) Open the back of the examination gown or garment. (3) Palpate for the inferior angle of the right scapula. (4) Grasp a fold of skin and subcutaneous adipose tissue directly below (1.0 cm) and medial to the inferior angle. This skinfold forms a line about 45° below the horizontal, extending diagonally toward the right elbow. (5) Place the jaws of the caliper perpendicular to the length of the fold, about 1.0 cm lateral to the fingers, with the top jaw of the caliper on the mark over the inferior angle of the scapula. (6) Measure the skinfold thickness to the nearest 1 mm while the fingers continue to hold the skinfold. (7) Record the measurement. If two measurements are within 4 mm of each other, record the mean. If the measurements are more than 4 mm apart, take four measurements and record the mean of all four.

Method: suprailiac skinfold. (1) Ask the patient to stand erect, with feet together and arms hanging loosely by the sides. If necessary, arms may be abducted slightly to improve access to the site. This measurement can be taken in the supine position for those unable to stand. The

Table 6. Selected Percentiles of Weight, Triceps and Subscapular Skinfolds, and Bone-Free Upper Arm Muscle Area (AMA) for US Men and Women With Small Frames (55 to 74 Years Old)

Height			Weight (kg)							Triceps (mm)							Subscapular (mm)							Bone-Free AMA (cm^2)						
Inches	cm	n	5†	10	15	50	85	90	95	5†	10	15	50	85	90	95	5†	10	15	50	85	90	95	5†	10	15	50	85	90	95
Men																														
62	157	47	45*	49*	56	61	68	73*	77*			6	9	12				11	16	23					38	46	52			
63	160	78	47*	49	51	62	71	71	79*		5	5	10	16	17			6	6	12	21	22			34	35	43	54	55	
64	163	107	47	50	54	63	72	74	80	4	4	4	9	20	21	22	6	7	7	14	24	25	29	26	30	31	44	53	54	56
65	165	132	48	54	59	70	80	90	90	5	6	7	11	18	19	24	6	8	8	16	28	28	29	26	30	34	48	57	60	62
66	168	112	51	55	59	68	77	80	84	5	6	7	11	16	20	20	7	7	8	15	25	26	30	25	31	35	45	54	58	64
67	170	128	55	60	61	69	79	81	88	5	6	6	10	15	17	25	7	8	9	13	22	25	31	30	36	37	45	53	55	59
68	173	95	54*	54	58	70	79	81	86*		5	5	10	15	17			7	7	13	21	22			35	35	43	55	60	
69	175	47	56*	59*	63	75	81	84*	88*			8	10	15				10	16	27						38	47	62		
70	178	29	57*	61*	63*	76	83*	86*	89*				11						13								48			
71	180	14	59*	62*	65*	69	85*	87*	91*				9						10								43			
72	183	6	60*	64*	66*	76*	86*	89*	92*																					
73	185	1	62*	65*	68*	78*	88*	90*	94*																					
74	188	1	63*	67*	69*	77*	89*	92*	95*																					
Women																														
58	147	85	39*	46	48	54	63	65	71*		14	16	21	31	34			8	9	18	32	33			22	23	29	40	42	
59	150	122	41	45	48	55	66	68	74	11	13	15	21	30	31	33	6	7	9	19	29	30	33	22	23	24	30	39	40	44
60	152	157	43	45	47	54	67	70	73	10	11	13	20	29	31	35	5	7	8	15	27	32	36	20	22	23	30	37	41	44
61	155	145	43	43	45	56	65	70	71	10	12	14	22	29	29	32	6	7	8	17	29	31	34	18	21	23	28	36	40	42
62	157	158	47	49	52	58	67	69	73	11	11	12	21	29	30	32	7	8	9	17	25	26	30	20	23	24	30	37	40	43
63	160	89	42*	45	49	58	67	68	74*		12	13	20	29	30			6	7	14	25	27			19	20	27	35	36	
64	163	50	43*	47	49	60	68	70	75*		12	13	21	27	29			6	7	18	24	25			21	21	28	37	42	
65	165	26	43*	47*	49*	60	69*	72*	75*				18							13							28			
66	168	12	44*	48*	50*	68	70*	72*	76*				23							13							33			
67	170	1	45*	48*	51*	61*	71*	73*	77*																					
68	173	1	45*	49*	51*	61*	71*	74*	77*																					
69	175	0	46*	49*	52*	62*	72*	74*	78*																					
70	178	0	47*	50*	52*	63*	73*	75*	79*																					

*Values estimated through linear regression equation.

†Numbers refer to percentiles of the normal population from the NHANES study. In general, the body weights of normal individuals at the 50th percentile who have the same height, gender, age range, and skeletal frame size as the patient in question are used as the standard.

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suprailiac skinfold is measured in the midaxillary line immediately superior to the iliac crest. (2) Palpate for the iliac crest. (3) Grasp the skin at an oblique angle, just posterior to the midaxillary line below the natural cleavage lines of the skin. Align the skinfold inferomedially at 45° to the horizontal. (4) Gently apply the caliper jaws about 1 cm from the fingers holding the skinfold. (5) Record the skinfold to the nearest 0.1 cm. If two measurements are within 4 mm of each other, record the mean. If the measurements are more than 4 mm apart, take four measurements and record the mean of all four.

The suprailiac skinfold, as well as the biceps skinfold, may be more useful in the research setting than in most clinical settings. It may be more difficult to obtain the suprailiac skinfold than the other skinfold measurements due to the potential reluctance of patients to expose that site. However, the Tables 9 and 10 are provided for those who may wish to incorporate these measurements as a component of the anthropometric assessment of MD or CRF patients. The method for estimating body fat from these four skinfold measurements is shown below.

Estimating Body Fat and Fat-Free Mass According to the Method of Durnin and Wormersley[260]

Method. (1) Determine the patient's age and weight (in kilograms). (2) Measure the following skinfolds (in millimeters): biceps, triceps, subscapular, and suprailiac. (3) Compute the sum

Table 7. Selected Percentiles of Weight, Triceps and Subscapular Skinfolds, and Bone-Free Upper Arm Muscle Area (AMA) for US Men and Women With Medium Frames (55 to 74 Years Old)

Height			Weight (kg)							Triceps (mm)							Subscapular (mm)							Bone-Free AMA (cm^2)						
Inches	cm	n	5†	10	15	50	85	90	95	5†	10	15	50	85	90	95	5†	10	15	50	85	90	95	5†	10	15	50	85	90	95
Men																														
62	157	49	50*	54*	59	68	77	81*	85*			5	12	25				11	19	27						39	48	61		
63	160	89	51*	57	60	70	80	82	87*		7	7	11	20	23		8	10	15	26	28				36	38	50	60	63	
64	163	210	55	59	62	71	82	83	91	5	6	6	10	17	20	26	6	7	9	15	25	27	35	35	39	40	51	64	66	71
65	165	335	56	60	64	72	83	86	89	5	6	7	11	17	19	24	7	8	9	17	25	29	31	35	38	41	52	63	65	72
66	168	405	57	62	66	74	83	84	89	6	6	7	12	18	19	22	7	9	10	16	25	28	31	34	39	42	51	60	62	67
67	170	509	59	64	66	78	87	89	94	5	6	7	12	18	20	23	7	9	10	17	26	29	34	35	39	42	52	65	67	70
68	173	413	62	66	68	78	89	95	101	6	7	8	12	18	21	23	7	9	10	17	26	29	32	37	40	42	52	65	67	70
69	175	366	62	66	68	77	90	93	99	5	6	7	12	19	22	25	6	8	9	16	25	28	30	31	36	40	51	62	65	72
70	178	248	62	68	71	80	90	95	101	6	7	7	11	18	19	21	7	9	10	16	25	27	30	36	41	44	53	63	65	68
71	180	146	68	70	72	84	94	97	101	5	6	6	11	16	17	20	7	9	10	15	25	26	31	36	42	44	56	65	67	71
72	183	81	66*	65	69	81	96	97	101*		6	8	11	19	20		8	10	16	28	30				27	39	50	58	59	
73	185	35	68*	72*	79	88	93	99*	103*			8	13	16				10	15	26						43	56	67		
74	188	11	69*	73*	76*	95	98*	101*	104*				11						18								56			
Women																														
58	147	105	40	44	49	57	72	82	85	5	13	17	28	40	40	41	3	7	10	25	37	43	48	21	23	25	32	46	47	51
59	150	198	47	49	52	62	74	78	86	12	15	18	26	34	38	41	8	9	11	23	32	36	43	24	26	27	35	44	48	48
60	152	358	47	50	52	65	76	79	86	13	17	18	25	33	34	38	8	10	12	22	34	36	40	21	24	26	35	45	49	57
61	155	543	49	51	54	64	78	81	86	13	16	18	25	35	37	42	8	10	10	20	33	36	42	22	24	26	34	44	49	52
62	157	576	49	53	54	64	78	82	88	13	15	17	24	33	36	39	7	8	10	20	33	36	38	24	25	26	35	45	47	54
63	160	551	52	54	55	65	79	83	89	12	14	16	24	32	35	38	8	8	10	18	32	37	41	24	26	27	35	44	45	51
64	163	406	51	54	57	66	78	81	87	12	14	16	25	33	34	37	7	9	10	17	30	33	38	21	24	26	33	44	46	49
65	165	307	54	56	59	67	78	84	88	14	16	17	24	33	35	39	7	8	9	17	30	35	37	24	25	27	34	44	45	50
66	168	119	54	57	57	66	79	85	88	12	13	16	24	33	33	36	6	7	8	16	30	31	34	24	26	27	33	41	43	49
67	170	63	51*	59	61	72	82	85	89*		17	17	27	35	35			9	10	19	35	35			27	28	32	41	43	
68	173	28	52*	56*	59*	70	83*	86*	90*				25							16							36			
69	175	5	53*	57*	60*	72*	84*	87*	91*																					
70	178	1	54*	58*	61*	73*	85*	88*	92*																					

*Values estimated through linear regression equation.

†Numbers refer to percentiles of the normal population from the NHANES study. In general, the body weights of normal individuals at the 50th percentile who have the same height, gender, age range, and skeletal frame size as the patient in question are used as the standard.

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(Σ) by adding the four skinfolds. (4) Compute the logarithm of the sum (Σ). (5) Apply one of the equations from Table 10 (age- and sex-adjusted) to compute body density (D, g/mL). (6) Fat mass is calculated as follows:

$$\text{Fat mass (kg)} = \text{body weight (kg)} \times [(4.95/D) - 4.5] \quad \text{Equation 32}$$

where D is obtained from the formulas shown in Table 10. (7) Fat-free body mass (FFM) is calculated as follows:

$$\text{FFM (kg)} = \text{body weight (kg)} - \text{fat mass (kg)} \quad \text{Equation 33}$$

Mid-Arm Muscle Area, Diameter, and Circumference

Anthropometric measures of skeletal muscle mass are an indirect assessment of muscle protein. Approximately 60% of total body protein is located in skeletal muscle—the body's primary source of amino acids in response to poor nutritional intake.[83]

Estimates of muscle mass in an individual, for comparison with a reference population, eg, NHANES, is made by measuring the arm at the midpoint from the acromion to the olecranon. From measurements of both the mid-arm circumference (MAC) and the triceps skinfold (TSF), a calculated estimate of the mid-arm muscle circumference (MAMC) (that includes the bone)

Table 8. Selected Percentiles of Weight, Triceps and Subscapular Skinfolds, and Bone-Free Upper Arm Muscle Area (AMA) for US Men and Women With Large Frames (55 to 74 Years Old)

Height			Weight (kg)							Triceps (mm)							Subscapular (mm)							Bone-Free AMA (cm^2)						
Inches	cm	n	5†	10	15	50	85	90	95	5†	10	15	50	85	90	95	5†	10	15	50	85	90	95	5†	10	15	50	85	90	95
Men																														
62	157	7	54*	59*	63*	77*	91*	95*	100*																					
63	160	12	55*	60*	64*	80	92*	96*	101*				15							20							57			
64	163	20	57*	62*	65*	77	94*	97*	102*				21							31							44			
65	165	36	58*	63*	73	79	89	98*	103*			11	14	22					14	19	27					44	59	66		
66	168	58	59*	67	73	80	101	102	105*		7	8	13	21	25			9	11	20	31	35			43	47	56	67	72	
67	170	114	65	71	73	85	103	108	112	6	8	9	16	21	25	27	8	11	12	20	35	35	38	41	43	44	56	71	73	79
68	173	128	67	71	73	83	95	98	111	6	7	8	13	20	21	23	8	10	11	18	27	30	32	41	43	46	57	69	70	74
69	175	131	65	70	74	84	96	98	105	6	7	8	12	18	20	23	7	11	11	19	27	30	33	40	45	45	58	70	72	79
70	178	144	68	73	77	87	102	104	117	5	6	8	14	22	25	31	9	11	13	20	30	33	37	43	48	50	59	70	71	87
71	180	95	65*	70	70	84	102	109	111*		6	6	13	18	22			8	9	15	30	30			46	47	54	70	75	
72	183	72	67*	76	81	90	108	112	112*		8	8	13	23	26			8	9	20	28	31			47	48	59	73	78	
73	185	23	68*	73*	76*	88	105*	108*	113*				11							19							59			
74	188	15	69*	74*	78*	89	106*	109*	114*				12							15							54			
Women																														
58	147	14	53*	59*	63*	92	95*	99*	104*				45							44							50			
59	150	26	54*	59*	63*	78	95*	99*	105*				36							31							49			
60	152	72	54*	65	69	78	87	88	105*		25	26	35	44	45			19	21	31	42	45			28	33	41	58	60	
61	155	117	64	68	69	79	94	95	106	18	22	24	33	40	44	46	13	16	19	29	40	43	48	31	32	34	44	59	61	71
62	157	126	59	61	63	82	93	101	111	19	24	24	32	40	43	50	13	19	22	30	39	48	53	28	29	34	43	59	63	76
63	160	154	61	65	67	80	100	102	118	20	24	25	33	41	43	45	13	15	16	29	40	45	51	27	32	33	41	56	62	67
64	163	147	60	65	67	77	97	102	119	18	22	23	29	42	46	50	10	12	16	24	41	46	55	28	29	32	41	54	60	78
65	165	117	60	66	69	80	98	102	111	15	17	20	30	43	44	46	8	9	12	26	42	46	48	29	32	32	42	53	57	65
66	168	64	57*	60	63	82	98	105	109*		18	18	27	35	40			9	12	26	34	36			31	31	40	57	58	
67	170	40	58*	64*	68	80	105	104*	109*			22	32	44					14	25	46					30	40	58		
68	173	17	58*	64*	68*	79	100*	104*	110*				26							21							48			
69	175	7	59*	65*	69*	85*	101*	105*	110*																					
70	178	2	60*	65*	69*	85*	101*	105*	111*																					

*Values estimated through linear regression equation.

†Numbers refer to percentiles of the normal population from the NHANES study. In general, the body weights of normal individuals at the 50th percentile who have the same height, gender, age range, and skeletal frame size as the patient in question are used as the standard.

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can be made using the following formula (Table 11)[83]:

$$\text{MAMC (cm)} = \text{MAC (cm)} - (\pi \times \text{TSF (cm)}) \quad \text{Equation 34}$$

A more accurate assessment of muscle mass is obtained by estimating bone-free arm muscle area (AMA). Corrected AMA may be calculated from TSF thickness and MAC using the following formulas[263]:

$$\text{AMA (corrected for males)} = [(\text{MAC (cm)} - \pi \times \text{TSF (cm)})^2/4\pi] - 10 \quad \text{Equation 35}$$

$$\text{AMA (corrected for famales)} = [(\text{MAC (cm)} - \pi \times \text{TSF (cm)})^2/4\pi] - 6.5 \quad \text{Equation 36}$$

AMA estimates may be inaccurate in obese and elderly subjects (Tables 3 through 8).[89]

Methods for Performing Mid-Arm Muscle Area, Diameter, and Circumference

Equipment. Flexible, nonstretchable (eg, metal) tape measure.

Method. (1) Ask the patient to stand with his/her elbow relaxed, with the right arm hanging freely to the side. (2) Place the tape around the upper arm, directly over the pencil mark at the midpoint on the posterior aspect (back) of the upper arm. Keep the tape perpendicular to the shaft of the upper arm. (3) Pull the tape just snugly enough around the arm to ensure contact with the medial side of the arm and elsewhere.

Table 9. Equivalent Fat Content, as Percentage of Body Weight, for a Range of Values for the Sum of Four Skinfold Measurements

Skinfolds (mm)	Men (y)				Women (y)			
	17-29	30-39	40-49	50+	16-29	30-39	40-49	50+
15	4.8				10.5			
20	8.1	12.2	12.2	12.6	14.1	17.0	19.8	21.4
25	10.5	14.2	15.0	15.6	16.8	19.4	22.2	24.0
30	12.9	16.2	17.7	18.6	19.5	21.8	24.5	26.6
35	14.7	17.7	19.6	20.8	21.5	23.7	26.4	28.5
40	16.4	19.2	21.4	22.9	23.4	25.5	28.2	30.3
45	17.7	20.2	23.0	24.7	25.0	26.9	29.6	31.9
50	19.0	21.5	24.6	26.5	26.5	28.2	31.0	33.4
55	20.1	22.5	25.9	27.9	27.8	29.4	32.1	34.6
60	21.2	23.5	27.1	29.2	29.1	30.6	33.2	35.7
65	22.2	24.3	28.2	30.4	30.2	31.6	34.1	36.7
70	23.1	25.1	29.3	31.6	31.2	32.5	35.0	37.7
75	24.0	25.9	30.3	32.7	32.2	33.4	35.9	38.7
80	24.8	26.6	31.2	33.8	33.1	34.3	36.7	39.6
85	25.5	27.2	32.1	34.8	34.0	35.1	37.5	40.4
90	26.2	27.8	33.0	35.8	34.8	35.8	38.3	41.2
95	26.9	28.4	33.7	36.6	35.6	36.5	39.0	41.9
100	27.6	29.0	34.4	37.4	36.4	37.2	39.7	42.6
105	28.2	29.6	35.1	38.2	37.1	37.9	40.4	43.3
110	28.8	30.1	35.8	39.0	37.8	38.6	41.0	43.9
115	29.4	30.6	36.4	39.7	38.4	39.1	41.5	44.5
120	30.0	31.1	37.0	40.4	39.0	39.6	42.0	45.1
125	31.0	31.5	37.6	41.1	39.6	40.1	42.5	45.7
130	31.5	31.9	38.2	41.8	40.2	40.6	43.0	46.2
135	32.0	32.3	38.7	42.4	40.8	41.1	43.5	46.7
140	32.5	32.7	39.2	43.0	41.3	41.6	44.0	47.2
145	32.9	33.1	39.7	43.6	41.8	42.1	44.5	47.7
150	33.3	33.5	40.2	44.1	42.3	42.6	45.0	48.2
155	33.7	33.9	40.7	44.6	42.8	43.1	45.4	48.7
160	34.1	34.3	41.2	45.1	43.3	43.6	45.8	49.2
165	34.5	34.6	41.6	45.6	43.7	44.0	46.2	49.6
170	34.9	34.8	42.0	46.1	44.1	44.4	46.6	50.0
175	35.3					44.8	47.0	50.4
180	35.6					45.2	47.4	50.8
185	35.9					45.6	47.8	51.2
190						45.8	48.2	51.6
195						46.2	48.5	52.0
200						46.5	48.9	52.4
205							49.1	52.7
210							49.4	53.0

Biceps, triceps, subscapular and suprailiac of men and women of different ages.
Adapted and reprinted with permission from Durnin and Womersley.[260]

Make sure that the tape is not too tight that it causes dimpling of the skin. (4) Record the measurement to the nearest millimeter. (5) Check to see if the two measurements are within 0.4 cm of each other. If they are not, take two more measurements and record the mean of all four.

Table 10. Equations for Estimating Body Density From the Sum of Four Skinfold Measurements

Age Range (y)	Equations for Men	Age Range (y)	Equations for Women
17-19	$D = 1.1620 - 0.0630 \times (\log \Sigma)$*	17-19	$D = 1.1549 - 0.0678 \times (\log \Sigma)$*
20-29	$D = 1.1631 - 0.0632 \times (\log \Sigma)$	20-29	$D = 1.1599 - 0.0717 \times (\log \Sigma)$
30-39	$D = 1.1422 - 0.0544 \times (\log \Sigma)$	30-39	$D = 1.1423 - 0.0632 \times (\log \Sigma)$
40-49	$D = 1.1620 - 0.0700 \times (\log \Sigma)$	40-49	$D = 1.1333 - 0.0612 \times (\log \Sigma)$
50+	$D = 1.1715 - 0.0779 \times (\log \Sigma)$	50+	$D = 1.1339 - 0.0645 \times (\log \Sigma)$

Four skinfolds are biceps, triceps, subscapular, and suprailiac.

*Σ = sum of 4 skinfolds (biceps, triceps, subscapular, suprailiac).

Data from Durnin and Womersley[260] and reprinted with permission from Wright and Heymsfield (eds): Nutritional Assessment, 1984, Blackwell Science, Inc.

Table 11. Mid-Arm Muscle Circumference for Adult Men and Women in the United States (18 to 74 Years)

Age Group (y)	Sample Size	Estimated Population (millions)	Mean (cm)	Percentile						
				5th	10th	25th	50th	75th	90th	95th
Men										
18-74	5,261	61.18	28.0	23.8*	24.8	26.3	27.9	29.6	31.4	32.5
18-24	773	11.78	27.4	23.5	24.4	25.8	27.2	28.9	30.8	32.3
25-34	804	13.00	28.3	24.2	25.3	26.5	28.0	30.0	31.7	32.9
35-44	664	10.68	28.8	25.0	25.6	27.1	28.7	30.3	32.1	33.0
45-54	765	11.15	28.2	24.0	24.9	26.5	28.1	29.8	31.5	32.6
55-64	598	9.07	27.8	22.8	24.4	26.2	27.9	29.6	31.0	31.8
65-74	1,657	5.50	26.8	22.5	23.7	25.3	26.9	28.5	29.9	30.7
Women										
18-74	8,410	67.84	22.2	18.4*	19.0	20.2	21.8	23.6	25.8	27.4
18-24	1,523	12.89	20.9	17.7	18.5	19.4	20.6	22.1	23.6	24.9
25-34	1,896	13.93	21.7	18.3	18.9	20.0	21.4	22.9	24.9	26.6
35-44	1,664	11.59	22.5	18.5	19.2	20.6	22.0	24.0	26.1	27.4
45-54	836	12.16	22.7	18.8	19.5	20.7	22.2	24.3	26.6	27.8
55-64	589	9.96	22.8	18.6	19.5	20.8	22.6	24.4	26.3	28.1
65-74	1,822	7.28	22.8	18.6	19.5	20.8	22.5	24.4	26.5	28.1

Numbers refer to percentiles of the normal population from the NHANES I study. In general, the body weights of normal individuals at the 50th percentile who have the same height, gender, age range, and skeletal frame size as the patient in question are used as the standard. Measurements made in the right arm.

*Values are in units of cm.

Adapted and reprinted with permission from Bishop et al.[317]

Appendix VIII. Serum Transferrin and Bioelectrical Impedance Analysis

Two indicators of protein-energy status (serum transferrin and bioelectrical impedance analysis) were not deemed valid measures of nutritional status in MD patients by the a priori definition (median panel rating 7 or above), but were considered by the Work Group to be worthy of brief discussion. Both were limited by a lack of specificity as nutritional indicators.

Serum Transferrin

Serum transferrin has been used extensively as a marker of nutritional status, and particularly the visceral protein pools, in individuals with or without CRF.[17] It has been suggested that serum transferrin may be more sensitive than albumin as an indicator of nutritional status, possibly because transferrin has a shorter half-life than albumin (~8 versus ~20 days, respectively).[17] Transferrin is a negative acute-phase reactant and is limited by many of the same conditions that limit albumin and prealbumin as indicators of nutritional status. Moreover, the serum transferrin concentration is affected by iron status (ie, serum transferrin increases in iron deficiency and declines following iron loading). Thus, increased iron requirements induced by chronic blood loss from sequestration of blood in the hemodialyzer, blood drawing, or gastrointestinal bleeding and by erythropoietin therapy and the frequent intravenous administration of iron may complicate interpretation of serum transferrin levels.

There is insufficient evidence that serum transferrin is a more sensitive index of PEM than serum albumin in MD patients. Furthermore, its lesser degree of specificity renders it less clinically useful than other serum proteins in this population. Serum transferrin may be more useful in nondialyzed patients with advanced CRF who are less likely to have increased blood loss and who are not receiving erythropoietin or iron therapy.[85]

Bioelectrical Impedance Analysis (BIA)

BIA is an attractive tool for nutritional assessment of individuals undergoing MD because it is relatively inexpensive to perform, noninvasive and painless, requires minimal operator training, and provides input data that has been correlated with several aspects of body composition.[261] Numerous population-based studies have shown a strong direct correlation ($r > 0.9$) between BIA (height-adjusted resistance) and total body water (TBW). The estimation of other, more complex body compartments (eg, edema-free lean body mass and body cell mass) has proved more difficult, in part because of the relative unavailability of gold standards for estimating compartment sizes. Population-specific regression equations for edema-free lean body mass and body cell mass have not been developed in ESRD. Therefore, systematic bias might magnify the error obtained using regression models derived from nonrenal populations. Errors may compound if multiple compartments are estimated (eg, body cell mass = lean body mass − extracellular water). Therefore, using regression-adjusted BIA parameters (resistance and reactance) to estimate body composition is not sufficiently reliable or valid to recommend its use in MD patients, in contrast to DXA (Guideline 11).

A more compelling argument for the use of BIA is the evidence linking phase angle* with survival in hemodialysis patients.[200,264] Although phase angle has been shown to correlate with some nutritional variables (eg, SGA, anthropometric measures, nPNA, and serum albumin, prealbumin, and creatinine), the physiologic basis for the correlation between phase angle and protein-energy nutritional status is not clearly established.[200] As with other nutritional indicators (eg, serum albumin; Guideline 3, Rationale), it is not clear that the relation between phase angle and survival is related to nutritional status.

Exploring the link between reactance, resistance, and derivations thereof (eg, phase angle), survival, and nutritional status represents an exciting area of inquiry. If BIA is to be used in the clinical setting, it is recommended that focus be placed on these direct impedance parameters, rather than on regression estimates of edema-free lean body mass or other body compartments.

*Phase angle reflects the relative contributions of fluid (resistance, or R) and cell membranes (reactance, or Xc) to the observed impedance in a biological system. Mathematically, phase angle equals the arc tangent of Xc/R.[264]

Appendix IX. Estimation of Glomerular Filtration Rate

Several guideline statements refer to glomerular filtration rates (GFR) below which certain monitoring strategies or therapies should be instituted. The inulin clearance is considered to be the most accurate measure of the GFR. However, it is a laborious and rather expensive measurement. We describe here recommended methods for determining GFR that are more useful under clinical conditions.

GFR can be estimated from the serum creatinine concentration and other factors, or determined more precisely using either timed urine collections or radioisotope elimination methods.[265-267] For the purposes recommended in these guidelines, the estimated GFR will usually be sufficient to provide a useful ''ballpark'' value for the GFR (ie, $<$25 mL/min). Direct urinary clearance measurements will be more useful in determining the degree of renal dysfunction at lower levels of clearance, when the need for renal replacement therapy is entertained.

The most widely used method for estimating GFR is the Cockcroft-Gault equation.[266] This equation considers the effects of age, sex, and body weight on creatinine generation (ie, on average, increased age, female sex, and decreased weight associated with reduced creatinine generation; Guideline 5), thereby adjusting serum creatinine values to more accurately reflect creatinine clearance.

$$\begin{aligned}\text{GFR} = {} & [(140 - \text{age}) \times \text{body weight (kg)} \\ & \times 0.85 \text{ if famale}] \\ & \div [72 \times \text{serum creatinine (mg/dL)}]\end{aligned}$$

Equation 37

More recently, an equation was derived from data obtained from the MDRD study, GFR measured by iothalamate clearances as the standard of measurement.[267] In addition to incorporating the influence of age and gender, the effects of race, and three (rather than one) biochemical measures are included:

$$\begin{aligned}\text{GFR} = {} & 170 \times \text{serum creatinine}^{-0.999} \\ & \times \text{age}^{-0.176} \times \text{female}^{0.762} \\ & \times (1.18 \times \text{black race}) \\ & \times \text{SUN}^{-0.17} \times \text{serum albumin}^{0.318}\end{aligned}$$

Equation 38

Timed urine collections are considered by most investigators to be valuable, albeit flawed measurements of GFR. Creatinine clearance is the value most frequently employed. As the GFR falls, however, the creatinine clearance progressively overestimates GFR, to a degree that may approach twice the true GFR value ($<$15 to 20 mL/min). At these levels of renal function, a more valid approximation of the GFR can be obtained using an average of the creatinine and urea clearances. Others have advocated the use of a creatinine clearance after administration of cimetidine, a drug known to block creatinine secretion. The accuracy of the timed urine collection is dependent on the integrity of the collection (among other factors). The creatinine index (Guideline 5) is often used to confirm whether a collection is appropriate, insufficient, or in excess. Radioisotope elimination methods (eg, ethylenediaminetetraaceticacid [EDTA], iothalamate) can be more accurate, but are limited by time constraints and expense.

Appendix X. Potential Uses for L-Carnitine in Maintenance Dialysis Patients

Prior Evaluation and Therapy of Proposed Indications

Although there is evidence that L-carnitine administration may favorably affect the management of anemia (see below), it is essential that other potential issues be resolved before proceeding with L-carnitine therapy. For example, patients with persistent anemia despite the provision of erythropoietin should be thoroughly investigated for causes of erythropoietin resistence, including iron, folate, and vitamin B12 deficiency, chronic infection or inflammatory disease, advanced secondary hyperparathyroidism, and underdialysis. Efforts to correct these abnormalities (eg, iron supplementation, increase in dialysis dose) should be implemented before L-carnitine is used to treat anemia.

Intradialytic hypotension should be managed with meticulous attention to the dialysis procedure, and modification of the dialysis procedure should be considered. Prolongation of dialysis time, ultrafiltration profiling, sodium modeling, modification of dialysate sodium and calcium concentrations, and modification of dialysate temperature are among the changes in management that could be considered.

Causes of low cardiac output in ESRD patients should be thoroughly investigated. Pericarditis with tamponade is a life-threatening complication that can be diagnosed by careful physical examination and echocardiography. Left ventricular dysfunction should be managed with agents that provide afterload reduction (eg, angiotensin converting enzyme inhibitors) and have been shown to enhance survival in non-ESRD patients.[268] Other agents proven effective in cardiomyopathy (eg, β-adrenergic antagonists) should also be considered.[269] Symptoms of heart failure with normal or high cardiac output may be seen with conditions such as severe anemia, hyperthyroidism, and large or multiple arteriovenous shunts.

Malaise, asthenia, weakness, fatigue, and low exercise capacity are more complex entities, with few broadly effective therapies. Before considering L-carnitine for these conditions, underdialysis, abnormalities of thyroid function, primary neurologic diseases, sleep disturbances (including restless legs syndrome), depression, and other nutrient deficiencies should be considered and treated if present.

Specific Indications

For most potential indications, there was insufficient evidence from carefully conducted clinical trials to provide strong support for the use of L-carnitine. What follows below is a description of the evidence used by the Work Group to reach is conclusions. The level of detail provided roughly corresponds to the quantity and quality of available evidence.

Elevated serum triglycerides. The Work Group agreed that there was insufficient evidence to support or refute the use of L-carnitine for dialysis-associated hypertriglycedemia. Thirty-two studies were reviewed.[270-301] Among 681 subjects, 55 maintenance hemodialysis patients served as controls. Thirty-one studies evaluated the serum triglycerides alone and one also reported on serum total cholesterol levels. L-carnitine treatment allocation was randomly assigned in 9 studies.[270,272,274-277,279,280,301] L-carnitine was administered intravenously in 17 studies,[270, 272, 275, 277, 280, 281, 284, 286, 287, 289-291, 294, 296, 297, 299, 301] orally in 13 studies,[271,273,276,279,285,288,289,292,293,295,296,298, 300] and via the dialysate in 7 studies.[274,278,282,283,287,292,298] Peritoneal dialysis patients were studied in one report.[290] The average number of subjects was 21 per study (range, 6 to 97). The duration of L-carnitine treatment was heterogeneous, ranging from 1 week to 12 to 15 months, with the mean duration being 3 to 6 months. When administered intravenously, the dose of L-carnitine ranged from 1 mg/kg body weight to 2 g at the end of each dialysis session, usually thrice weekly. Oral L-carnitine was administered in one to three daily doses, from 10 mg/kg body weight per day to 3 g per day. When L-carnitine was added into the dialysate, the final dialysate L-carnitine concentration was approximately 75 μmol/L or 150 μmol/L, corresponding to 2 g or 4 g of L-carnitine for each dialysis session, respectively.

There was no significant change in serum triglycerides in 23 of 32 studies. In a single study in which 3 g per day of oral L-carnitine were administered, there was a significant increase in serum triglycerides (+ 22%) over a 5-week time

period. A decrease in serum triglycerides was observed in seven studies; in some of these, the significant decrease was observed in patient subgroups only, based on dialysate buffer,[278] starting HDL concentrations,[291] or the final dose of L-carnitine.[280] The small sample sizes, heterogeneity in L-carnitine route of administration and dose, variable durations of study and methods of analysis, and the inclusion of patients with normal triglyceride levels in most studies make interpretation of these data difficult.

Cardiac function and arrhythmias. Cardiac and skeletal muscle myocyte metabolism is largely oxidative and dependent on free fatty acid delivery and mitochondrial transport. Moreover, the myocyte has one of the highest intracellular carnitine concentrations in the body. Experimental models of cardiomyopathy have been corrected with the administration of L-carnitine, and primary carnitine deficiency has been associated with left ventricular hypertrophy in animal models.

Cardiovascular disease accounts for approximately 50% of deaths in the ESRD population, and complications of left ventricular dysfunction and left ventricular hypertrophy lead to considerable morbidity.[302] For these reasons, L-carnitine therapy has been explored as a treatment for cardiovascular disease in ESRD.

Two studies of L-carnitine treatment evaluated ejection fraction as an index of left ventricular function.[303,304] Van Es et al[303] showed a statistically significant increase in ejection fraction among 13 patients (mean, 48.6% versus 42.4%) after 3 months of L-carnitine therapy (1 g IV after each hemodialysis session). The patients had all undergone hemodialysis for greater than 1 year, using high-flux, bicarbonate dialysis, with hematocrit >30% and with no change in hemodialysis frequency or time over the course of the study. The study was not randomized, and there was no concurrent control. Fagher et al[304] conducted a 6-week, randomized placebo-controlled trial in 28 hemodialysis patients, who received either 2 g IV of L-carnitine or placebo after each hemodialysis session. There was no difference in ejection fraction comparing baseline and post-treatment values and no difference between L-carnitine and placebo groups. Furthermore, there was no difference in heart volumes. Although randomized and placebo-controlled, the study was short-term, and the patients included did not have evidence of myocardial dysfunction (mean ejection fraction, 62%).

Table 12. Studies Evaluating the Effect of L-Carnitine Administration on Dialysis-Related Symptoms

Study Reference	Route	Dose and Duration of Treatment
Fagher et al[308]	IV	2 g after dialysis for 6 wk
Sohn et al[277]	IV	1-1.5 g after dialysis for 2 mo
Ahmad et al[305]	IV	20 mg/kg after dialysis for 6 mo
Sakurauchi et al[306]	PO	0.5 g/d for 3 mo
Casciani et al[307]	PO	1 g/d for 2 mo
Bellinghieri et al[276]	PO	2 g/d for 2 mo
Sloan et al[309]	PO	1 g before, 1 g after dialysis for 6 mo

As part of a multicenter, long-term (6 months), double-blind, placebo-controlled randomized clinical trial of 82 maintenance hemodialysis patients (see below),[272] Holter monitoring was performed during a single dialysis period during the baseline (nontreatment) period, during the treatment period, and at the end of the treatment phase. Individual data were not available for review, but the authors noted that there were very few arrythmias at baseline in their study subjects, and no significant change in dialysis-associated arrhythmias was observed.

Malaise, asthenia, muscle cramps, weakness, and fatigue. Seven studies reported the effects of L-carnitine on either postdialysis fatigue,[276,305-308] muscle weakness,[306] muscle cramps,[277] or well-being.[277,309] Only the study reported by Sloan et al[309] included a well-accepted scale of health-related quality of life (the Medical Outcomes Study Short Form-36 instrument). The duration of treatment ranged from 2 to 6 months. The dose and route of delivery was widely variable, making comparison across studies difficult (Table 12).

In a double-blind, randomized, placebo-controlled study, Ahmad et al[305] showed significant improvement over time in postdialysis asthenia in both L-carnitine–and placebo-treated patients; there was no significant difference in the response to treatment between the groups. However, it was only among the L-carnitine–treated patients that the authors found a significant reduction in intradialytic muscle cramps and hypotension. Sakurauchi et al[306] reported that symptoms of fatigue were reduced in 14 of 21 patients, and

muscle weakness improved in 14 of 24 patients ($P < 0.05$) after 3 months of L-carnitine treatment. There was no control group, and the methods of symptom assessment were neither adequately described nor validated. Sohn et al[277] reported significant improvements in muscle cramps and sense of well-being comparing L-carnitine to placebo in 30 hemodialysis patients, although their methods of assessment were likewise not described. Casciani et al[307] performed an 18-patient, nonrandomized cross-over study, and showed a significant improvement in asthenia after 2 months of L-carnitine administration, regardless of the order of drug administration. Bellinghieri et al[276] evaluated muscle fatigability immediately postdialysis and during the interdialytic interval. They showed that postdialysis asthenia was markedly reduced as early as 15 days after commencing L-carnitine therapy, whereas intradialytic asthenia was only improved after 30 days of treatment. When L-carnitine was stopped, asthenia resumed within 15 to 30 days.[276] By contrast, Fagher et al[308] found no subjective improvement in fatigue in 14 patients treated with L-carnitine for 6 weeks.

Sloan et al[309] provided oral L-carnitine (1 g before and 1 g after each dialysis treatment) to 101 maintenance hemodialysis patients and evaluated their health-related quality of life with the SF-36. In this study, oral L-carnitine had a perceived positive effect on the SF-36 general health ($P < 0.02$) and physical function ($P < 0.03$) subscales, although the effects were not sustained after 6 months of treatment.

In summary, although most studies of ''subjective'' symptoms suggest a beneficial effect of L-carnitine supplementation for maintenance dialysis patients, the Work Group concluded that the heterogeneity of study design, and the difficulty in measuring these and related symptoms in an unbiased manner render the available evidence in this area inconclusive. Nevertheless, several members of the Work Group felt that a short-term trial of L-carnitine was reasonable in selected patients with these symptoms who are unresponsive to other therapies, in light of its favorable side effect profile, lack of alternative effective therapies, and the findings from some studies of improvement in these symptoms with L-carnitine therapy.

Exercise capacity. Correction of anemia, hyperparathyroidism, and 1, 25-OH vitamin D3 deficiency and provision of adequate dialysis do not fully restore muscle function and exercise capacity in ESRD patients. Carnitine is abundant in skeletal muscle, and muscle carnitine content has been reported to decrease with dialysis vintage.[277] Therefore, provision of L-carnitine might help to restore muscle mass and function. Five studies describing various aspects of physical activity were reviewed in detail. Physical activity was assessed by a patient activity score,[310] exercise time, maximal oxygen consumption and mid arm muscle area,[305] a measurement of maximum strength,[308] exercise workload,[308] and subjective muscle strength.[280]

The duration of treatment ranged from 1 to 6 months. L-carnitine was administered either IV at the end of each dialysis session, 2 g for 6 weeks[307] or 6 months,[311] 20 mg/kg for 6 months,[305] or PO 0.9 g/d for 2 months[298] and 3 g/d for 30 days.[280]

Each study assessed physical activity in a different manner. Siami et al[310] observed a trend ($P = 0.07$) toward improvement in subjective physical activity (on a scale from 1 [normal] to 5 [total incapacity]) after dosing L-carnitine, 2 g IV after dialysis for 6 months. Ahmad et al[305] reported a significant increase in mid-arm muscle area ($P = 0.05$) in carnitine-treated patients and no change in placebo-treated patients. In the L-carnitine–treated patients, there was a significant increase in the maximal oxygen consumption (mean increase, 111 mL/min; $P < 0.03$) and a trend toward increased exercise time. Fagher et al[308] observed an improvement in maximum muscular strength from baseline ($P < 0.01$) only in the group receiving L-carnitine 2 g IV after dialysis for 6 weeks, although there was no significant difference between treatment and placebo arms in this study. Mioli et al[298] reported an increase in maximum work load after 45 days of oral L-carnitine administration that was sustained after 60 days of treatment ($P < 0.05$). Finally, Albertazzi[311] reported a subjective improvement in physical activity (not quantified) in 10 patients receiving 3 g L-carnitine PO per day for 30 days and no change in 10 control subjects.

In summary, as with the more subjective symptoms of malaise, asthenia, muscle cramps, weakness and fatigue, there is inconclusive evidence

regarding the role of L-carnitine supplementation on muscle function in ESRD. Although most of the published studies suggest a modest beneficial effect, relatively few studies are well-controlled, the methods of assessment are not validated, and assessment may be insensitive to important changes induced by a variety of therapies, including L-carnitine itself. The Work Group members were also concerned about the effect of publication bias on the available medical literature. In other words, it might be less likely for investigators to submit studies with a nil effect, and less likely that journal editors would publish such papers. The Work Group agreed that there was insufficient evidence to support the use of L-carnitine to enhance muscle strength or exercise capacity in patients on dialysis. However, the Work Group agreed that a short-term trial of L-carnitine (3 to 4 months) was reasonable in selected patients to enhance muscle strength and exercise capacity, in light of its favorable side effect profile, lack of alternative effective therapies, and benefits shown in several studies. More research is required in this area.

Anemia. It has been proposed that carnitine deficiency might reduce erythrocyte half-life, by adversely influencing the integrity of the erythrocyte membrane. Kooistra et al[312] showed a relation between anemia and erythropoietin requirements and low serum free carnitine levels in dialysis patients. Despite the availability of recombinant erythropoietin and the more liberal use of intravenous iron dextran in recent years, a large proportion of maintenance dialysis patients continue to suffer from anemia or require large doses of erythropoietin to maintain blood hemoglobin concentrations within the recommended range. Epidemiologic studies have consistently shown a mortality advantage among patients with hematocrits in the 30% to 36% range, and the NKF-DOQI Work Group on Anemia Management recommended a target hematocrit of 33% to 36% based on the expert panels' detailed literature review.

Ten studies involving carnitine and anemia were reviewed in detail. Four studies[272,314-316] (36 patients total) compared hemoglobin or hematocrit at baseline and after about 2 months of L-carnitine treatment (three studies using oral L-carnitine and one study using a combination of oral and intravenous L-carnitine). A fifth study[292] was a nonrandomized trial in which 12 patients were treated with oral L-carnitine (1 g per day) and 11 patients were dialyzed against a bath supplemented with L-carnitine (concentration, ~100 μmol/L) for 6 months. Although three of the five studies showed significant improvement in blood hemoglobin or hematocrit, the Work Group discounted these studies due to flaws in design. A single cross-over study was performed.[276] In only one of the two sequences was there a significant increase in hematocrit. There were 14 patients overall (7 in each sequence). The rather small sample size limited statistical power, and there was no consideration given to blood loss, iron status, or other clinical factors. It is noteworthy that in none of the six studies cited above were the hematologic effects of L-carnitine the primary outcome of interest.

Four randomized, placebo-controlled clinical trials[272,275,315,316] were conducted in which the effect of L-carnitine on hemoglobin concentration or hematocrit was evaluated. In three of the four studies,[272,314,316] treatment of anemia was the primary focus of the work. The total number of patients studied was 109. Nillson-Ehle et al[275] treated 28 patients for 6 weeks with L-carnitine 2 g IV after each dialysis session. There were no significant differences in hemoglobin concentration in either group. No mention was made of serum levels or intake of iron, vitamins, or other factors known to affect management of this condition. In a randomized, placebo-controlled, double-blind trial, Labonia[272] treated 13 patients with L-carnitine 1 g IV after each dialysis session for 6 months and compared the results with 11 patients given a placebo control. Inclusion criteria included a stable dialysis regimen, ''normal'' iron status, ''usual'' treatment with folic acid and vitamin B12, and the absence of ''severe'' hyperparathyroidism. In each patient, efforts were made to periodically reduce the dose of erythropoietin, but any reduction in the erythropoietin dose was maintained only if the hematocrit did not decrease. The target hematocrit was 28% to 33% throughout the study, and a protocol for erythropoietin dosing was established. There were defined, accepted criteria for the provision of iron supplements. The hematocrit remained stable in the L-carnitine–treated group, but dropped slightly (and significantly) in the placebo group (mean, 29.5% to 27.9%; $P < 0.05$).

The erythropoietin dose requirements were reduced by 38% in the L-carnitine–treated patients and unchanged in the placebo-treated group. Roughly the same proportion of patients received iron during the course of the study, although the ferritin concentration (a marker of iron stores and of inflammation) was higher on average in the placebo group. There were no changes in endogenous erythropoietin or in erythrocyte osmotic fragility; thus, there was not a clear mechanism for what appeared to be a large clinical effect.

Trovato et al[315] showed even more dramatic results in a placebo-controlled randomized study conducted before the availability of erythropoietin. In the control group, the mean hematocrit was 24.0% at baseline and dropped to 21.8% after 12 months. In the L-carnitine group, the mean hematocrit was 25.5% and increased to 37.4% after 12 months. All patients received folic acid, vitamin B12, and sodium ferrigluconate at the end of each dialysis session.

Finally, Caruso et al[316] led a placebo-controlled randomized clinical trial in 31 hemodialysis patients, looking at erythropoietin dose and hematocrit. Patients received 1 g of L-carnitine IV after each dialysis session. The overall study results showed no significant effect of L-carnitine. When examining the subgroup of patients older than 65 years of age ($n = 21$), there were significant increases in hematocrit (mean, 32.8% versus 28.1%) and lowering of the erythropoietin dose (mean, 92.8 versus 141.3 U/kg) in the L-carnitine–treated patients compared with placebo-treated controls. It is worth noting that the Trovato et al[315] and Caruso et al[316] studies both employed per protocol analyses, compared with the more conventional ''intent to treat'' methods.

Some members of the Work Group felt that an empiric trial of oral or intravenous L-carnitine ($\sim$1 g after dialysis) was reasonable in selected patients with anemia and/or very large erythropoietin requirements. A 4-month trial was considered to be of sufficient length to reliably assess the response to L-carnitine.

D. REFERENCES (ADULT GUIDELINES)

Note: Asterisks indicate the citations that were used in the structured review of the literature.

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E. Index of Equations and Tables (Adult Guidelines)

Abbreviations: HD, hemodialysis; Kt/V, measure of dialysis where K is the membrane clearance, t is the time on dialysis, and V is the volume of urea distribution; CPD, chronic peritoneal dialysis; PNA, protein equivalent of total nitrogen appearance; GFR, glomerular filtration rate.

II. PEDIATRIC GUIDELINES

GUIDELINE 1

Patient Evaluation of Protein-Energy Nutritional Status

The most valid measures of protein and energy nutrition status in children treated with maintenance dialysis include: *(Evidence and Opinion)*

- Dietary interview/diary *(Opinion)*
- Serum Albumin *(Opinion)*
- Height or length *(Evidence and Opinion)*
- Estimated dry weight *(Evidence and Opinion*)
- Weight/Height Index *(Opinion)*
- Mid-arm circumference and muscle circumference or area *(Opinion)*
- Skinfold thickness *(Opinion)*
- Head circumference (3 years or less) *(Evidence and Opinion)*
- Standard deviation score (SDS or Z score) for height *(Evidence and Opinion)*

RATIONALE

Assessment of the nutritional status of children receiving MD utilizes standard techniques from both normal children and adult dialysis populations. Monitoring energy and protein status in dialysis patients requires multiple indices measured concurrently and evaluated collectively. No single measure has been proven to provide a complete picture of protein-energy status in children treated with dialysis. The role of serum albumin is described in Guideline 1 of the adult guidelines. Growth parameters are a fundamental component and must be measured according to standardized protocols with consistent equipment and are preferably performed by the same person.[14]

The following parameters are directly measured: recumbent length, height, weight, head circumference, mid-arm circumference (MAC), and skinfold thickness. Formulas for calculating mid-arm muscle circumference (MAMC) and area and standard deviation scores (SDS) for height are included in Appendix I, along with tables of normal values. The Work Group was unable to agree on the optimum frequency for calculating SDS scores for weight. However, tables for calculating such scores are provided in Appendix I.

Dietary intake data provide a quantitative and qualitative analysis of the nutrient content of the diet. There are several limitations to using dietary recalls and diaries to assess protein and/or energy intake; however, they are the only component of the nutrition assessment by which actual nutrient intake can be evaluated. The validity and reliability of the diet information obtained from the patient depends on the accuracy of the nutrient intake data and the extent to which it represents typical eating patterns. Registered Dietitians (RDs) are skilled and well trained in obtaining dietary information and are able to educate patients on providing an accurate record of their food intake. The nutrient intake data is calculated for amounts of macronutrients and

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micronutrients and then used to develop or evaluate compliance with the diet prescription.

The most common methods for obtaining dietary intake data are the 24-hour dietary recall and the 3-day food record. An advantage of the recall method is that the respondent (child or family member) will not have the opportunity to deliberately modify his or her usual food behavior. Disadvantages include the potential for inability to remember details and quantities of foods, and the day in question may not represent typical intake. Food intake records are written reports of foods eaten during a specified length of time, typically 3 days. Records kept for more than 3 days increase the likelihood of inaccurate reporting. Inclusion of 1 weekend day is recommended. Food records must be very detailed, especially with regard to quantities of foods, to increase their validity. They are more time-consuming for both the patient and dietitian, but provide a more accurate assessment of dietary intake than the 24-hour recall.

The dietary interview should be conducted with the patient and/or primary caretaker by an experienced RD to obtain the following information: dietary intake data; presence or absence of nausea, vomiting, diarrhea, or constipation; consumption of non-food items such as paper or dirt; compliance with medication intake; eating patterns (availability and consumption) at school, home, and daycare; who prepares food for the family; facilities for food preparation; presence of economic resources for food purchasing; frequency of eating away from home (fast food, other restaurants); previous diet restrictions; change in appetite or the taste of food; mouth pain or difficulty swallowing; physical eating skills; and activity level. The information from the food recall or diary can be quantified for calorie and protein levels. The condition of the hair, nails, skin, tongue, teeth, and breath may give additional information about the patient's nutritional status.[14] Children on dialysis require nutrition evaluation by a renal dietitian with skills in age-appropriate data collection and interpretation, counseling, monitoring, and modifying treatment goals on a regular basis.

Each child must be evaluated individually with regard to the degree to which serum albumin reflects nutritional status. Many factors affect serum albumin levels, including decreased synthesis secondary to inflammation, infection, malnutrition, acidosis, hormonal influences, and liver disease; increased losses due to peritoneal losses, persistent proteinuria, and blood loss; and altered distribution secondary to overhydration.[15] Albumin used as blood pressure support during HD or in the treatment of nephrotic syndrome may falsely raise albumin levels.

A number of other measures to assess nutritional status were considered by the Work Group, including pre-albumin, body mass index (BMI), protein equivalent of total nitrogen appearance (PNA), alpha-1-acid glycoprotein (α1-AG), IGF-I, and dual energy x-ray absorptiometry (DXA). The reasons for not accepting these as valid measures of assessment at this time fell into the following categories: (1) lack of information on interpretation in renal disease; (2) inadequate standardization in children; (3) not responsive to the fluid compartment changes of growing children; and/or (4) impractical for clinical practice (eg, expensive facilities required, extensive expertise required to interpret, or substantial patient cooperation required). Normal values for BMI (weight in kilograms divided by height in meters squared) in children are to be included in new growth charts set to be released in 2001, or later, and may be recommended for inclusion in a standard nutrition assessment at that time.

Reasons for assessing protein and energy status more frequently include:

- Dietary interview in MD patients that identifies warning flags such as persistent decreased appetite; increase in nausea or vomiting; or change in social structure (eg, new baby or divorce with shared custody) or economic status.
- Decrease in estimated dry weight or weight for height secondary to known (infection, surgery) or unknown reasons.

The expected result would be implementation of a plan to achieve or surpass recommended levels of protein and energy using foods normally consumed or nutritional supplements.

RECOMMENDATIONS FOR RESEARCH

1. Investigation in the following areas to standardize interpretation in children with renal disease:

- PNA
- Subjective Global Assessment (SGA) for pediatric patients
- Prealbumin

GUIDELINE 2

Management of Acid-Base Status

Because acidemia exerts a detrimental effect on growth and nutritional status, serum bicarbonate levels below 22 mmol/L should be corrected with oral administration of alkali therapy and/or the use of higher sodium bicarbonate dialysate solution in patients treated with maintenance hemodialysis. *(Evidence and Opinion)*

RATIONALE

Metabolic acidosis (total venous carbon dioxide content less than 20 mmol/L) was encountered in one half of children 5 to 17 years of age who were treated with MHD. In only 50% of these patients was acidosis corrected after an HD treatment.[16] Patients treated with peritoneal dialysis have more normal serum bicarbonate levels than do patients receiving chronic HD.[17] Acidosis may play a significant role in the continuing growth retardation in children with end-stage renal disease (ESRD), despite the appropriate use of vitamin D metabolites to reverse secondary hyperparathyroidism.

The beneficial effect of correction of acidosis on growth retardation was initially described in children with renal tubular acidosis and normal renal function.[18] Such results have been extrapolated to patients with ESRD. However, there are no published data that specifically address the effects of acidosis on growth in MD patients. Blunted GH response to a standard clonidine stimulus has been demonstrated in children with renal tubular acidosis. The often-profound growth failure seen in these patients has been thought to be secondary to inhibition of GH secretion or expression in the presence of chronic metabolic acidosis. In addition, the degree of acidosis has a significant influence on proteolysis in human volunteers and experimental animals.[19,20]

Recent experimental data support the contention that the growth retardation of acidosis is related to the primary effect of acidosis on the GH/IGF axis, primarily by altering the pattern of GH secretion.[21] Metabolic acidosis not only reduces pulsatile pituitary secretion of GH, but also decreases hepatic GH-receptor mRNA and IGF-I mRNA. In addition, acidosis directly reduces IGF-I expression in chondrocytes of the growth plate of the long bone in experimental animals.

In acidotic uremic animals, depressed serum IGF-I levels returned to normal with sodium bicarbonate correction of the uremic acidosis. Significantly, the food intake did not differ between the uremic nonacidotic and the uremic acidotic group.[22] These multiorgan effects of metabolic acidosis may explain the growth failure observed in children who are acidotic, including those receiving MD.

It is recommended, therefore, that serum bicarbonate levels below 22 mmol/L be corrected in all children treated with MD. The use of high sodium

bicarbonate concentrations in dialysate as well as oral administration of sodium citrate or sodium bicarbonate to maintain steady-state serum bicarbonate levels should be individualized. Attention should be paid to the potential concomitant use of aluminum containing antacids and sodium citrate, because citrate salts enhance intestinal absorption of aluminum and thus the risk of aluminum intoxication.

RECOMMENDATIONS FOR RESEARCH

1. Studies are needed to delineate the role of acidosis on growth retardation in the setting of ESRD in children.

2. Whether or not correction of acidosis may improve the poor response to recombinant human GH in pediatric patients treated with MD needs to be elucidated.

GUIDELINE 3

Urea Kinetic Modeling

Urea kinetic modeling may have a role in the nutritional assessment and management of children treated with maintenance dialysis. Although PNA is useful to assess and follow nutritional status in adults, there is currently insufficient evidence to recommend its routine use in pediatric patients. ***(Evidence and Opinion)***

RATIONALE

Urea kinetic modeling is an important tool in the measurement of dialysis delivery and, therefore, for the assessment of dialysis adequacy.[23] However, there are limited data that clearly and definitively correlate PNA (or protein catabolic rate [PCR]) to dietary intake and to nutritional outcomes in children receiving MD.

A correlation between measured net PNA and the combination of urea generation rate and body weight has been demonstrated in children treated with HD.[24] In a prospective study on two children undergoing HD, kinetically determined PNA increased from 0.8 to 1.1 g/kg/d when protein and energy intake were increased in one subject, with a consequent 78% increase in nitrogen balance. The second child was given additional nonprotein calories, and the kinetically derived PNA decreased from 1.22 to 0.81 g/kg/d, with a 257% increase in nitrogen balance.[25]

A correlation has also been shown between protein balance (dietary protein intake [DPI] from diet diaries minus the kinetically derived PNA) and energy intake in children treated with maintenance hemodialysis (MHD).[26] PNA alone did not correlate with either protein intake or energy intake for the group as a whole. When subdivided by nitrogen balance, a correlation with PNA did exist. Children in positive nitrogen balance had lower PNAs than did children in negative nitrogen balance.[26] However, 10 of the 43 balance periods had PNA values not anticipated by the children's protein and energy intake. Knowledge of either PNA or protein intake alone was felt to be insufficient to predict the protein balance of children.[26] Recently, the combination of increased dialysis and adequate nutrition have been shown to have a beneficial effect on growth in children undergoing MHD.[27] Moreover, the characteristics of peritoneal solute transport may play a role in growth and nutritional status in children treated with MD.[28]

Studies performed in seven children on automated peritoneal dialysis showed no correlation between Kt/V and DPI or between normalized PNA (nPNA) and DPI. There was a correlation between Kt/V and energy intake.[29] An additional study was performed in 12 children undergoing continuous ambulatory peritoneal dialysis (CAPD) and eight children undergoing continu-

ous cyclic peritoneal dialysis (CCPD). DPI was reported to be higher in the children treated with CCPD. The two groups had equal weekly total creatinine clearances (57 L/wk/1.73 m^2), but the children treated with CCPD had a mean weekly total Kt/V urea that was greater than those on CAPD (2.45 versus 1.75).[30]

Despite the information provided in these studies, there is insufficient evidence at this time to recommend the routine determination of PNA (nPNA) as a means of nutritional assessment in children.

RECOMMENDATIONS FOR RESEARCH

1. Appropriate correlations between calculated and measured data need to be established. The impact of the PNA on growth needs to be better defined, and the need to normalize the data to some measure of body size must be assessed. Longitudinal data of PNA, along with dietary protein and energy intake, must be collected and correlated against accepted parameters of growth and nutritional status.

2. There is a need for the development of a validated formula to calculate V in children treated with peritoneal dialysis. The reported studies described above calculated the urea volume of distribution based on formulas developed in normal children. It is not clear whether children with renal failure and on peritoneal dialysis are characterized by the same formula.

3. Assess the ability of a kinetic model of solute removal for children treated with CAPD and automated peritoneal dialysis to accurately reflect the nutritional status of these patients and establish a valid model for children treated with all forms of peritoneal dialysis. The relationship between weekly creatinine clearance and weekly Kt/V for children treated with CAPD is not the same as that for children treated with automated peritoneal dialysis. Correlations may differ between modalities.

GUIDELINE 4

Interval Measurements

Scheduled, interval measurements of growth and nutrition parameters should be obtained to provide optimal care of the nutritional needs of children on maintenance peritoneal dialysis or hemodialysis. *(Evidence and Opinion)*

RATIONALE

Dialysis and nutrition prescriptions are based on objective and subjective measures that determine how well the child is growing and developing. To optimize the care of children treated with MD, a series of parameters associated with nutritional adequacy have been defined by the Work Group (Table 1). The recommended intervals are minimum ones, and the clinician is encouraged to obtain them more frequently if it is felt that the patient may benefit. Infants in particular may need very close follow-up (every 1 to 2 weeks initially) to monitor adequacy of the diet prescription, feeding tolerance, and growth parameters.[31,32]

RECOMMENDATIONS FOR RESEARCH

1. The use of bioelectrical impedance (BIA) and DXA technologies to measure body composition should be explored.

2. The measurement of IGF-I or IGF-binding protein levels to reflect nutritional adequacy should be explored.

3. The value of using a selective dietary interview/diary and the use of nPNA to assess DPI should be determined.

Table 1. Nutritional Parameters and Appropriate Minimum Schedule of Testing or Measurement for Patients Treated With HD and PD

	Minimum Interval	
Parameter	Below 2 y	2 y and Over
Length	Monthly	Not applicable*†
Standing height	Not applicable	3-4 mo
Head circumference	Monthly	3-4 mo until age 36 mo†
Estimated dry weight	Monthly	3-4 mo*†
Weight/height index	Monthly	3-4 mo†
Z score or SDS height for chronologic age	Monthly	3-4 mo†
Serum albumin	Monthly	Monthly†
Serum bicarbonate	Monthly	Monthly*†
Skinfold thickness	No agreement	3-4 mo†
Midarm muscle circumference, area	3-4 mo	3-4 mo†
Dietary interview	Monthly	3-4 mo†
Urea kinetic modeling	3-4 mo	3-4 mo†

*Evidence.
†Opinion.

GUIDELINE 5

Energy Intake for Children Treated With Maintenance Dialysis

The initial prescribed energy intake for children treated with maintenance hemodialysis or peritoneal dialysis should be at the Recommended Dietary Allowance (RDA) level for chronological age. Modifications should then be made depending upon the child's response. ***(Evidence and Opinion)***

RATIONALE

The Recommended Dietary Allowance (RDA) for energy intake in children[33] is a guide based on extrapolated data (Table 2). These allowances have been designed so that children who receive that quantity of calories are highly unlikely to be calorie deficient. RDAs are meant to be applied to children as a group, rather than to the individual child, and therefore include a wide margin of safety. The American Academy of Pediatrics' Committee on Nutrition states that RDAs cannot be used as a measure of nutritional adequacy in children.[34]

There is no consistent evidence that daily energy intake for children treated with MD should exceed the RDA for age, at least initially. Children who demonstrate energy malnutrition, however, will require ''catch-up'' energy supplementation to achieve the RDA or higher. The Pediatric Nutrition Handbook of the American Academy of Pediatrics suggests a formula for such energy supplementation that is based on the child's weight age.[34] There are no data to support this approach in children with CRF, and it is recommended that such supplementation be based on the child's chronological age and adjusted according to his or her response.

The calories derived from the dialysate glucose concentration should be included to the total dietary calorie intake in those patients treated with peritoneal dialysis. The peritoneal dialysate glucose absorption will increase the total calorie intake by 7 to 10 kcal/kg.[35,36] Energy recommendations based on height age should be used as the basis for energy intake goals only if the patient does not gain weight appropriately with consistent caloric intake at the RDA for chronological age.

Energy supplementation exceeding the RDA for age has been administered to stable children treated with dialysis, but there are no data that demonstrate a consistent improvement in growth velocity. Assessment of growth has been routinely utilized as the outcome for energy supplementation in the published studies.[37,38] In the absence of malnutrition, energy supplementation has demonstrated no other benefits in outcomes such as increased albumin levels, decreased morbidity, or decreased mortality. Attention to adequate amounts of non-protein calories is impor-

Table 2. Estimated Energy Allowances for Children and Infants

	Age (y)	kcal/kg/d
Infants	0-0.5	108
	0.5-1	98
Children	1-3	102
	4-6	90
	7-10	70
Males	11-14	55
	15-18	45
	18-21	40*
Females	11-14	47
	15-18	40
	18-21	38*

*Based on Recommended Dietary Allowances and increased physical activity.

tant for protein-sparing effects. A retrospective analysis of 31 children treated with dialysis (16 HD and 15 peritoneal dialysis), using multiple linear regression analysis, demonstrated that the growth velocity standard deviation scores correlated positively with caloric intake and negatively with protein intake.[39] The regressions suggested a greater impact for suboptimal calories than for excess protein. It is expected that ongoing monitoring will result in adjustment of calorie levels upward or downward as necessary.

Energy requirements for children have also been established based on age and height and reported as kcal/cm/d.[34] This measure was used in a small study of children treated with MHD,[26] which suggests that height may be a better standard than age for practical reasons: because height does not fluctuate from dialysis to dialysis, it is independent of fluctuations in total body water and/or body fat; and, because children with advanced renal failure are often stunted, it may be more appropriate to compare such children with others of the same height age.[35] Sufficient normative data are not available to support the use of a height standard for energy prescriptions.

Many events may necessitate the admission of a child on MD to the hospital. A clearly definable severity scale of illness in a child on MD is not available and neither is there a body of data concerning nutrition needs in such children. It is recognized that it is not always medically indicated or necessary to deliver full nutrition to a patient in the first few days of hospitalization. Accordingly, it is recommended that as soon as it is medically appropriate to initiate nutrition in a hospitalized child, the nutrition provided should at least equal that prescribed for the child when he or she is an outpatient.

RECOMMENDATIONS FOR RESEARCH

1. Given the lack of specificity of the RDA for calories, and the fact that the RDA was devised to apply to a population of normal children, clearer data on the actual energy expenditure of children treated with dialysis are necessary. Indirect calorimetry can be utilized and resting energy and basal energy expenditure can be measured and compared with the RDA. The impact of the dialysis process on the children's energy expenditure should be assessed in this patient population. The availability of such information would allow a more appropriate initial diet prescription for such patients.

2. Prospective interventional trials should be designed to better understand the impact of various energy intakes on growth and nutritional status.

GUIDELINE 6

Protein Intake for Children Treated With Maintenance Dialysis

Children treated with maintenance hemodialysis should have their initial dietary protein intake based on the Recommended Dietary Allowances for chronological age and an additional increment of 0.4 g/kg/d. ***(Evidence and Opinion)***

Children treated with maintenance peritoneal dialysis should have their initial dietary protein intake based on the Recommended Dietary Allowances for their chronological age plus an additional increment based on anticipated peritoneal losses. ***(Evidence and Opinion)***

RATIONALE

Limited data are available to demonstrate the optimal amount of protein for dialysis-dependent children. Patients undergoing chronic HD should be prescribed the RDA for age plus an increment of 0.4 g/kg/d to consistently achieve a positive nitrogen balance (Table 3).[40] This recommendation is based on studies performed in adult patients on MHD who demonstrated the presence of malnutrition when they received 0.75 g/kg/d and in whom the ingestion of 1.1 g/kg/d of protein of high biological value was not adequate to maintain nitrogen balance.[41] Moreover, the use of dietary protein restriction has lead to poor growth in children undergoing HD.[37] There are no data, however, that demonstrate any advantage of protein supplemented at a rate above the combination of the RDA and the assumed dialysate losses with regard to growth rate or other measures of nutritional status.

The DPI is higher for patients treated with peritoneal dialysis than for those on HD because there is constant loss of protein and amino acids through the peritoneal membrane (Table 3).[35,36,42,43] The recommendations for daily protein intake in children undergoing chronic maintenance peritoneal dialysis are based on expert opinion. These recommendations were derived somewhat empirically in 1982[44] based on older

Table 3. Recommended Dietary Protein for Children on Maintenance Dialysis

	Age (y)	RDA*	Protein Intake* for HD	Protein Intake* for PD
Infants	0-0.5	2.2	2.6	2.9-3.0
	0.6-1.0	1.6	2.0	2.3-2.4
Children	1-3	1.2	1.6	1.9-2.0
	4-6	1.2	1.6	1.9-2.0
	7-10	1.0	1.4	1.7-1.8
Males	11-14	1.0	1.4	1.7-1.8
	15-18	0.9	1.3	1.4-1.5†
	19-21	0.8	1.2	1.3†
Females	11-14	1.0	1.4	1.7-1.8
	15-18	0.8	1.2	1.4-1.5†
	19-21	0.8	1.2	1.3†

*Values are expressed in grams of protein per kilogram per day.

†Based on growth potential.

RDA recommendations,[33] dialysate protein losses,[35,36,42] and nitrogen balance studies performed in adult patients treated with CAPD.[45] The Work Group could find no studies to suggest any basis other than the RDA. The supplemental factor for replacement of transperitoneal loss is based on clinical data.[35,36,42] These data suggest that protein loss is inversely related to age and size, so that smaller and, therefore, younger children have proportionately higher losses. An initial diet prescription at the higher end of the recommendation for infants and toddlers and the lower end for older children and adolescents would be appropriate. Given the wide variability in transperitoneal protein losses in children, careful monitoring and appropriate adjustments in diet prescription are mandatory.

It should be noted that the recommended ranges are for children at the initiation of dialysis. Follow-up evaluations and routine measures of protein and calorie nutritional status as recommended in other guidelines within this document may necessitate adjustments.

RECOMMENDATIONS FOR RESEARCH

1. What is the optimal DPI for a child on HD or peritoneal dialysis?
2. What is the optimal ratio of protein to non-protein calories?
3. How can the impact of interventions on protein intake best be monitored?

GUIDELINE 7

Vitamin and Mineral Requirements

The recommended dietary intake should achieve 100% of the Dietary Reference Intakes for thiamin (B_1), riboflavin (B_2), pyridoxine (B_6), vitamin B_{12}, and folic acid. An intake of 100% of the Recommended Dietary Allowance should be the goal for vitamins A, C, E, and K, copper, and zinc. *(Evidence and Opinion)*

RATIONALE

Vitamins and minerals are essential for normal growth and development. Studies conducted in the adult dialysis population have provided evidence of low blood concentrations of water-soluble vitamins and minerals because of inadequate intake, increased losses, and increased needs.[46-48]

The Dietary Reference Intakes (DRIs) for a number of nutrients have recently replaced the RDAs and are based on four sources: the RDA, the Tolerable Upper Intake Level, the Estimated Average Requirement, and the Adequate Intake.[49] DRIs are reference values that are quantitative estimates of nutrient intakes used for planning and assessing diets for healthy individuals. It has been proposed that the RDA and average intake may each serve as a further basis for adjusting individual recommendations for patients with special health care needs.[48] In the case of nutrients for which DRIs are not yet developed, the previously published RDAs remain the standard.[33]

No published studies have assessed the blood vitamin levels of children undergoing maintenance peritoneal dialysis or HD in the absence of the use of a vitamin supplement. Therefore, recent practice has been to routinely provide a water-soluble vitamin supplement to children receiving dialysis. Whereas dietary intakes below the DRI have been documented for vitamins B_6 and B_2, the needs for the other water-soluble vitamins are regularly met by dietary intake alone. Consequently, the combination of dietary and supplemental vitamin intake is routinely associated with blood concentrations that meet or exceed normal values.[50-52]

Accordingly, it is recommended that an intake of 100% of the DRI is a reasonable starting point for water-soluble vitamin requirements in children on MD (Table 4). It is also recommended that the nutritional status of water-soluble vitamin be monitored. Supplementation should be considered if the dietary intake alone does not meet or exceed the DRI, if measured blood vitamin levels are below normal values, or if clinical evidence of deficiency is present (eg, low folic acid or vitamin B_{12} levels giving rise to poor responsiveness to recombinant human erythropoietin).

Table 4. Dietary Reference Intakes for Children and Adolescents[49]

Category	Thiamin (mg)	Riboflavin (mg)	Pyridoxine* (mg)	Folate (µg)	Vitamin B_{12} (µg)
Infants					
0-6 mo	0.2	0.3	0.1	65	0.4
7-12 mo	0.3	0.4	0.3	80	0.5
Children					
1-3 y	0.5	0.5	0.5	150	0.9
4-8 y	0.6	0.6	0.6	200	1.2
Males					
9-13 y	0.9	0.9	1.0	300	1.8
14-18 y	1.2	1.3	1.3	400	2.4
Females					
9-13 y	0.9	0.9	1.0	300	1.8
14-18 y	1.0	1.0	1.2	400	2.4

*Refers to the quantity of free pyroxidone and not pyroxidone hydrochloride.

Table 5. Recommended Dietary Allowances for Children and Adolescents[33]

Category	Vitamin A (µg, RE)	Vitamin E (mg α-TE)	Vitamin K (µg)	Vitamin C (mg)	Zinc (mg)	Copper (mg)
Infants						
0.0-0.5 mo	375	3	5	30	5	0.4-0.6
0.5-1.0 mo	375	4	10	35	5	0.6-0.7
Children						
1-3 y	400	6	15	40	10	0.7-1.0
4-6 y	500	7	20	45	10	1.0-1.5
7-10 y	700	7	30	45	10	1.0-2.0
Males						
11-14 y	1,000	10	45	50	15	1.5-2.5
15-18 y	1,000	10	65	60	15	1.5-2.5
Females						
11-14 y	800	8	45	50	12	1.5-2.5
15-18 y	800	8	55	60	12	1.5-2.5

The blood levels of fat-soluble vitamins A and E are normal or elevated in pediatric patients receiving dialysis despite the lack of excessive dietary intake or vitamin supplementation (Table 5). The loss of clearance of vitamin A metabolites by the normal kidney places dialysis patients at risk for symptoms of hypervitaminosis A. This is an important consideration when selecting a multivitamin that contains a combination of water- and fat-soluble vitamins. Limited data are available on the status of vitamin K in the ESRD population, although it is possible that a child's vitamin K status could be compromised by a poor dietary vitamin K intake, particularly during antibiotic therapy, which suppresses intestinal bacteria that synthesize vitamin K.[53]

A dietary intake below the RDA has been noted for zinc and copper in children receiving peritoneal dialysis.[50] It is recommended that the intake of these minerals be monitored every 4 to 6 months, because supplementation may be required in patients whose dietary intake is particularly low, for those undergoing MD for prolonged periods of time, or for those who demonstrate laboratory or clinical evidence of trace metal deficiency.[34]

RECOMMENDATIONS FOR RESEARCH

1. The vitamin and mineral needs of children undergoing MD should be determined by prospective, longitudinal studies conducted in patients not yet receiving vitamin and mineral supplementation.

GUIDELINE 8

Nutrition Management

Every dialysis patient and appropriate family member (or caretaker) should receive intensive nutrition counseling based on an individualized plan of care, which includes relevant, standardized measurements of growth and physical development, developed prior to or at the time of initiation of maintenance dialysis. ***(Opinion)***

The nutrition plan of care developed during the early phase of maintenance dialysis therapy should be re-evaluated frequently and modified according to progress. The maximum time between such updates is 3 to 4 months. ***(Opinion)***

RATIONALE

The nutrition plan of care synthesizes information obtained from the evaluation of growth and physical development, dietary interview, and other sources listed below. This information is evaluated, and short- and long-term goals are determined, from which the nutrition prescription is developed, which contains specific recommendations for the patient to follow. These recommendations are updated and reinforced frequently. The plan of care is updated at least every 3 to 4 months and is shared with the patient, family, and multidisciplinary team.

Nutrition counseling is performed based on the nutrition prescription. Initiation of MD generally requires modification of dietary nutrient intake from normal to maintain adequate nutrition and optimize growth and development. Such changes in dietary intake may include alteration of phosphorus, sodium, potassium, protein, and fluid in the diet. Diet restrictions for children treated with dialysis should be individualized and minimized as much as possible to optimize nutrient intake.

Nutrition counseling is recommended at the initiation of dialysis (ideally within the first week) and on an ongoing basis, because of the dynamic nature of the child's medical condition and food preferences. Family members and primary caretakers must be involved in the process to enable the patient to have appropriate foods available and to provide support for food and fluid limitations (when appropriate) as well as encouragement for nutrient consumption. Counseling must be targeted at the appropriate education level of the child and family member.

The components evaluated to develop an individualized nutrition plan of care include[14]:

- Assessment and evaluation of growth parameters according to standardized protocols (see Appendix 1)
- Dietary interview (see Guideline 1)
- Estimates of actual nutrient intake for macronutrients (such as energy and protein) from oral and/or enteral feeds
- Comparison of actual intake with estimated needs
- Medical history
- Urine, stool, emesis, and ostomy output
- Medications

- Laboratory values associated with nutrient intake
- Psychosocial status
- Questions regarding consumption of unusual non-food substances such as paper
- Blood pressure
- Fluid balance
- Physical eating skills
- Appearance of hair, tongue, skin, and teeth and smell of breath

Conditions that could dictate a more frequent evaluation of the nutrition plan of care include dry-weight loss, ongoing decrease in oral intake, change in gastrointestinal function, significant change in standard deviation scores (such as a 0.5 standard deviation decrease in SDS for height), elevated or suboptimal laboratory values related to nutrients, ongoing excess interdialytic weight gain, concern for appropriate compliance with recommendations, change in psychosocial situation, or when placement of a tube for feeding is under consideration. In these cases, monthly or more often updates to the care plan may be necessary.

A registered dietitian with renal experience should be a central and integral part of the dietary management. Registered dietitians are proficient in the assessment and ongoing evaluation of the patient's nutrition status and the development of the nutrition plan of care and diet prescription. In addition, the pediatric population requires a registered dietitian skilled in the evaluation of growth as well as physical, developmental, educational, and social needs. At a minimum, registered dietitians should be responsible for assessing the child's nutritional status; developing the nutrition plan of care; providing education and counseling at the appropriate age level for patients, family members, and/or caretakers; monitoring the patient's nutritional status; evaluating adherence to the nutrition prescription; assessing and monitoring adequacy of dialysis; and documentation of these services. Registered dietitians should manage the nutrition care and provide nutrition counseling for patients prior to starting dialysis and for those who have lost a kidney transplant and are returning to dialysis.

Compliance with the nutrition prescription and recommendations from other team members are important at any age, especially in adolescents. Integrating the treatment goals of the dietitian, social worker, child development specialist, nurse, and physician helps to maximize patient and family adherence to the overall plan of care.

RECOMMENDATIONS FOR RESEARCH

1. Would adaptation of an SGA tool specifically for the pediatric population be useful for evaluating nutrition status of children?
2. Studies are needed to evaluate strategies to enhance compliance, with particular emphasis on the adolescent age group.

GUIDELINE 9

Nutritional Supplementation for Children Treated With Maintenance Dialysis

Supplemental nutritional support should be considered when a patient is not growing normally (eg, does not have normal height velocity) or fails to consume the Recommended Dietary Allowances for protein and/or energy. Supplementation by the oral route is preferred followed by enteral tube feeding. *(Evidence and Opinion)*

RATIONALE

Poor oral intake is common in children undergoing chronic dialysis. The reasons behind the inadequate intake are multifactorial. Metabolic derangements and medications may affect taste, appetite, and gastrointestinal function.[15] Abdominal fullness from the peritoneal dialysate solutions may result in the active refusal of food. Gastroesophageal reflux is particularly common in infants and may further impair feeding activity.[54]

During infancy, oral supplementation can be achieved by increasing the caloric density of the formula using modular components of carbohydrate, fat, and protein.[32;55] In older children and adolescents, energy and protein supplementation can be accomplished using modular components or using commercial enteral products in liquid or bar form.

Enteral tube feeding should be considered in those who are unable to meet nutritional goals by the oral route alone. Nasogastric or gastrostomy tube or button and gastrojejunostomy tubes have all been used successfully to provide additional formula or oral supplements by intermittent bolus or continuous infusion. Each has associated advantages and disadvantages.[56-58] The nasogastric tube has been used most frequently in infants and young children, is easily inserted, and is generally well tolerated.[56] The use of this route of therapy is not aesthetically pleasing, however, and is often complicated by recurrent emesis and the need for frequent tube replacement. The gastrostomy tube or button is hidden beneath clothing and can be used within days of placement, even in the patient receiving peritoneal dialysis.[58;59] Reported complications associated with nasogastric and gastrostomy tubes or button feeding include emesis, exit-site infection, leakage, and peritonitis.[60] Gastrojejunostomy feeding should be considered in the child receiving enteral tube feeding when gastroesophageal reflux is severe and not amenable to medical therapy. Surgical repair of gastroesophageal reflux may also be considered in this situation.

A prolonged and potentially difficult transition from tube to oral feeding can occur in infants who use any form of enteral tube feeding.[61;62] Regular non-nutritive sucking and repetitive oral stimulation are recommended for all tube-fed infants. A multidisciplinary feeding team (eg, dietitian, occupational therapist, or behavioral psychologist) may be needed to facilitate the transition from tube to oral feeding.

To date, intraperitoneal nutrition with the use of dialysate solutions substituting amino acids as an alternative to glucose has been evaluated in only a limited number of children receiving peritoneal dialysis and has been used in individual patients for periods of time that do not exceed 6 to 12 months.[63-65] The quantity of amino acids absorbed from the dialysate routinely exceeds the protein lost in the dialysate. Future studies may prove this route of nutritional supplementation to be a valuable adjunct to the oral and enteral routes of therapy.

RECOMMENDATIONS FOR RESEARCH

1. The use of amino acid–based peritoneal dialysis solutions is potentially an attractive means of nutrition support. Studies should be conducted to determine the optimal dialysate amino acid profile and whether the amino acids should be combined with dextrose for better utilization of the protein source. Even with the addition of both dextrose and amino acids to dialysate, the total tolerable osmolality of the dialysate solution prevents the solutions from providing much energy. Thus, the solutions are more effective at providing an adequate amino acid or protein load than a sufficient energy intake.

2. The impact of this therapy on the nutrient intake of patients, solute clearance, and patient growth when used on a long-term basis also requires further study.

GUIDELINE 10

Recommendations for the Use of Recombinant Human Growth Hormone (hGH) for Children Treated With Maintenance Dialysis

Treatment with recombinant hGH in dialysis patients with growth potential should be considered under the following conditions: *(Evidence and Opinion)*

- Children who have (1) a height for chronological age more negative than 2.0 standard deviation scores (SDS) or (2) a height velocity for chronological age SDS more negative than 2.0 SDS, (3) growth potential documented by open epiphyses, and (4) no other contraindication for recombinant hGH use.
- Prior to consideration of the use of recombinant hGH, there should be correction of (1) insufficient intake of energy, protein, and other nutrients, (2) acidosis, (3) hyperphosphatemia (the level of serum phosphorus should be less than 1.5× the upper limit for age), and (4) secondary hyperparathyroidism.

RATIONALE

Serum GH levels are elevated in uremia, yet growth retardation is a frequent accompaniment of chronic renal insufficiency (CRI) in infants, children, and adolescents. An apparent GH-resistant state is thought to result from a combination of reduced GH-receptor expression, especially in the liver, with subsequent decreased IGF-I production and increased IGF-binding protein levels, which reduce the availability of free IGF-I. Because IGF-I is the primary stimulus for the increase in linear growth, it is probable that both reduced hepatic GH-receptor expression and increased IGF-binding protein levels contribute to the GH-resistant state in uremia.[66,67]

Pharmacologic doses of exogenous recombinant hGH (0.05 mg/kg/d; Genentech, South San Francisco, CA; 30 IU/m^2/wk; Kabi-Pharmacia, Stockholm, Sweden) administered subcutaneously improve linear growth in children with CRI[68] and those undergoing peritoneal dialysis[69] or HD during the first year of treatment.[70] However, the magnitude of improvement in linear growth in patients treated with dialysis is not as great as that observed in children with stable CRF.[71,72] Furthermore, the gain in height during subsequent years of recombinant hGH treatment is diminished.[69,70] Therefore, the efficacy of long-term recombinant hGH therapy remains to be established in children receiving MD.

A lack of response to recombinant hGH therapy has been seen with suboptimal energy or protein intakes or in children with metabolic acidemia. Correction of these abnormalities is essential before initiation of recombinant hGH therapy. A serum bicarbonate value below 22 mmol/L requires exogenous alkali therapy (see Guideline 2). An expected effect of recombinant hGH therapy is to increase intact parathyroid hormone (PTH) levels in the first 6 months of therapy.[73] Therefore, to prevent potentially deleterious effects of worsening secondary hyperparathyroidism in children, attempts to control elevated serum PTH levels (intact assay values less than 500 pg/mL; normal range, 10 to 55 pg/mL) is necessary prior to initiation of recombinant hGH

therapy. Additionally, it is suggested that monitoring of intact PTH levels be performed at least every 3 months during the first 6 months of recombinant hGH therapy in these children. Severe hyperphosphatemia also impairs the action of recombinant hGH, and it is important to maximize the control of serum phosphorus levels in these patients prior to initiating treatment with recombinant hGH.

If the patient does not respond to recombinant hGH after 12 months of treatment, discontinuation of recombinant hGH should be considered. A lack of response to recombinant hGH is defined as gain of growth velocity by less than or equal to 2 cm compared with that observed during the previous year. Prior to discontinuation of recombinant hGH therapy, a thorough evaluation of the patient should be undertaken to assure that other causes that contribute to growth retardation in children with CRF have been corrected. Continuation of recombinant hGH at this point would depend on correction of these other factors.

If the patient reaches the 50th percentile for target height following recombinant hGH treatment, it is advisable to discontinue recombinant hGH treatment and monitor the patient. If the height SDS decreases by 0.25 during a subsequent observation period, it is advisable to consider reinstitution of recombinant hGH therapy.

RECOMMENDATIONS FOR RESEARCH

1. Studies are needed to better define the response to recombinant hGH in patients treated with MD, and whether higher doses of recombinant hGH would have a beneficial effect on linear growth remains to be established.

2. Although it is recognized that control of secondary hyperparathyroidism is important prior to the initiation of therapy with recombinant hGH, serum PTH levels increase during therapy with recombinant hGH despite treatment with calcitriol. Thus, further studies should define the appropriate serum PTH levels that correspond to indices of bone remodeling during therapy with calcitriol and recombinant hGH in children treated with MD.

B. APPENDIX (PEDIATRIC GUIDELINES)

Appendix I. Procedures for Measuring Growth Parameters

(Adapted from Pediatric Nutrition Handbook [ed 4]. Committee on Nutrition, American Academy of Pediatrics. Elk Grove Village, IL, American Academy of Pediatrics, 1998, pp 168-174.)

GROWTH PARAMETERS TO BE MEASURED

Recumbent Length

Measured in children up to approximately 24 months of age or in older children who are unable to stand without assistance.

Equipment. Infant stature board with a fixed headboard and a moveable footboard positioned perpendicular to the table surface, and a rule along one side; pen and paper for recording. Two persons are necessary: one to hold the head and another to measure.

Procedure. (1) The infant may be measured in light clothing, without foot coverings. (2) Place the infant on the table, lying on his back. (3) Hold the crown of the infant's head and bring it gently in contact with the fixed headboard. Align the external auditory meatus and the lower margin of the eye orbit perpendicular to the table. (4) While the head remains in contact with the headboard, a second measurer grasps one or both feet at the ankle. (5) Move the footboard close to the infant's feet as the legs are gently straightened. Bring the footboard to rest firmly against the infant's heels, making sure the toes point straight upward and the knees are pressed down on the table. (6) Read the markings on the side of the measuring board and record the value to the nearest 0.1 cm.

Height

Measures the child who is able to stand unassisted.

Equipment. Fixed measuring device attached to a wall (stadiometer); block squared at right angles or moveable head projection attached at right angle to the board; pen and paper for recording.

Procedure. (1) Have the child remove his or her shoes and stand on the floor, facing away from the wall with heels together, back as straight as possible, arms straight down; heels, buttocks, shoulders, and head touching the wall or vertical surface of the measuring device. A family member or other measurer may be necessary to hold the child's ankles and knees steadily in place. The child's axis of vision should be horizontal, with the child looking ahead and the external auditory meatus and lower margin of the orbit aligned horizontally. (2) Place the head projection at the crown of the head. (3) Hold the block steady and have the child step away from the wall. (4) Note the measurement, and record it to the nearest 0.1 cm. (5) Perform three measurements which are within 0.2 cm of each other and use the average of the three for the final value.

Weight Using an Infant Scale

Equipment. Infant scale that allows infant to lay down; pen and paper for recording.

Procedure. (1) Ask the mother to undress the infant. (2) Place a clean paper liner in the tray of the scale. (3) Calibrate the scale to zero. (4) Lay or sit the infant in the tray. (5) Read the weight according to the type of scale. Make sure the infant is unable to touch the wall or surrounding furniture. (6) Record the weight to the nearest 0.1 kg.

Standing Weight

Equipment. Scale; pen and paper for recording.

Procedure. (1) The child should be weighed in light clothing without footwear. (2) Assist the child onto the platform of the scale. (3) Calibrate the scale to zero. (4) Instruct the child to stand in the center of the platform with feet flat and heels touching, as erect as possible. (5) If using a beam scale, adjust the beam of the scale with the main and fractional poise as necessary until the beam swings freely and comes to rest parallel to the scale platform. Activate the digital scale, if this is the scale used. (6) Read the measurement from the scale, looking squarely at the increments rather than from an angle. (7) Record the weight to the nearest 0.1 kg.

Head Circumference

Measured in children up to 36 months of age.

Equipment. Firm, nonstretchable measuring tape; pen and paper for recording.

Procedure. (1) Have the person assisting hold the infant so that the head is upright. (2) Locate the occipital bone at the back of the head, also

the supra-orbital ridges. (3) Apply the tape firmly around the head just above the supra-orbital ridges at the same level on both sides to the occiput. Move the tape up or down slightly to obtain the maximum circumference. The tape should have sufficient tension to press the hair against the skull. (4) Record the measurement to the nearest 0.1 cm.

Mid-Arm Circumference

NOTE: The tables of normal values for MAC and triceps skinfold (TSF) use the right arm. The nondominant arm or arm without hemodialysis access can also be used. Consistent use of the same arm is the most critical factor.

Equipment. Firm, nonstretchable measuring tape; pen and paper for recording.

Procedure. (1) Position at the time of measurement: The mother or substitute sits comfortably on a chair. The child is held, facing forward, by the mother on her lap. The child's right hand is grasped gently but firmly by the mother's hand and placed on the child's hip so that the child's elbow is flexed at about a right angle. Older children who are cooperative need not be held. (2) Briefly explain the purpose of the measurement. (3) Have the mother or substitute bare the child's arm and shoulder. (4) Sit or stand so that the child's arm is relaxed with the elbow point and shoulder facing the measurer. (5) Place the zero end of the measuring tape at the acromium process of the scapula of the arm being measured. Measure to the olecrenon (elbow tip) and note the midpoint. Place a pen mark at the midpoint. (6) Measure around the arm at the level of the mark, with firm and uniform contact with the skin surface. Do not compress the soft tissue of the area. (7) Read the value on the tape and record to the nearest 0.1 cm.

Triceps Skinfold Thickness

Equipment. Lange or other skinfold caliper; firm, nonstretchable measuring tape; pen and paper for recording.

Procedure. (1) Briefly explain the purpose of this measurement. Demonstrate how the caliper is used by applying the jaws to your finger, mother's finger, or the child's finger if possible. (2) This measurement directly follows the MAC measurement. The positioning is the same. (3) Align a long pencil or equivalent directly up the back of the upper arm from the elbow point. Mark along this line at the region of the MAC mark previously made. The two lines should cross at a right angle. (4) The child's arm should be relaxed and hanging at his side. Gently but firmly grasp the fold of skin and subcutaneous adipose tissue approximately 0.1 cm above the point at which the skin is marked, with the skinfold parallel to the long axis of the upper arm. Do not pinch underlying muscle, only the skin. (5) Lift the fatfold enough to clear it from underlying tissue felt deeply with your fingertips. Flex the child's arm to make sure the muscle tissue is not being pinched. (6) Depress the lever of the calipers gently so that the jaws separate. Apply the jaws just below the pinch to the part of the fatfold at the midpoint (defined in number 3) at the same depth as the pinch but about 1 cm down the arm. The jaws should be perpendicular to the length of the fold. (7) Remove the caliper, keeping the left thumb and index finger in position. (8) Repeat the procedure two more times, or until 3 measurements agree within 0.2 mm; record to the nearest 0.1 mm.

EVALUATION OF MEASUREMENTS

Evaluation of these measurements is done by determining percentiles and comparing them with values from healthy children of the same chronological age and sex, because there are no separate agreed-on standards for growth in children on MD at this time. Standardized growth charts[74] and normal tables[75] provide the reference data for comparison (Tables 6 through 18). One-time measurements reflect size, whereas serial measurements are necessary for the assessment of growth.

The following are plotted on growth charts on the appropriate graph: standing height or recumbent length, weight, weight for height, and head circumference. Weight for height is determined by plotting the weight and height (or length) measurements on the appropriate grid on the growth chart and noting the percentile. Low weight for height, low height for chronological age, or a low head circumference in proportion to height may reflect chronic nutritional deficits. Parental heights and ethnic backgrounds should be considered when interpreting growth charts.

The mid-arm muscle circumference (MAMC) is calculated from the MAC and TSF measurements according to the following formula:

$$\text{MAMC (cm)} = \text{MAC (cm)} - (3.14 \times \text{TSF in cm}) \quad \text{Equation 1}$$

The mid-arm muscle area (MAMA) can be calcu-

Table 6. Mid-Arm Circumference (MAC) and Estimated Mid-Arm Muscle Circumference (MAMC) in Males

	Arm Circumference (MAC; mm), Percentiles							Arm Muscle Circumference (MAMC; mm), Percentiles						
Age (y)	5	10	25	50	75	90	95	5	10	25	50	75	90	95
1-1.9	142	146	150	159	170	176	183	110	113	119	127	135	144	147
2-2.9	141	145	153	162	170	178	185	111	114	122	130	140	146	150
3-3.9	150	153	160	167	175	184	190	117	123	131	137	143	148	153
4-4.9	149	154	162	171	180	186	192	123	126	133	141	148	156	159
5-5.9	153	160	167	175	185	195	204	128	133	140	147	154	162	169
6-6.9	155	159	167	179	188	209	228	131	135	142	151	161	170	177
7-7.9	162	167	177	187	201	223	230	137	139	151	160	168	177	180
8-8.9	162	170	177	190	202	220	245	140	145	154	162	170	182	187
9-9.9	175	178	187	200	217	249	257	151	154	161	170	183	196	202
10-10.9	181	184	196	210	231	262	274	156	160	166	180	191	209	221
11-11.9	186	190	202	223	244	261	280	159	165	173	183	195	205	230
12-12.9	193	200	214	232	254	282	303	167	171	182	195	210	223	241
13-13.9	194	211	228	247	263	286	301	172	179	196	211	226	238	245
14-14.9	220	226	237	253	283	303	322	189	199	212	223	240	260	264
15-15.9	222	229	244	264	284	311	320	199	204	218	237	254	266	272
16-16.9	244	248	262	278	303	324	343	213	225	234	249	269	287	296
17-17.9	246	253	267	285	308	336	347	224	231	245	258	273	294	312
18-18.9	245	260	276	297	321	353	379	226	237	252	264	283	298	324
19-24.9	262	272	288	308	331	355	372	238	245	257	273	289	309	321

Data from Frisancho.[75]

lated from the TSF and MAC using the following formula:

MAMA (for males):

$$[(\text{MAC (cm)} - 3.14 \times \text{TSF})^2/4 \times 3.14] - 10 \quad \text{Equation 2}$$

MAMA (females):

$$[(\text{MAC (cm)} - 3.14 \times \text{TSF})^2/4 \times 3.14] - 6.5 \quad \text{Equation 3}$$

The MAC, MAMC, MAMA, and TSF are evaluated according to tables of normal values for

Table 7. Mid-Arm Circumference (MAC) and Estimated Mid-Arm Muscle Circumference (MAMC) in Females

	Arm Circumference (MAC; mm), Percentiles							Arm Muscle Circumference (MAMC; mm), Percentiles						
Age (y)	5	10	25	50	75	90	95	5	10	25	50	75	90	95
1-1.9	138	142	148	156	164	172	177	105	111	117	124	132	139	143
2-2.9	142	145	152	160	167	176	184	111	114	119	126	133	142	147
3-3.9	143	150	158	167	175	183	189	113	119	124	132	140	146	152
4-4.9	149	154	160	169	177	184	191	115	121	128	136	144	152	157
5-5.9	153	157	165	175	185	203	211	125	128	134	142	151	159	165
6-6.9	156	162	170	176	187	204	211	130	133	138	145	154	166	171
7-7.9	164	167	174	183	199	216	231	129	135	142	151	160	171	176
8-8.9	168	172	183	195	214	247	261	138	140	151	160	171	183	194
9-9.9	178	182	194	211	224	251	260	147	150	158	167	180	194	198
10-10.9	174	182	193	210	228	251	265	148	150	159	170	180	190	197
11-11.9	185	194	208	224	248	276	303	150	158	171	181	196	217	223
12-12.9	194	203	216	237	256	282	294	162	166	180	191	201	214	220
13-13.9	202	211	223	243	271	301	338	169	175	183	198	211	226	240
14-14.9	214	223	237	252	272	304	322	174	179	190	201	216	232	247
15-15.9	208	221	239	254	279	300	322	175	178	189	202	215	228	244
16-16.9	218	224	241	258	283	313	334	170	180	190	202	216	234	249
17-17.9	220	227	241	264	295	324	350	175	183	194	205	221	239	257
18-18.9	222	227	241	258	281	312	325	174	179	191	202	215	237	245
19-24.9	221	230	247	265	290	319	345	179	185	195	207	221	236	249

Data from Frisancho.[75]

Table 8. Estimates of Mid-Arm Muscle Area (MAMC)

	Mid-Arm Muscle Area (mm^2), Percentiles													
	Males							Females						
Age (y)	5	10	25	50	75	90	95	5	10	25	50	75	90	95
1-1.9	956	1014	1133	1278	1447	1644	1720	885	973	1084	1221	1378	1535	1621
2-2.9	973	1040	1190	1345	1557	1690	1787	973	1029	1119	1269	1405	1595	1727
3-3.9	1095	1201	1357	1484	1618	1750	1853	1014	1133	1227	1396	1563	1690	1846
4-4.9	1297	1264	1408	1579	1747	1926	2008	1058	1171	1313	1475	1644	1832	1958
5-5.9	1298	1411	1550	1720	1884	2089	2285	1238	1301	1423	1598	1825	2012	2159
6-6.9	1360	1447	1605	1815	2056	2297	2493	1354	1414	1513	1683	1877	2182	2323
7-7.9	1497	1548	1808	2027	2246	2494	2886	1330	1441	1602	1815	2045	2332	2469
8-8.9	1550	1664	1895	2089	2296	2628	2788	1513	1566	1808	2034	2327	2657	2996
9-9.9	1811	1884	2067	2288	2657	3053	3257	1723	1788	1976	2227	2571	2987	3112
10-10.9	1930	2027	2182	2575	2903	3486	3882	1740	1784	2019	2296	2583	2873	3093
11-11.9	2016	2156	2382	2670	3022	3359	4226	1784	1987	2316	2612	3071	3739	3953
12-12.9	2216	2339	2649	3022	3496	3968	4640	2092	2182	2579	2904	3225	3655	3847
13-13.9	2363	2546	3044	3553	4081	4502	4794	2269	2426	2657	3130	3529	4081	4568
14-14.9	2830	3147	3586	3963	4575	5368	5530	2418	2562	2874	3220	3704	4294	4850
15-15.9	3138	3317	3788	4481	5134	5631	5900	2426	2518	2847	3248	3689	4123	4756
16-16.9	3625	4044	4352	4951	5753	6576	6980	2308	2567	2865	3248	3718	4353	4946
17-17.9	3998	4252	4777	5286	5950	6886	7726	2442	2674	2996	3336	3883	4552	5251
18-18.9	4070	4481	5066	5552	6374	7067	8355	2398	2538	2917	3243	3694	4461	4767
19-24.9	4508	4777	5274	5913	6660	7606	8200	2538	2728	3026	3406	3877	4439	4940

Data from Frisancho.[75]

Table 9. Triceps Skinfold Thickness (TSF)

	Triceps Skinfold Thickness, Percentiles (mm)															
	Males								Females							
Age (y)	n	5	10	25	50	75	90	95	n	5	10	25	50	75	90	95
1-1.9	228	6	7	8	10	12	14	16	204	6	7	8	10	12	14	16
2-2.9	223	6	7	8	10	12	14	15	208	6	8	9	10	12	15	16
3-3.9	220	6	7	8	10	11	14	15	208	7	8	9	11	12	14	15
4-4.9	230	6	6	8	9	11	12	14	208	7	8	8	10	12	14	16
5-5.9	214	6	6	8	9	11	14	15	219	6	7	8	10	12	15	18
6-6.9	117	5	6	7	8	10	13	16	118	6	6	8	10	12	14	16
7-7.9	122	5	6	7	9	12	15	17	126	6	7	9	11	13	16	18
8-8.9	117	5	6	7	8	10	13	16	118	6	8	9	12	15	18	24
9-9.9	121	6	6	7	10	13	17	18	125	8	8	10	13	16	20	22
10-10.9	146	6	6	8	10	14	18	21	152	7	8	10	12	17	23	27
11-11.9	122	6	6	8	11	16	20	24	117	7	8	10	13	18	24	28
12-12.9	153	6	6	8	11	14	22	28	129	8	9	11	14	18	23	27
13-13.9	134	5	5	7	10	14	22	26	151	8	8	12	15	21	26	30
14-14.9	131	4	5	7	9	14	21	24	141	9	10	13	16	21	26	28
15-15.9	128	4	5	6	8	11	18	24	117	8	10	12	17	21	25	32
16-16.9	131	4	5	6	8	12	16	22	142	10	12	15	18	22	26	31
17-17.9	133	5	5	6	8	12	16	19	114	10	12	13	19	24	30	37
18-18.9	91	4	5	6	9	13	20	24	109	10	12	15	18	22	26	30
19-24.9	531	4	5	7	10	15	20	22	1060	10	11	14	18	24	30	34

Data from Frisancho.[75]

Table 10. Table of 50th Percentile for Height in Boys to Be Used in Calculating SDS Scores for Height

Age (y)	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
2	86.8	87.5	88.2	88.9	89.7	90.4	91.3	92.2	93.1	94.0
3	94.9	95.7	96.6	97.4	98.3	99.1	99.8	100.6	101.4	102.1
4	102.9	103.6	104.4	105.1	105.9	106.6	107.3	107.9	108.6	109.2
5	109.9	110.5	111.2	111.8	112.5	113.1	113.7	114.3	114.9	115.5
6	116.1	116.7	117.3	117.8	118.4	119.0	119.5	120.1	120.6	121.2
7	121.7	122.2	122.8	123.3	123.8	124.4	124.9	125.4	125.9	126.5
8	127.0	127.5	128.0	128.6	129.1	129.6	130.1	130.6	131.2	131.7
9	132.2	132.7	133.2	133.8	134.3	134.8	135.3	135.9	136.4	136.9
10	137.5	138.1	138.6	139.2	139.7	140.3	140.9	141.5	142.1	142.7
11	143.3	143.9	144.5	145.2	145.8	146.4	147.0	147.7	148.4	149.0
12	149.7	150.4	151.0	151.7	152.3	153.0	153.7	154.4	155.1	155.3
13	156.5	157.2	157.9	158.5	159.2	159.9	160.5	161.2	161.8	162.6
14	163.1	163.7	164.3	164.9	165.6	166.2	166.8	167.3	167.9	168.4
15	169.0	169.5	170.0	170.5	171.0	171.5	171.9	172.3	172.7	173.1
16	173.5	173.8	174.2	174.5	174.9	175.2	175.4	175.6	175.8	176.0
17	176.2	176.3	176.4	176.5	176.6	176.7	176.7	176.7	176.8	176.8
18	176.8	176.8	176.8	176.8	176.8	176.8	176.8	176.8	176.8	176.8

Data from the NCHS Growth Curves for Children, Birth-18 years. DHEW Publication N. PHS 78-1650. Washington, DC, US Department of Health, Education and Welfare, Public Health Service, National Center for Health Statistics, 1977.

children of the same age and sex.[75] The most common skinfold thickness measured in children is the TSF because of available normal values and ease of measurement.

Standard Deviation Scores (SDS) are calculated using the patient's actual height compared with control values of the same chronological age and sex (Tables 10 through 17), according to the following equation:

$$\text{SDS} = [\text{Patient's actual value}] - \text{value at 50th percentile for controls} / \text{standard deviation of the control subjects} \quad \text{Equation 4}$$

The control subjects used for comparison are of the same chronological age and gender.

Table 11. Table of Standard Deviation Values for Height in Boys to Be Used in Calculating SDS Scores for Height

Age (y)	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
2	3.6	3.63	3.67	3.7	3.74	3.77	3.81	3.84	3.88	3.91
3	3.95	3.99	4.02	4.06	4.09	4.13	4.28	4.43	4.58	4.73
4	4.28	4.31	4.34	4.38	4.41	4.44	4.46	4.49	4.51	4.54
5	4.56	4.58	4.61	4.63	4.66	4.68	4.70	4.73	4.75	4.78
6	4.8	4.82	4.85	4.87	4.89	4.92	4.95	4.98	5.02	5.05
7	5.08	5.10	5.13	5.15	5.18	5.20	5.23	5.26	5.29	5.32
8	5.35	5.39	5.43	5.48	5.52	5.56	5.59	5.63	5.67	5.70
9	5.74	5.78	5.83	5.87	5.92	5.96	6.0	6.06	6.10	6.15
10	6.20	6.26	6.32	6.38	6.44	6.50	6.56	6.61	6.67	6.72
11	6.78	6.86	6.93	7.01	7.08	7.16	7.23	7.3	7.37	7.44
12	7.51	7.58	7.65	7.73	7.79	7.87	7.93	7.99	8.06	8.12
13	8.18	8.23	8.28	8.32	8.37	8.42	8.43	8.44	8.46	8.47
14	8.48	8.46	8.43	8.41	8.38	8.36	8.31	8.26	8.21	8.16
15	8.11	8.04	7.98	7.91	7.85	7.78	7.70	7.62	7.55	7.47
16	7.39	7.32	7.25	7.19	7.12	7.05	7.00	6.95	6.91	6.86
17	6.81	6.79	6.76	6.74	6.71	6.69	6.68	6.68	6.67	6.67
18	6.66	6.66	6.66	6.66	6.66	6.66	6.66	6.66	6.66	6.66

Data from the NCHS Growth Curves for Children, Birth-18 years. DHEW Publication N. PHS 78-1650. Washington, DC, US Department of Health, Education and Welfare, Public Health Service, National Center for Health Statistics, 1977.

Table 12. Table of 50th Percentile for Height in Girls to Be Used in Calculating SDS Scores for Height

Age (y)	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
2	86.8	87.4	88.1	88.7	89.4	90.0	90.8	91.6	92.5	93.3
3	94.1	94.9	95.6	96.4	97.1	97.9	98.6	99.4	100.1	100.9
4	101.6	102.3	102.9	103.6	104.3	105.0	105.7	106.4	107.0	107.7
5	108.4	109.0	109.7	110.3	110.9	111.6	112.2	112.8	113.4	114.0
6	114.6	115.2	115.8	116.4	117.0	117.6	118.2	118.8	119.4	120.0
7	120.6	121.1	121.8	122.3	122.9	123.5	124.1	124.7	125.2	125.8
8	126.4	126.9	127.6	128.1	128.7	129.3	129.9	130.5	131.0	131.6
9	132.2	132.8	133.1	134.0	134.6	135.2	135.8	136.4	137.1	137.7
10	138.3	138.9	139.6	140.2	140.9	141.5	142.2	142.8	143.2	144.1
11	144.8	145.5	146.2	146.8	147.5	148.2	148.9	149.5	150.2	150.8
12	151.5	152.1	152.7	153.4	153.9	154.6	155.1	155.6	156.1	156.6
13	157.1	157.5	157.9	158.2	158.6	159.0	159.3	159.6	159.8	160.1
14	160.4	160.6	160.7	160.9	161.0	161.2	161.3	161.4	161.6	161.7
15	161.8	161.9	161.9	161.9	162.0	162.1	162.2	162.2	162.3	162.3
16	162.4	162.5	162.5	162.6	162.6	162.7	162.8	162.9	162.9	163.0
17	163.1	163.2	163.2	163.3	163.3	163.4	163.5	163.5	163.6	163.6
18	163.7	163.7	163.7	163.7	163.7	163.7	163.7	163.7	163.7	163.7

Data from the NCHS Growth Curves for Children, Birth-18 years. DHEW Publication N. PHS 78-1650. Washington, DC, US Department of Health, Education and Welfare, Public Health Service, National Center for Health Statistics, 1977.

SDS for height compares growth rates over specific time intervals.

EXAMPLE: A 7.2-year-old boy has a body weight of 20 kg and a height of 118.5 cm. His SDS for height (Tables 10 and 11) and weight (Tables 14 and 15) are calculated in the following manner:

Height SDS = 118.5 − 122.8 (Table 10)/5.13 (Table 11)

Height SDS = −0.84

Weight SDS = 20 − 23.32 (Table 14)/3.70 (Table 15)

Weight SDS = −0.89

An SDS within two standard deviations encom-

Table 13. Table of Standard Deviation Values for Height in Girls to Be Used in Calculating SDS Scores for Height

Age (y)	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
2	3.65	3.65	3.65	3.65	3.65	3.65	3.67	3.69	3.7	3.72
3	3.74	3.77	3.80	3.83	3.86	3.89	3.92	3.95	3.98	4.01
4	4.04	4.08	4.11	4.15	4.18	4.22	4.26	4.29	4.33	4.37
5	4.41	4.56	4.51	4.55	4.60	4.65	4.69	4.75	4.79	4.84
6	4.89	4.94	4.99	5.04	5.09	5.14	5.19	5.24	5.28	5.33
7	5.38	5.43	5.48	5.52	5.57	5.62	5.67	5.72	5.77	5.82
8	5.87	5.92	5.97	6.01	6.06	6.11	6.15	6.19	6.24	6.28
9	6.32	6.36	6.39	6.43	6.46	6.50	6.54	6.58	6.61	6.65
10	6.69	6.71	6.74	6.76	6.79	6.81	6.83	6.85	6.86	6.88
11	6.90	6.91	6.92	6.94	6.95	6.96	6.96	6.96	6.96	6.96
12	6.96	6.96	6.96	6.96	6.96	6.96	6.96	6.96	6.96	6.96
13	6.96	6.95	6.95	6.94	6.94	6.93	6.92	6.91	6.89	6.88
14	6.87	6.86	6.86	6.85	6.85	6.84	6.83	6.82	6.80	6.79
15	6.78	6.76	6.74	6.73	6.71	6.69	6.67	6.65	6.64	6.62
16	6.60	6.57	6.54	6.50	6.47	6.44	6.42	6.39	6.37	6.34
17	6.32	6.29	6.26	6.23	6.20	6.17	6.15	6.13	6.12	6.10
18	6.08	6.08	6.08	6.08	6.08	6.08	6.08	6.08	6.08	6.08

Data from the NCHS Growth Curves for Children, Birth-18 years. DHEW Publication N. PHS 78-1650. Washington, DC, US Department of Health, Education and Welfare, Public Health Service, National Center for Health Statistics, 1977.

Table 14. Table of 50th Percentile for Weight in Boys to Be Used in Calculating SDS Scores for Weight

Age (y)	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
2	12.34	12.58	12.81	13.05	13.30	13.52	13.74	13.95	14.17	14.38
3	14.60	14.81	15.03	15.25	15.46	15.68	15.88	16.08	16.29	16.49
4	16.69	16.89	17.09	17.29	17.49	17.69	17.89	18.08	18.28	18.47
5	18.67	18.87	19.07	19.27	19.47	19.67	19.87	20.08	20.28	20.49
6	20.69	20.90	21.11	21.32	21.53	21.74	21.96	22.18	22.41	22.63
7	22.85	23.09	23.32	23.56	23.79	24.03	24.28	24.54	24.79	25.05
8	25.30	25.56	25.82	26.08	26.34	26.66	26.95	27.25	27.54	27.84
9	28.13	28.45	28.77	29.09	29.41	29.73	30.07	30.41	30.76	31.09
10	31.44	31.81	32.18	32.56	32.93	33.30	33.70	34.10	34.50	34.90
11	35.30	35.73	36.16	36.59	37.03	37.46	37.92	38.39	38.85	39.32
12	39.78	40.28	40.78	41.27	41.77	42.27	42.81	43.34	43.88	44.41
13	44.95	45.52	46.09	46.67	47.24	47.81	48.40	48.99	49.59	50.18
14	50.77	51.37	51.97	52.56	53.16	53.76	54.35	54.94	55.53	56.12
15	56.71	57.35	57.99	58.63	59.27	59.51	60.03	60.55	61.06	61.58
16	62.10	62.56	63.02	63.47	63.93	64.39	64.77	65.16	65.54	65.93
17	66.31	66.60	66.90	67.19	67.49	67.78	68.00	68.22	68.44	68.66
18	68.88	68.88	68.88	68.88	68.88	68.88	68.88	68.88	68.88	68.88

Data from the NCHS Growth Curves for Children, Birth-18 years. DHEW Publication N. PHS 78-1650. Washington, DC, US Department of Health, Education and Welfare, Public Health Service, National Center for Health Statistics, 1977.

passes about 95% of healthy North American children; an SDS greater than +2.0 or more negative than −2.0 is associated with either an abnormal increase or decrease in height or weight.[15,76]

The estimated dry weight can be challenging to ascertain, because weight gain is expected in growing children. Five parameters are helpful in the estimation process: weight, presence of edema, blood pressure, certain laboratory values, and dietary interview. The mid-week, postdialysis weight is used for evaluation purposes in the HD patient, and the weight at a monthly visit (minus dialysis fluid in the peritoneal cavity) is used for the child on peritoneal dialysis. The estimated dry weight is challenging to evaluate

Table 15. Table of Standard Deviation Values for Weight in Boys to Be Used in Calculating SDS Scores for Weight

Age (y)	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
2	1.52	1.54	1.56	1.58	1.60	1.62	1.64	1.67	1.69	1.72
3	1.74	1.77	1.79	1.82	1.84	1.87	1.90	1.93	1.96	1.99
4	2.02	2.05	2.08	2.12	2.15	2.18	2.22	2.26	2.30	2.34
5	2.38	2.42	2.47	2.51	2.56	2.60	2.65	2.70	2.76	2.81
6	2.86	2.92	2.98	3.04	3.10	3.16	3.23	3.29	3.36	3.42
7	3.49	3.59	3.70	3.81	3.91	4.02	4.07	4.13	4.18	4.24
8	4.29	4.38	4.48	4.57	4.67	4.76	4.86	4.96	5.07	5.17
9	5.27	5.38	5.49	5.59	5.70	5.81	5.92	6.03	6.14	6.25
10	6.36	6.47	6.59	6.70	6.82	6.93	7.04	7.16	7.27	7.39
11	7.50	7.61	7.72	7.83	7.94	8.05	8.16	8.26	8.37	8.47
12	8.58	8.68	8.78	8.88	8.98	9.08	9.17	9.26	9.36	9.45
13	9.54	9.62	9.69	9.77	9.85	9.93	10.01	10.08	10.16	10.23
14	10.31	10.38	10.44	10.51	10.57	10.64	10.70	10.76	10.82	10.88
15	10.94	10.99	11.06	11.11	11.17	11.23	11.29	11.34	11.39	11.45
16	11.51	11.57	11.63	11.68	11.74	11.80	11.82	11.84	11.87	11.89
17	11.91	12.01	12.11	12.21	12.31	12.41	12.47	12.53	12.58	12.64
18	12.70	12.70	12.70	12.70	12.70	12.70	12.70	12.70	12.70	12.70

Data from the NCHS Growth Curves for Children, Birth-18 years. DHEW Publication N. PHS 78-1650. Washington, DC, US Department of Health, Education and Welfare, Public Health Service, National Center for Health Statistics, 1977.

Table 16. Table of 50th Percentile for Weight in Girls to Be Used in Calculating SDS Scores for Weight

Age (y)	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
2	11.80	12.05	12.29	12.54	12.78	13.03	13.24	13.46	13.67	13.89
3	14.10	14.29	14.49	14.68	14.88	15.07	15.25	15.43	15.60	15.78
4	15.96	16.13	16.30	16.47	16.64	16.81	16.98	17.15	17.32	17.49
5	17.66	17.84	18.02	18.20	18.38	18.56	18.75	18.94	19.14	19.33
6	19.52	19.74	19.96	20.17	20.39	20.61	20.86	21.10	21.35	21.59
7	21.84	22.12	22.41	22.69	22.98	23.26	23.58	23.89	24.21	24.52
8	24.84	25.19	25.54	25.88	26.23	26.58	26.96	27.33	27.71	28.09
9	28.46	28.86	29.26	29.65	30.05	30.45	30.87	31.29	31.71	32.13
10	32.55	32.98	33.42	33.85	34.29	34.72	35.17	35.61	36.06	36.50
11	36.95	37.41	37.86	38.32	38.77	39.23	39.69	40.15	40.61	41.07
12	41.53	41.99	42.45	42.92	43.38	43.84	44.29	44.74	45.19	45.65
13	46.10	46.53	46.96	47.39	47.83	48.26	48.66	49.07	49.47	49.88
14	50.23	50.64	51.01	51.37	51.74	52.10	52.42	52.73	53.05	53.37
15	53.68	53.94	54.19	54.45	54.70	54.96	55.15	55.33	55.52	55.70
16	55.89	56.00	56.11	56.22	56.33	56.44	56.49	56.54	56.59	56.64
17	56.69	56.69	56.70	56.70	56.71	56.71	56.69	56.67	56.65	56.63
18	56.62	56.62	56.62	56.62	56.62	56.62	56.62	56.62	56.62	56.62

Data from the NCHS Growth Curves for Children, Birth-18 years. DHEW Publication N. PHS 78-1650. Washington, DC, US Department of Health, Education and Welfare, Public Health Service, National Center for Health Statistics, 1977.

in patients prone to edema and must be done in conjunction with a physical examination. Excess fluid may be visible in the periorbital, pedal, and other regions of the body. Edema may affect evaluation of both skinfold and body weight measurements, because expansion in extracellular fluid volume can obscure the effect of altered nutrient intake and metabolism on muscle and adipose tissue mass.[76] Hypertension which resolves with dialysis can be indicative of excess fluid weight. Decreased serum sodium and albumin levels may be markers of overhydration. Rapid weight gain in the absence of significant increase in energy intake or decrease in physical activity must be critically evaluated before it is assumed to be dry weight gain.

Table 17. Table of Standard Deviation Values for Weight in Girls to Be Used in Calculating SDS Scores for Weight

Age (y)	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9
2	1.28	1.33	1.37	1.42	1.46	1.51	1.55	1.59	1.62	1.66
3	1.70	1.74	1.78	1.81	1.85	1.89	1.93	1.96	1.99	2.03
4	2.07	2.11	2.14	2.18	2.21	2.25	2.29	2.33	2.37	2.41
5	2.45	2.49	2.54	2.59	2.63	2.68	2.73	2.79	2.84	2.89
6	2.95	3.01	3.07	3.14	3.19	3.26	3.33	3.41	3.49	3.56
7	3.64	3.73	3.82	3.91	4.00	4.09	4.19	4.29	4.39	4.49
8	4.59	4.70	4.81	4.92	5.03	5.14	5.26	5.37	5.49	5.60
9	5.72	5.84	5.96	6.08	6.20	6.32	6.44	6.56	6.69	6.81
10	6.93	7.05	7.17	7.29	7.42	7.54	7.66	7.78	7.89	8.01
11	8.13	8.24	8.35	8.47	8.58	8.69	8.79	8.89	9.00	9.11
12	9.21	9.30	9.39	9.49	9.58	9.67	9.75	9.83	9.92	9.99
13	10.08	10.15	10.22	10.29	10.36	10.43	10.49	10.55	10.62	10.68
14	10.74	10.79	10.84	10.88	10.93	10.98	11.02	11.06	11.10	11.14
15	11.18	11.21	11.24	11.27	11.30	11.33	11.35	11.37	11.38	11.40
16	11.42	11.43	11.44	11.45	11.46	11.47	11.47	11.47	11.46	11.46
17	11.46	11.45	11.44	11.43	11.42	11.41	11.39	11.37	11.35	11.33
18	11.31	11.31	11.31	11.31	11.31	11.31	11.31	11.31	11.31	11.31

Data from the NCHS Growth Curves for Children, Birth-18 years. DHEW Publication N. PHS 78-1650. Washington, DC, US Department of Health, Education and Welfare, Public Health Service, National Center for Health Statistics, 1977.

Table 18. Length for Infant Boys and Girls for Calculating SDS Scores[74]

	Boys		Girls	
Age (y)	Length (cm)	Std Dev	Length (cm)	Std Dev
0	50.5	2.29	49.9	2.17
0.25	61.1	2.65	59.5	2.49
0.5	67.8	2.69	65.9	2.64
0.75	72.3	2.65	70.4	2.73
1	76.1	2.70	74.3	2.84
1.25	79.4	2.85	77.8	2.95
1.5	82.4	3.04	80.9	3.07
1.75	85.1	3.23	83.8	3.18

C. REFERENCES (PEDIATRIC GUIDELINES)

Note: Asterisks indicate the citations that were used in the structured review of the literature.

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D. Index of Equations and Tables (Pediatric Guidelines)

III. Biographical Sketches of the Work Group Members

THE FOLLOWING ARE brief sketches that describe the professional training and experience of the Work Group members, particularly as they relate to the DOQI Nutrition Guidelines, as well as their principle business affiliations. All Work Group members completed a disclosure statement and certified that any potential conflict of interest would not influence their judgement or actions concerning the guidelines.

ADULT WORK GROUP

Suhail Ahmad, BSc, MB, BS, MD, is Associate Professor of Medicine and Medical Director for Dialysis and Apheresis at the University of Washington, Seattle, and Medical Director at the Scribner Kidney Center, Seattle. He completed his Fellowship at the University of Washington under Dr Belding Scribner and continued Dr Scribner's research after his retirement. Dr Ahmad has served on the Editorial Board of several nephrology journals and has published over 115 papers, including abstracts, book chapters, and one book on dialysis. He holds three patents related to dialysis technology. He is the current Chair of the Medical Review Board and Member of the Board of Directors for ESRD Network 16, current Chair of the Executive Committee of the Medical Staff of Northwest Kidney Center, Seattle, and past Member of the Executive Board of the ESRD Forum of Networks. Dr Ahmad is the recipient of the Excellent Teaching Award at the University of Washington and is listed in *Best Doctors*. He has received research grants and/or gives lectures for the following companies: Advanced Renal Technologies, Hoechst Marion Roussel, Novartis, Sigma-Tau Pharmaceuticals, Inc, Astra Zeneca, and Searle.

Jerrilynn D. Burrowes, MS, RD, CDN, is Research Coordinator for the Division of Nephrology and Hypertension at Beth Israel Medical Center in New York City. Ms Burrowes has has worked to improve the nutritional status and outcome of patients with ESRD for over a decade and has published several papers on these topics. Ms Burrowes is a doctoral candidate in the Department of Nutrition and Food Studies at New York University. She has also served on the Executive Committee for the National Kidney Foundation Council on Renal Nutrition and the Council on Renal Nutrition of Greater New York. Ms Burrowes is currently Chair of the CRN Program for the NKF Clinical Nephrology Meetings 2000. She is Study Coordinator at Beth Israel Medical Center for the NIH-sponsored Hemodialysis (HEMO) Study to evaluate the potential values of different dialysis doses and high versus low flux dialyzer membranes for maintenance hemodialysis patients. Ms Burrowes is an active member of the Nutrition Subcommittee that developed the nutrition component for this study.

Glenn M. Chertow, MD, MPH, is Assistant Professor of Medicine in Residence at the University of California, San Francisco (UCSF) and Director of Clinical Services in the Divisions of Nephrology at Moffitt-Long Hospitals and UCSF-Mt. Zion Medical Center. He is Medical Director of the Hemodialysis and Peritoneal Dialysis programs at both clinical sites. In addition to ABIM-certification in Internal Medicine and Nephrology, he has been designated a Certified Nutrition Support Physician (CNSP) by the American Society of Parenteral and Enteral Nutrition (ASPEN) and practices nutrition support in the critical care setting. Dr Chertow's research interests are focused on the epidemiology of acute and chronic renal failure, with a special interest in nutrition and renal diseases. He has written numerous papers on end-stage renal disease, dialysis therapy, and nutritional status. He is Associate Editor of the *Journal of Renal Nutrition*. He currently serves on the Board of Directors of the TransPacific Renal Network (ESRD Network #17), the Scientific Program Committee of the American Kidney Fund, and the Program Committee for NKF Clinical Nephrology 2000. Dr Chertow has served as a consultant for Amgen, Inc, and GelTex Pharmaceuticals, Inc, and has received research funding from GelTex Pharmaceuticals, Inc, and Genzyme, Inc.

David B. Cockram, MS, RD, LD, is a Research Scientist in Medical and Regulatory Affairs at the Ross Products Division of Abbott Laboratories. He has been actively conducting clinical trials in the areas of nutritional assessment and nutrition in renal disease for the past 12

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years. He has written more than 75 scientific publications and presentations. Mr Cockram is currently a PhD Candidate at Ohio State University and a member of the American Dietetic Association, the National Kidney Foundation Council on Renal Nutrition, the American Society for Nutritional Sciences, and the American Society of Clinical Nutrition.

Denis Fouque, MD, PhD, is Professor of Nephrology at the University Claude Bernard at Lyon, France, and Director of the Clinical Renal Unit at Hôpital Edouard Herriot. He is also the co-ordinating Editor of the Renal Group of the Cochrane Collaboration, based in Lyon. In addition to 10 years of clinical research on metabolism and nutrition in chronic renal failure, Dr Fouque has performed a number of meta-analyses and systematic reviews in the renal field, including the effects of low-protein diets on the role of progressive to end-stage renal failure in patients with chronic renal disease and the use of carnitine in hemodialysis patients. He has published more than 50 papers, including book chapters, on nutrition and renal diseases. He contributed to the French INSERM statement on malnutrition published in 1999 and to the European Nutritional Guidelines in Renal Disease (to be released). Dr Fouque is Associate Editor of the *Journal of Renal Nutrition*. Dr Fouque has received an Extramural grant from Baxter Healthcare, Inc, and has served as a consultant for them.

Charles J. Foulks, MD, FACP, FACN, is Professor of Medicine at Texas A&M University Health Sciences Center and College of Medicine and Director of the Division of Nephrology and Hypertension at Scott and White Hospital and Clinic in Temple, Texas. He served as Chairman of the Department of Internal Medicine at the University of North Dakota from 1996 to 1998. He has practiced clinical nephrology for over 20 years and has published numerous papers in the field of nutrition, particularly renal nutrition, with an emphasis on nutrition support and intradialytic parenteral nutrition. He was a member of the original HCFA Expert Panel on Quality in Dialysis. He has served on the National Kidney Foundation task forces on the initiation and withdrawal of dialysis, as well as the Expert Panel on Nutrition, which was a precursor to the DOQI Nutrition Work Group. He served as a member of the Medical Review Board for ESRD Network 14 of Texas from 1992 to 1996. Dr Foulks is also a member of the editorial board of the *Journal of Renal Nutrition* and is an associate editor of *Nutrition in Clinical Practice*. He has been a speaker for NMC and NMC Home Care and is currently on the Scientific Advisory Board for R&D Labs.

Joel D. Kopple, MD, FACP, (*Work Group Chair*) is Professor of Medicine and Public Health at the UCLA Schools of Medicine and Public Health and Chief of the Division of Nephrology and Hypertension at Harbor-UCLA Medical Center. Dr Kopple has published over 320 papers primarily in the fields of nutrition and metabolism, particularly as they relate to renal disease or renal failure. Dr Kopple is past President of the American Society for Parenteral and Enteral Nutrition, the International Society for Renal Nutrition and Metabolism and the Council of American Kidney Societies and is a past Director of the American Board of Nutrition. He is currently President of the National Kidney Foundation. Dr Kopple is a coeditor of 10 proceedings of meetings or symposia on general nutrition or nutrition and renal disease and is the coeditor of the book entitled *Nutritional Management of Renal Disease*. He has served as a reviewer or member of the editorial review boards of many journals. Dr Kopple has served as a consultant for many pharmaceutical or other health care companies, including Abbott Laboratories, Baxter Healthcare, Sigma-Tau Pharmaceuticals, Inc, and Total Renal Care, Inc.

Bradley Maroni, MD, is a Product Development Team Leader at Amgen, Inc. Prior to assuming that position he was a member of the Nephrology faculty at Emory University in Atlanta, Georgia, for 10 years. During that tenure he was active in NIH sponsored research investigating the impact of renal failure on protein metabolism and the dietary requirements of the patient with progressive chronic renal failure. He has published extensively in the field of nutrition and renal disease. Dr Maroni also served as a Co-Investigator for the NIH-sponsored Modification of Diet in Renal Disease (MDRD) Study and Principal Investigator at Emory University for the Morbidity and Mortality in Hemodialysis (HEMO) Study. Dr Maroni serves on several journal editorial boards and is active in many renal societies.

Linda W. Moore, RD, is currently Director of Scientific Publications for SangStat Medical Corporation. She has worked in dialysis and transplantation for many years at the University of Tennessee-Memphis where she focused on clinical outcomes in developing research protocols and patient care protocols. Ms Moore has published over 50 articles on renal nutrition and on transplantation for improving patient outcomes. Ms Moore is currently the Chair of the Council on Renal Nutrition for the National Kidney Foundation, serves as a work group member of the ESRD Core Indicators for the Health Care Finance Administration, and was a member of the NKF-DOQI Peritoneal Dialysis Adequacy Work Group.

Marsha Wolfson, MD, FACP, is Medical Director of the Renal Division at Baxter HealthCare. Prior to joining Baxter, she was Professor of Medicine at Oregon Health Sciences University and Chief of the Nephrology Section at the Portland VA Medical Center. She currently holds the title of Clinical Professor of Medicine in the Division of Nephrology and Hypertension at Oregon Health Sciences University. Her research interests have primarily focused on nutrition and metabolism in renal disease and she has numerous publications and book chapters in this area.

PEDIATRIC WORK GROUP

James C.M. Chan, MD, is Professor of Pediatrics and Professor of Biochemistry and Molecular Biophysics at Virginia Commonwealth University in Richmond. He has served on the faculties of the University of Southern California Children's Hospital of Los Angeles and George Washington University's Children's National Medical Center in Washington, DC. He has spent two sabbaticals at the National Institutes of Health (NIH). From 1983 to 1993, he led a consortium of 25 universities, funded by the NIH, to study the growth failure of children with renal diseases. In addition, Dr Chan has been funded since 1996 by the NIH to study progressive IgA nephropathy. Finally, he has been the director of a pediatric nephrology training program funded by the NIH since 1988 and coedited two textbooks: *Kidney Electrolyte Disorders* (Churchill-Livingstone) and *Phosphate in Pediatric Health and Disease* (CRC Press).

Richard N. Fine, MD, is Professor and Chairman of the Department of Pediatrics at the State University of New York at Stonybrook. Dr Fine has been involved in the clinical management of children with end-stage renal disease (ESRD) for more than 3 decades. He was instrumental in demonstrating that the duel therapeutic modalities of dialysis and renal transplantation were applicable to the treatment of children with ESRD. Dr Fine's research activities include the use of recombinant human growth hormone for children with growth retardation due to chronic renal insufficiency, dialysis or transplantation, and the utilization of peritoneal dialysis as an optimal therapeutic modality for infants, children, and adolescents. Dr Fine is past President of the American Society of Pediatric Nephrology and past member of the Council of the International Society for Peritoneal Dialysis, International Pediatric Nephrology Association, and International Transplant Society. He is currently a member of the Council of the American Society of Transplantation and the International Pediatric Transplantation Society. Dr Fine is on the Board of Directors for the Genentech Foundation.

Craig B. Langman, MD, is a Tenured Professor of Pediatrics at Northwestern University Medical School and Head of Nephrology and Mineral Metabolism and Director of Dialysis at Children's Memorial Medical Center in Chicago. Dr Langman's research has focused on the anatomical, biochemical and clinical expression of inherited or acquired disorders of calcium, phosphorus and vitamin D metabolism in infants, children, and adolescents. He has pioneered the use of noninvasive testing in children to assess bone cell function. Dr Langman has published more than 125 articles in his discipline and currently serves on the Editorial Advisory Boards of Advances in Renal Replacement Therapy and Pediatric Endocrinology. He previously served on the Editorial Advisory Board of Pediatric Nephrology. Dr Langman has served as President of the American Board of Pediatrics subboard of Pediatric Nephrology, the American Society of Pediatric Nephrology, and the Council of American Kidney Societies. He has served on the Scientific Advisory Board, Public Policy, and the Executive Committee of the Council of Pediatric Urology and Nephrology Committees, among others, of the National Kidney Foundation. He has also served on the Growth Advisory

Board of the North American Pediatric Renal Transplant Cooperative Study. Dr Langman serves on the Academic Advisory Board of Total Renal Care, Inc. He has served as a consultant for many pharmaceutical laboratories, health care companies, and health care related Foundations, including Merck USA, Roche Pharmaceuticals, Abbott Laboratories, and the Oxalosis and Hyperoxaluria Foundation.

Bruce Morgenstern, MD, is an Associate Professor of Pediatrics at the Mayo Clinic and Mayo Medical School in Rochester, MN, and Consultant in Pediatric Nephrology. Dr Morgenstern has a longstanding interest in clinical and basic research in peritoneal dialysis, as well as the evaluation and management of children with hypertension. He is currently the Principal Investigator of a multicenter study of peritoneal adequacy in children, involving the Pediatric Peritoneal Dialysis Study Consortium institutions. This study is partly funded by Baxter Healthcare.

Pauline Nelson, RD, is the Pediatric Renal Dietitian at the UCLA Center for the Health Sciences, working with children in the inpatient and outpatient settings on all modalities of ESRD care. She has participated in many clinical research studies related to growth and nutrition, especially in the areas of recombinant human growth hormone and peritoneal dialysis. Ms Nelson has written numerous professional and lay papers on various aspects of nutrition in ESRD, with a particular emphasis on practical approaches to the delivery of nutrients. She has been active in the American Dietetic Association and the Council on Renal Nutrition of the National Kidney Foundation on local and national levels.

Isidro B. Salusky, MD, FAAP, is Professor of Pediatrics at UCLA School of Medicine, Program Director of the UCLA General Clinic Research Center, and Director of the Pediatric Dialysis Program. He has a long-standing interest in the fields of growth and nutrition in children with renal failure that has ranged from experimental models to patients treated with maintenance dialysis. Dr Salusky has done extensive work to characterize the syndromes of renal osteodystrophy in children with chronic renal failure undergoing regular dialysis and postrenal transplantation. Dr Salusky has published more than 150 papers and is very active in many professional societies. During the course of these studies, Dr Salusky has been successful in obtaining funding from the National Institutes of Health, as well as from other profit and nonprofit organizations. He is a consultant for Genzyme, Inc, Bone Care International, and Abbott Laboratories.

Bradley A. Warady, MD, is Professor of Pediatrics at the University of Missouri-Kansas City School of Medicine and Chief of Nephrology and Director of Dialysis and Transplantation at the Children's Mercy Hospital. Dr Warady's clinical and research focus is end-stage renal disease with particular emphasis on peritoneal dialysis. He established the Pediatric Peritoneal Dialysis Study Consortium and currently codirects research projects on a number of topics, including growth hormone usage in pediatric dialysis patients, peritoneal dialysis adequacy in children, and intravenous iron therapy in pediatric patients receiving hemodialysis. He coedited the book *CAPD/CCPD in Children* and has published more than 150 papers. Dr Warady currently serves on the executive committees of the American Society of Pediatric Nephrology, the Pediatric Nephrology and Urology Committee of the National Kidney Foundation, and the Nephrology section of the American Academy of Pediatrics. Dr Warady is a member of the Editorial Board for *Advances of Renal Replacement Therapy*, and he is also a member of the NKF B DOQI Peritoneal Dialysis Adequacy Work Group. Dr Warady has had research funded by Baxter Health Care and Schein Pharmaceuticals.