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KDOQI

KIDNEY DISEASE OUTCOMES QUALITY INITIATIVE

KDOQI Clinical Practice Guideline for Nutrition in Children with CKD: 2008 Update

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Abstract

The 2008 update of the Kidney Disease Outcomes Quality Initiative (KDOQI) pediatric nutrition clinical practice guideline is intended to assist the practitioner caring for infants, children, and adolescents with chronic kidney disease (CKD) stages 2 to 5, on long-term dialysis therapy, or with a kidney transplant. The guideline contains recommendations for evaluation of nutritional status and growth and for counseling and selecting nutrition therapies that are appropriate to age and CKD stage. Therapeutic interventions considered include enteral feeding, intradialytic parenteral nutrition, growth hormone therapy, and restriction or supplementation of various macro- and micronutrients. The Work Group drafted narrative reviews based on its expertise and knowledge of the literature in the field and used references to support its write-up. Given the heterogeneity and often unique circumstances of the disease conditions in children with CKD, the Work Group adopted a perspective of issuing recommendations of potential use for improving patient survival, health, and quality of life. The recommendations also underwent both internal and external review. Tables of food and formula nutrient content, procedures for anthropometric measurements, copies of growth charts, and a list of resources for calculating energy requirements and anthropometric z scores are provided to assist with implementation. Furthermore, limitations to the recommendations are discussed; comparisons to other guidelines are made; and recommendations are provided for future research.

INDEX WORDS: Infants; children and adolescents; chronic kidney disease; dialysis; kidney transplantation; nutrition; guideline.

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CONTENTS

VOL 53, NO 3, SUPPL 2, MARCH 2009

KDOQI Clinical Practice Guideline for Nutrition in Children with CKD: 2008 Update

RECOMMENDATIONS

Continued

APPENDICES

WORK GROUP BIOGRAPHIES AND REFERENCES

NOTICE

SECTION I: USE OF THE CLINICAL PRACTICE GUIDELINE

This Clinical Practice Guideline document is based upon the best information available at the time of publication. It is designed to provide information and assist decision making. It is not intended to define a standard of care and should not be construed as one, nor should it 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 a type of practice. Every health care professional making use of these recommendations is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation. The recommendations for research contained within this document are general and do not imply a specific protocol.

SECTION II: DISCLOSURE

The National Kidney Foundation (NKF) makes every effort to avoid any actual or reasonably perceived conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the Work Group.

All members of the Work Group are required to complete, sign, and submit a disclosure and attestation form showing all such relationships that might be perceived or actual conflicts of interest. This document is updated annually and information is adjusted accordingly. All reported information is published in its entirety at the end of this publication in the Work Group members' Biographical and Disclosure Information section and is on file at the NKF.

In citing this document, the following format should be used: National Kidney Foundation. KDOQI Clinical Practice Guideline for Nutrition in Children with CKD: 2008 Update. Am J Kidney Dis 53: S1-S124, 2009 (suppl 2).

Tables

Figures

Abbreviations and Acronyms

ADL	Activities of daily living
AHA	American Heart Association
AI	Adequate intake
AMDR	Acceptable macronutrient distribution ranges
APD	Automated peritoneal dialysis
BIA	Bioelectrical impedance analysis
BMI	Body mass index
BSA	Body surface area
BUN	Blood urea nitrogen
CAPD	Continuous ambulatory peritoneal dialysis
CARI	Caring for Australasians with Renal Impairment
CCPD	Continuous cycler-assisted peritoneal dialysis
CDC	Centers for Disease Control and Prevention
CKD	Chronic kidney disease
CPD	Chronic peritoneal dialysis
CVD	Cardiovascular disease
DHA	Docosahexanoic acid
DPI	Dietary protein intakes
DRI	Dietary reference intake
DXA	Dual-energy X-ray absorptiometry
DV	Daily value
EAR	Estimated average requirement
ECF	Extracellular fluid
EER	Estimated energy requirement
EPA	Eicosapentanoic acid
ERT	Evidence Review Team
G	Urea generation rate
GFR	Glomerular filtration rate
HD	Hemodialysis
HDL	High-density lipoprotein
HPLC	High-performance liquid chromatography
IDL	Intermediate-density lipoprotein
IDPN	Intradialytic parenteral nutrition
IgA	Immunoglobulin A
IGF	Insulin-like growth factor
K	Potassium
KDIGO	Kidney Disease: Improving Global Outcomes
KDOQI	Kidney Disease Outcomes Quality Initiative
LDL	Low-density lipoprotein
MAC	Mid-arm circumference
MAMA	Mid-arm muscle area
MAMC	Mid-arm muscle circumference
MDRD	Modification of Diet in Renal Disease
mRNA	Messenger RNA
Na	Sodium
NAPRTCS	North American Pediatric Renal Trials and Collaborative Studies
ND	Not determined
NE	Nitrogen equivalent
n-3 FA	Omega-3 fatty acids
NCEP-C	National Cholesterol Expert Panel in Children and Adolescents

NKF	National Kidney Foundation
nPCR	Normalized protein catabolic rate
nPNA	Normalized protein nitrogen appearance
25(OH)D	25-Hydroxyvitamin D
$1,25(OH)_2D$	1,25-Dihydroxyvitamin D
PA	Physical activity coefficient
PAL	Physical activity level
PD	Peritoneal dialysis
PEM	Protein-energy malnutrition
PET	Peritoneal equilibration test
PTH	Parathyroid hormone
RDA	Recommended Dietary Allowance
rhGH	Recombinant human growth hormone
SD	Standard deviation
SDS	Standard deviation score(s)
SGA	Subjective Global Assessment
SGNA	Subjective Global Nutrition Assessment
TEE	Total energy expenditure
TG	Triglycerides
TNA	Total nitrogen appearance
TSF	Triceps skinfold thickness
UL	Tolerable upper intake level
USDA	US Department of Agriculture
VLDL	Very low-density lipoprotein
WHO	World Health Organization

Glossary of Definitions

Acceptable Macronutrient Distribution Ranges (AMDR): A range of intake for each energy source associated with reduced risk of chronic disease while providing adequate intake of essential nutrients. The AMDR is based on evidence that consumption greater or less than these ranges may be associated with nutrient inadequacy and increased risk of developing chronic diseases, such as coronary heart disease, obesity, diabetes, and/or cancer. The AMDR is expressed as a percentage of total energy intake because its requirement is not independent of other energy sources or of the individual's total energy requirement.

Adequate Intake (AI): The recommended average daily nutrient intake level based on observed or experimentally determined approximations or estimates of nutrient intake by a group (or groups) of apparently healthy people who are assumed to be maintaining an adequate nutritional state. The AI is expected to meet or exceed the needs of most individuals in a specific life-stage and gender group. When a Recommended Dietary Allowance (RDA) is not available for a nutrient, the AI can be used as the goal for usual intake by an individual. The AI is not equivalent to an RDA.

Children: Infants, children, and adolescents between the ages of birth and 19 years.

Dietary Reference Intakes (DRI): Set of 4 nutrient-based values that apply to the apparently healthy general population consisting of RDA, Estimated Average Requirement (EAR), AI, and Tolerable Upper Intake Level (UL).

Enteral Nutrition:* Nutrition provided through the gastrointestinal tract through a tube, catheter, or stoma that delivers nutrients distal to the oral cavity.

Estimated Energy Requirement (EER): An EER is defined as the average dietary energy intake that is predicted to maintain energy balance in healthy normal-weight individuals of a defined age, sex, weight, height, and level of physical activity consistent with good health. In children, the EER includes the needs associated with growth at rates consistent with good health. Relative body weight (ie, loss, stable, or gain) is the preferred indicator of energy adequacy.

Fiber: Combination of *dietary* fiber, the edible nondigestible carbohydrate and lignin components existing naturally in plant foods, and *functional* fiber, the isolated, extracted, or synthetic fiber that has proven health benefits. Fiber includes viscous or soluble forms that may decrease serum cholesterol levels (eg, oat bran and legumes/beans) and insoluble forms or bulking agents that prevent or alleviate constipation (eg, wheat bran, whole grains, vegetables, and fruits).

Height Age: The age at which the child's height would be on the 50th percentile.

Ideal Body Weight: The weight at the same percentile as the child's height percentile, for the same age and sex.

Macronutrients: Dietary fat, carbohydrate, protein, and fiber.

Nutrition Care:* Interventions and counseling of individuals on appropriate nutrition intake through the integration of information from the nutrition assessment.

Nutrition Care Plan:* A formal statement of the nutrition goals and interventions prescribed for an individual using the data obtained from a nutrition assessment. The plan, formulated by an interdisciplinary process, should include: statements of nutrition goals and monitoring parameters, the most appropriate route of administration of specialized nutrition support (oral, enteral, and/or parenteral), method of nutrition access, anticipated duration of therapy, and training and counseling goals and methods.

Nutrition Therapy:* A component of medical treatment that includes oral, enteral, and parenteral nutrition.

Obesity: Body mass index (BMI) for age at 95th percentile or greater.

Oral Nutrition:* Nutrition taken by mouth.

Overweight: BMI for age at 85th or greater and less than 95th percentiles.

Parenteral Nutrition:* The administration of nutrients intravenously.

Physical Activity Level (PAL): The ratio of total energy expenditure (TEE) to basal energy expenditure. PAL categories are defined as sedentary (PAL, 1.0 to 1.39), low active (PAL, 1.4 to 1.59), active (PAL, 1.6 to 1.89), and very active (PAL, 1.9 to 2.5). PAL should not be confused with the physical activity coefficient (PA values) used in the equations to estimate energy requirement.

Recommended Dietary Allowance (RDA): The intake that meets the nutrient needs of almost all (97% to 98%) individuals in a group. It may be used as a goal for individual intake.

Tolerable Upper Intake Level (UL): The highest average daily nutrient intake level likely to pose no risk of adverse health effects to almost all individuals in a given life-stage and sex group. The UL is not a recommended level of intake. As intake increases above the UL, the potential risk of adverse effects increases.

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* Source: Teitelbaum et al.[1]

Reference Key

Stages of Chronic Kidney Disease

Stage	Description	GFR (mL/min/1.73 m^2)	Treatment
1	Kidney damage with normal or ↑ GFR	≥90	
2	Kidney damage with mild ↓ GFR	60–89	1-5T if kidney transplant recipient
3	Moderate ↓ GFR	30–59	
4	Severe ↓ GFR	15–29	
5	Kidney failure	<15 (or dialysis)	5D if dialysis (HD or PD)

Abbreviations: CKD, chronic kidney disease; HD, hemodialysis; GFR, glomerular filtration rate; PD, peritoneal dialysis; ↑, increased; ↓, decreased.

Nomenclature and Description for Rating Guideline Recommendations

Strength of the Recommendation	Wording of the Recommendation	Prerequisite	Assumption	Expectation
A	An intervention "should be done"	The quality of the evidence is "high" or additional considerations support a "strong" recommendation	Most well-informed individuals will make the same choice	The expectation is that the recommendation will be followed unless there are compelling reasons to deviate from it in an individual. A strong recommendation may form the basis for a clinical performance measure
B	An intervention "should be considered"	The quality of the evidence is "high" or "moderate" or additional considerations support a "moderate" recommendation	A majority of well-informed individuals will make this choice, but a substantial minority may not	The expectation is that the recommendation will be followed in the majority of cases
C	An intervention is "suggested"	The quality of the evidence is "moderate," "low," or "very low" or additional considerations support a weak recommendation based predominantly on expert judgment	A majority of well-informed individuals will consider this choice	The expectation is that consideration will be given to following the recommendation

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Foreword

The publication of the Kidney Disease Outcomes Quality Initiative (KDOQI™) Clinical Practice Guideline for Nutrition in Children with Chronic Kidney Disease: Update 2008 represents the first update of the K/DOQI Nutrition and Chronic Renal Failure guidelines that were published in 2000.

The number of pediatric patients with chronic kidney disease (CKD) continues to grow. Patients with CKD are at significant risk of protein-energy malnutrition (PEM). Nutritional status in these children is especially important because it has a significant impact on linear growth, neurocognitive development, and sexual development. The effect of nutrition is especially important in infants because deficits in either linear growth or development that are acquired during infancy may not be fully correctable.

This guideline was developed to assist practitioners in Pediatric Nephrology in assessing the nutritional status of children with CKD, including patients on dialysis therapy or who have a kidney transplant; providing adequate macronutrient and micronutrient intake; and monitoring and treating complications of CKD, including bone mineral, vitamin D, fluid, and electrolyte derangements. This guideline will be of great importance to a broad audience of pediatric caregivers who endeavor to mitigate the effects of CKD on nutritional status and thus on the growth and development of these children.

This guideline has been developed by involving multiple disciplines from both US and international sources. These perspectives have been invaluable in ensuring a robust document with broad perspective. Each statement is graded based on the strength of recommendations (see the Reference Key on page S6 and Appendix 6). As for all KDOQI guidelines, these suggested interventions have been thoroughly discussed by all members of the Work Group to ensure they reflect state-of-the-art opinion on diagnosis, and management of these nutritional disorders. This final version of the document has undergone revision in response to comments during the public review process, an important and integral part of the KDOQI guideline process. Nonetheless, as with all guideline documents, there will be a need in the future for revision in the light of new evidence and, more importantly, a concerted effort to translate the guidelines into practice.

The recommendations are intended to serve as starting points for clinical decision making, and it is emphasized that the clinical judgment of the health care provider must always be included in the decision-making process and in the application of these recommendations. They are not to be considered as rules or standards of clinical practice, in keeping with the objectives of KDOQI. It is hoped that the information in this guideline document and the research recommendations provided will help improve the quality of care provided to children who have CKD and will stimulate additional research that will augment and refine this guideline in the future.

KDOQI is moving into an exciting new phase of activities. With the publication of the *Clinical Practice Guidelines and Clinical Practice Recommendations for Diabetes and Chronic Kidney Disease* in February 2007, KDOQI achieved its primary goal of producing evidence-based guidelines for the 12 aspects of CKD care most likely

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to improve patient outcomes. We now seek to apply the knowledge acquired in the development and refinement of the KDOQI processes to improve clinical practice through a broader range of activities that include directed research, public policy, guideline updates, commentaries on Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, publication forums, and new guidelines, if not being addressed by KDIGO or other guideline developers. We are looking forward to working with various members of the kidney health care community regarding these new and continuing KDOQI activities.

In a voluntary and multidisciplinary undertaking of this magnitude, many individuals make contributions to the final guideline document. It is impossible to acknowledge each of these individuals here, but to each and every one of them, I extend my sincerest appreciation. This limitation notwithstanding, the members of the Nutrition in Children with CKD Work Group and the Methods Consultants are to be commended for all their time and effort in reviewing the literature on pediatric nutrition since the release of the first nutrition guidelines in 2000 and for providing this update. Special thanks are given to the Co-Chairs, Dr Bradley Warady and Dr Donna Secker, for coordinating the activities of the Work Group. It is their commitment and dedication to the KDOQI process that has made this document possible.

Michael Rocco, MD, MSCE
KDOQI Chair

EXECUTIVE SUMMARY

INTRODUCTION

Regular evaluation of nutritional status and provision of adequate nutrition are key components in the overall management of children with CKD. The traditional and predominant focus of nutritional management for children with impaired kidney function is to prevent the development of PEM and meet the patient's vitamin and mineral needs. More recently, overnutrition characterized by obesity and the long-term implications of unbalanced dietary and lifestyle practices are of increasing concern to the pediatric CKD population, and attention to this issue must be incorporated into the nutrition management scheme. Thus, the focus of nutritional care for children across the spectrum of CKD must always be centered on the achievement of the following goals:

- Maintenance of an optimal nutritional status (ie, achievement of a normal pattern of growth and body composition by intake of appropriate amounts and types of nutrients).
- Avoidance of uremic toxicity, metabolic abnormalities, and malnutrition.
- Reduction of the risk of chronic morbidities and mortality in adulthood.

This publication represents the first revision of the K/DOQI Pediatric Clinical Practice Guidelines for Nutrition in Chronic Renal Failure and is a completely revised and expanded document. The revision of the document published in 2000 was considered necessary for the following reasons:

- To modify prior guideline statements based upon the availability of information published subsequent to the development of the 2000 guidelines.
- To expand the target population with recommendations to address patients with CKD stages 2 to 5 and kidney transplant recipients, in addition to the dialysis population addressed in the prior publication.
- To address a variety of topics not covered in the original guidelines, such as the dietary modification of sodium, potassium, fluid, calcium, and phosphorus, all of which can have a profound impact on patient outcomes.
- To incorporate references to dietary recommendations, anthropometric reference values, and growth charts for the healthy population that replaced those on which the 2000 guidelines were based.
- To reconcile discrepancies in recommendations for nutrient modification that exist between the pediatric nutrition guidelines and recent KDOQI guidelines on Hypertension and Dialysis Adequacy.

One of the challenges for the Work Group in revising the 2000 K/DOQI Pediatric Nutrition Guidelines was the remarkable lack of published data available for the topic of nutrition in children with all stages of CKD. In addition, the quality of evidence in pediatric nephrology studies related to the issues addressed in these guidelines was frequently low due to small sample size, the lack of randomized controlled trials, and the lack of information for both short- and long-term clinical outcomes. Thus, the Work Group has generated a set of guideline recommendations to provide guidance to practitioners on the clinical aspects of nutrition management while at the same time recognizing the limited evidence that exists. These recommendations are based on available evidence, such as it exists; they also rely heavily on the opinion of the Work Group members and are graded accordingly. All submitted suggestions from physicians, nurses, and dietitians who participated in the public review of the draft recommendations were carefully reviewed and considered for incorporation into the recommendations by the Work Group Chairs and individual Work Group members. Most importantly, the absence of randomized controlled trials to support the recommendations made precludes the subsequent development of clinical performance measurements by oversight bodies on most, if not all, of the issues addressed by the guidelines.

The process of revising the guidelines has also provided a unique opportunity to detect and highlight deficiencies in the scientific literature and to identify much needed areas of research for

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clinicians and scientists to undertake in the future. Areas of uncertainty arose for several reasons. For some issues, research in the pediatric CKD population has never been undertaken. For others, studies have provided indeterminate results, either because of small sample size or because infants, children, and adolescents were considered together, precluding the ability to relate outcomes to specific age groups. Studies that are rigorously designed to consider these issues and more and that address such topics as the role of inflammation on the nutritional status of children, the contribution of nutrition management to modification of cardiovascular risk, and the impact of frequent hemodialysis (HD) on energy, protein, and vitamin needs are required to ensure that future recommendations are truly evidence based.

The charge to the Work Group was to develop comprehensive guideline recommendations that could provide valuable assistance to all clinicians (eg, dietitians, physicians, and nurses) involved in the nutritional management of children with CKD. We believe we have accomplished that goal. Of course, the primary use of these recommendations is to complement—but not replace—clinical judgment and to recognize that this is a "living document" that requires regular modification as new information becomes available. When used in this manner, we are confident that the information contained in this document will contribute to improved clinical management and outcomes of children with CKD.

Finally, the Work Group expresses its appreciation to Michael Cheung, Dekeya Slaughter-Larkem, and Donna Fingerhut of the NKF-KDOQI Management Team and to Katrin Uhlig and Ethan Balk at the Tufts Center for Kidney Disease Guideline Development and Implementation for their guidance and assistance in the development of this guideline.

RECOMMENDATIONS

Recommendation 1: Evaluation of Growth and Nutritional Status

1.1 The nutritional status and growth of all children with CKD stages 2 to 5 and 5D should be evaluated on a periodic basis. ***(A)***

1.2 The following parameters of nutritional status and growth should be considered in combination for evaluation in children with CKD stages 2 to 5 and 5D. ***(B)***

- **i Dietary intake (3-day diet record or three 24-hour dietary recalls)**
- **ii Length- or height-for-age percentile or standard deviation score (SDS)**
- **iii Length or height velocity-for-age percentile or SDS**
- **iv Estimated dry weight and weight-for-age percentile or SDS**
- **v BMI-for-height-age percentile or SDS**
- **vi Head circumference-for-age percentile or SDS (≤3 years old only)**
- **vii Normalized protein catabolic rate (nPCR) in hemodialyzed adolescents with CKD stage 5D.**

1.3 It is suggested that the frequency of monitoring nutritional and growth parameters in all children with CKD stages 2 to 5 and 5D be based on the child's age and stage of CKD (Table 1). ***(C)*** **In general, it is suggested that assessments be performed at least twice as frequently as they would be performed in a healthy child of the same age.** ***(C)*** **Infants and children with polyuria, evidence of growth delay, decreasing or low BMI, comorbidities influencing growth or nutrient intake, or recent acute changes in medical status or dietary intake may warrant more frequent evaluation.** ***(C)***

Recommendation 2: Growth

2.1 Identification and treatment of existing nutritional deficiencies and metabolic abnormalities should be aggressively pursued in children with CKD stages 2 to 5 and 5D, short stature (height SDS < −1.88 or height-for-age < 3rd percentile), and potential for linear growth. ***(A)***

2.2 Serum bicarbonate level should be corrected to at least the lower limit of normal (22 mmol/L) in children with CKD stages 2 to 5 and 5D. ***(B)***

2.3 Recombinant human growth hormone (rhGH) therapy should be considered in children with CKD stages 2 to 5 and 5D, short stature (height SDS < −1.88 or

height-for-age < 3rd percentile), and potential for linear growth if growth failure (height velocity-for-age SDS < −1.88 or height velocity-for-age < 3rd percentile) persists beyond 3 months despite treatment of nutritional deficiencies and metabolic abnormalities. ***(B)***

Recommendation 3: Nutritional Management and Counseling

3.1 Nutrition counseling, based on an individualized assessment and plan of care, should be considered for children with CKD stages 2 to 5 and 5D and their caregivers. ***(B)***

3.2 Nutritional intervention that is individualized according to results of the nutritional assessment and with consideration of the child's age, development, food preferences, cultural beliefs, and psychosocial status should be considered for children with CKD stages 2 to 5 and 5D. ***(B)***

3.3 Frequent reevaluation and modification of the nutrition plan of care is suggested for children with CKD stages 2 to 5 and 5D. ***(C)*** **More frequent review is indicated for infants and children with advanced stages of CKD, relevant comorbidities influencing growth or nutrient intake, evidence of inadequate intake or malnutrition, or if acute illness or adverse events occur that may negatively impact on nutritional status.** ***(C)***

3.4 Nutritional management, coordinated by a dietitian who ideally has expertise in pediatric and renal nutrition, is suggested for children with CKD stages 2 to 5 and 5D. ***(C)*** **It is suggested that nutritional management be a collaborative effort involving the child, caregiver, dietitian, and other members of the multidisciplinary pediatric nephrology team (ie, nurses, social workers, therapists, and nephrologists).** ***(C)***

Recommendation 4: Energy Requirements and Therapy

4.1 Energy requirements for children with CKD stages 2 to 5 and 5D should be considered to be 100% of the EER for chronological age, individually adjusted for PAL and body size (ie, BMI). ***(B)*** **Further adjustment to energy intake is suggested based upon the response in rate of weight gain or loss.** ***(B)***

4.2 Supplemental nutritional support should be considered when the usual intake of a child with CKD stages 2 to 5 or 5D fails to meet his or her energy requirements and the child is not achieving expected rates of weight gain and/or growth for age. ***(B)***

4.3 Oral intake of an energy-dense diet and commercial nutritional supplements should be considered the preferred route for supplemental nutritional support for children with CKD stages 2 to 5 and 5D. ***(B)*** **When energy requirements cannot be met with oral supplementation, tube feeding should be considered.** ***(B)***

4.4 A trial of intradialytic parenteral nutrition (IDPN) to augment inadequate nutritional intake is suggested for malnourished children (BMI-for-height-age < 5th percentile) receiving maintenance HD who are unable to meet their nutritional requirements through oral and tube feeding. ***(C)***

4.5 A balance of calories from carbohydrate and unsaturated fats within the physiological ranges recommended as the AMDR of the DRI is suggested when prescribing oral, enteral, or parenteral energy supplementation to children with CKD stages 2 to 5 and 5D. ***(C)***

4.6 Dietary and lifestyle changes are suggested to achieve weight control in overweight or obese children with CKD stages 2 to 5 and 5D. ***(C)***

Recommendation 5: Protein Requirements and Therapy

5.1 It is suggested to maintain dietary protein intake (DPI) at 100% to 140% of the DRI for ideal body weight in children with CKD stage 3 and at 100% to 120% of the DRI in children with CKD stages 4 to 5. ***(C)***

5.2 In children with CKD stage 5D, it is suggested to maintain DPI at 100% of the DRI for ideal body weight plus an allow-

ance for dialytic protein and amino acid losses. ***(C)***

5.3 The use of protein supplements to augment inadequate oral and/or enteral protein intake should be considered when children with CKD stages 2 to 5 and 5D are unable to meet their protein requirements through food and fluids alone. ***(B)***

Recommendation 6: Vitamin and Trace Element Requirements and Therapy

6.1 The provision of dietary intake consisting of at least 100% of the DRI for thiamin (B_1), riboflavin (B_2), niacin (B_3), pantothenic acid (B_5), pyridoxine (B_6), biotin (B_8), cobalamin (B_{12}), ascorbic acid (C), retinol (A), α-tocopherol (E), vitamin K, folic acid, copper, and zinc should be considered for children with CKD stages 2 to 5 and 5D. ***(B)***

6.2 It is suggested that supplementation of vitamins and trace elements be provided to children with CKD stages 2 to 5 if dietary intake alone does not meet 100% of the DRI or if clinical evidence of a deficiency, possibly confirmed by low blood levels of the vitamin or trace element, is present. ***(C)***

6.3 It is suggested that children with CKD stage 5D receive a water-soluble vitamin supplement. ***(C)***

Recommendation 7: Bone Mineral and Vitamin D Requirements and Therapy

7.1: Calcium

7.1.1 In children with CKD stages 2 to 5 and 5D, it is suggested that the total oral and/or enteral calcium intake from nutritional sources and phosphate binders be in the range of 100% to 200% of the DRI for calcium for age. ***(C)***

7.2: Vitamin D

7.2.1 In children with CKD stages 2 to 5 and 5D, it is suggested that serum 25-hydroxyvitamin D levels be measured once per year. ***(C)***

7.2.2 If the serum level of 25-hydroxyvitamin D is less than 30 ng/mL (75 nmol/L), supplementation with vitamin D_2 (ergocalciferol) or vitamin D_3 (cholecalciferol) is suggested. ***(C)***

7.2.3 In the repletion phase, it is suggested that serum levels of corrected total calcium and phosphorus be measured at 1 month after initiation or change in dose of vitamin D and at least every 3 months thereafter. ***(C)***

7.2.4 When patients are replete with vitamin D, it is suggested to supplement vitamin D continuously and to monitor serum levels of 25-hydroxyvitamin D yearly. ***(C)***

7.3: Phosphorus

7.3.1 In children with CKD stages 3 to 5 and 5D, reducing dietary phosphorus intake to 100% of the DRI for age is suggested when the serum parathyroid hormone (PTH) concentration is above the target range for CKD stage and the serum phosphorus concentration is within the normal reference range for age. ***(C)***

7.3.2 In children with CKD stages 3 to 5 and 5D, reducing dietary phosphorus intake to 80% of the DRI for age is suggested when the serum PTH level is above the target range for CKD stage and the serum phosphorus concentration exceeds the normal reference range for age. ***(C)***

7.3.3 After initiation of dietary phosphorus restriction, it is suggested that serum phosphorus concentration be monitored at least every 3 months in children with CKD stages 3 to 4 and monthly in children with CKD stage 5 and 5D. ***(C)*** **In all CKD stages, it is suggested to avoid serum phosphorus concentrations both above and below the normal reference range for age.** ***(C)***

Recommendation 8: Fluid and Electrolyte Requirements and Therapy

8.1 Supplemental free water and sodium supplements should be considered for children with CKD stages 2 to 5 and 5D and polyuria

to avoid chronic intravascular depletion and to promote optimal growth. *(B)*

8.2 Sodium supplements should be considered for all infants with CKD stage 5D on peritoneal dialysis (PD) therapy. *(B)*

8.3 Restriction of sodium intake should be considered for children with CKD stages 2 to 5 and 5D who have hypertension (systolic and/or diastolic blood pressure ≥ 95th percentile) or prehypertension (systolic and/or diastolic blood pressure ≥ 90th percentile and < 95th percentile). *(B)*

8.4 Fluid intake should be restricted in children with CKD stages 3 to 5 and 5D who are oligoanuric to prevent the complications of fluid overload. *(A)*

8.5 Potassium intake should be limited for children with CKD stages 2 to 5 and 5D who have or are at risk of hyperkalemia. *(A)*

Recommendation 9: Carnitine

9.1 In the opinion of the Work Group, there is currently insufficient evidence to suggest a role for carnitine therapy in children with CKD stage 5D.

Recommendation 10: Nutritional Management of Transplant Patients

10.1 Dietary assessment, diet modifications, and counseling are suggested for children with CKD stages 1 to 5T to meet nutritional requirements while minimizing the side effects of immunosuppressive medications. *(C)*

10.2 To manage posttransplantation weight gain, it is suggested that energy requirements of children with CKD stages 1 to 5T be considered equal to 100% of the EER for chronological age, adjusted for PAL and body size (ie, BMI). *(C)* Further adjustment to energy intake is suggested based upon the response in rate of weight gain or loss. *(C)*

10.3 A balance of calories from carbohydrate, protein, and unsaturated fats within the physiological ranges recommended by the AMDR of the DRI is suggested for children with CKD stages 1 to 5T to prevent or manage obesity, dyslipidemia, and corticosteroid-induced diabetes. *(C)*

10.4 For children with CKD stages 1 to 5T and hypertension or abnormal serum mineral or electrolyte concentrations associated with immunosuppressive drug therapy or impaired kidney function, dietary modification is suggested. *(C)*

10.5 Calcium and vitamin D intakes of at least 100% of the DRI are suggested for children with CKD stages 1 to 5T. *(C)* In children with CKD stages 1 to 5T, it is suggested that total oral and/or enteral calcium intake from nutritional sources and phosphate binders not exceed 200% of the DRI (see Recommendation 7.1). *(C)*

10.6 Water and drinks low in simple sugars are the suggested beverages for children with CKD stages 1 to 5T with high minimum total daily fluid intakes (except those who are underweight, ie, BMI-for-height-age < 5th percentile) to avoid excessive weight gain, promote dental health, and avoid exacerbating hyperglycemia. *(C)*

10.7 Attention to food hygiene/safety and avoidance of foods that carry a high risk of food poisoning or food-borne infection are suggested for immunosuppressed children with CKD stages 1 to 5T. *(C)*

RECOMMENDATION 1: EVALUATION OF GROWTH AND NUTRITIONAL STATUS

INTRODUCTION

Normal growth and development are major goals of pediatric CKD management. Because adequate nutritional status is important in achieving these goals, careful monitoring of nutritional status is essential. Nutritional status is a complex concept that cannot be adequately summarized by a single measurement. Multiple measures, considered collectively, are required to give a complete and accurate picture of nutritional status. Growth parameters are particularly important in children and should be accurately measured using calibrated equipment and standardized techniques (see Appendix 1).

1.1 The nutritional status and growth of all children with CKD stages 2 to 5 and 5D should be evaluated on a periodic basis. ***(A)***

1.2 The following parameters of nutritional status and growth should be considered in combination for evaluation in children with CKD stages 2 to 5 and 5D. ***(B)***

- **i Dietary intake (3-day diet record or three 24-hour dietary recalls)**
- **ii Length- or height-for-age percentile or standard deviation score (SDS)**
- **iii Length or height velocity-for-age percentile or SDS**
- **iv Estimated dry weight and weight-for-age percentile or SDS**
- **v BMI-for-height-age percentile or SDS**
- **vi Head circumference-for-age percentile or SDS (≤3 years old only)**
- **vii Normalized protein catabolic rate (nPCR) in hemodialyzed adolescents with CKD stage 5D.**

1.3 It is suggested that the frequency of monitoring nutritional and growth parameters in all children with CKD stages 2 to 5 and 5D be based on the child's age and stage of CKD (Table 1). ***(C)*** **In general, it is suggested that assessments be performed at least twice as frequently as they would be performed in a healthy child of the same age.** ***(C)*** **Infants and children with polyuria, evidence of growth delay, decreasing or low BMI, comorbidities influencing growth or nutrient intake, or re-**

Table 1. Recommended Parameters and Frequency of Nutritional Assessment for Children with CKD Stages 2 to 5 and 5D

	Minimum Interval (mo)									
	Age 0 to <1 y			Age 1-3 y			Age >3 y			
Measure	CKD 2-3	CKD 4-5	CKD 5D	CKD 2-3	CKD 4-5	CKD 5D	CKD 2	CKD 3	CKD 4-5	CKD 5D
Dietary intake	0.5-3	0.5-3	0.5-2	1-3	1-3	1-3	6-12	6	3-4	3-4
Height or length-for-age percentile or SDS	0.5-1.5	0.5-1.5	0.5-1	1-3	1-2	1	3-6	3-6	1-3	1-3
Height or length velocity-for-age percentile or SDS	0.5-2	0.5-2	0.5-1	1-6	1-3	1-2	6	6	6	6
Estimated dry weight and weight-for-age percentile or SDS	0.5-1.5	0.5-1.5	0.25-1	1-3	1-2	0.5-1	3-6	3-6	1-3	1-3
BMI-for-height-age percentile or SDS	0.5-1.5	0.5-1.5	0.5-1	1-3	1-2	1	3-6	3-6	1-3	1-3
Head circumference-for-age percentile or SDS	0.5-1.5	0.5-1.5	0.5-1	1-3	1-2	1-2	N/A	N/A	N/A	N/A
nPCR	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1*

Abbreviation: N/A, not applicable.

*Only applies to adolescents receiving HD.

cent acute changes in medical status or dietary intake may warrant more frequent evaluation. ***(C)***

RATIONALE

1.1: The nutritional status and growth of all children with CKD stages 2 to 5 and 5D should be evaluated on a periodic basis. (A)

1.2: The following parameters of nutritional status and growth should be considered in combination for evaluation in children with CKD stages 2 to 5 and 5D. (B)

Because of the high prevalence of growth retardation in children with CKD, nutrition has always been a primary focus of pediatric CKD care. Early studies emphasized the importance of adequate energy intake in maintaining normal growth in pediatric CKD. However, no study demonstrated a growth advantage to a caloric intake greater than about 75% of the RDA,[2-4] which corresponds approximately to 100% of the EER in children older than 3 months. Interestingly, the prevalence of undernutrition in children with CKD is unknown. This is likely due, in part, to an inadequate definition of undernutrition in this population. In children with CKD, the prevalence of undernutrition has been demonstrated to vary widely—from 2% to 65%—depending on the definition used.[5] In the general population, the World Health Organization (WHO) has defined undernutrition as weight-for-age, height-for-age, and weight-for-height 2 SDs or greater less than the Centers for Disease Control and Prevention (CDC) reference median,[6] in recognition of the fact that long-term undernutrition may lead to wasting (low weight-for-height) and/or stunting (low height-for-age). However, this definition may be inappropriate in children with CKD. Whereas stunting can be reasonably attributed solely to long-term undernutrition in otherwise healthy children, the multifactorial cause of stunting in children with CKD makes it a poor choice as a definition of undernutrition in this group. In the CKD population, anthropometric definitions of undernutrition are complicated; consideration must be given to the appropriateness of measures for both age and height of the child.

Body composition has yet to be well characterized in pediatric CKD. Few high-quality studies are available in which measures of body composition were adequately adjusted for height and appropriately compared with a healthy reference population.[7-12] Of these, lean mass deficits were observed in some studies,[11] but not others.[7] Fat mass appears to be increased relative to height in children with CKD.[11] Preliminary evidence in small numbers of children suggests that use of growth hormone may result in lower fat mass and higher lean mass for height.[11]

Interpretation of many prior studies of nutrition and growth in pediatric CKD is difficult because most studies considered infants and older children together as a uniform group. There are reasons to believe that infants younger than 2 to 3 years behave very differently from older children. At a theoretical level, there are 2 main considerations. First, a much larger proportion of the daily energy requirement is devoted to growth in infants compared with older children. Second, growth is driven primarily by nutrition during infancy, whereas growth hormone and sex hormones have a dominant influence during childhood and adolescence, respectively.[13-16] On a practical level, there is evidence to support the notion that infants and older children behave differently. Inadequate spontaneous calorie intake has been clearly demonstrated in infants with CKD[17-19]; energy intakes for older children usually are normal relative to body size.[9] In studies separating children by age, weight-for-height indices, and BMI-for-age, z scores were low in younger children, but normal in older children.[10,12] Lean mass deficits were also more likely in younger than older children.[7,8,10] Routine calorie and/or protein supplementation have been shown to improve growth in infants with CKD.[17-19] However, there is no clear evidence that routine nutritional supplements have a similar effect in older children.

Because of these differences between infants and older children, the present recommendations emphasize the importance of considering the age of the child when planning nutritional monitoring and interventions.

Historically, the main focus of malnutrition in children with CKD has been undernutrition; there is some evidence that obesity is beginning to be a problem in the CKD population.[20-22]

Dietary Intake

It is suggested that dietary intake be assessed regularly by a skilled registered dietitian by means of a 3-day diet diary. Three 24-hour recalls may be preferable in adolescents. Dietary intake data provide useful information about the quantity and quality of nutrients ingested. The 2 most practical and clinically feasible ways to determine usual daily intake are the prospective 3-day dietary diary and the retrospective 24-hour dietary recall. From either of these, daily intake of calories, macronutrients (carbohydrate, protein, and fat), vitamins, and minerals can be estimated. Each of the methods has its own limitations. Dietary diaries have been shown to give unbiased estimates of energy intake in normal-weight children younger than 10 years; however, underreporting is common in adolescents.[23,24] Twenty-four–hour recalls may be better suited to adolescents. The most important limitation of the 24-hour recall method is its poor ability to capture the day-to-day variability in dietary intake. Children may be even more susceptible to this limitation than adults because they tend to have more day-to-day variability.[25] It may be useful to obtain three 24-hour recalls to more completely evaluate the food-intake pattern. One weekend day should be included in a 3-day diet diary and as 1 of three 24-hour recalls. Despite their limitations, dietary recall interviews conducted by a skilled pediatric registered dietitian or dietary diaries completed by the patient and/or parent as instructed by a registered dietitian provide useful general information about the pattern of food intake. Information about dietary intake allows the treating team to evaluate the adequacy of a patient's intake before significant adverse changes in body composition result.

Poor intake is expected in infants with CKD and should prompt immediate initiation of nutritional supplements if there is any evidence of inadequate weight gain or growth. When spontaneous intake is low in a poorly growing older child, consideration also must be given to the possibility that the poor intake is a result of the poor growth, rather than the cause. Spontaneous calorie intake increased by almost 12% in a study of 33 children with CKD during treatment with rhGH.[26]

Length- or Height-for-Age Percentile or SDS

Length (infants $<$ 2 years) or height (children $>$ 2 years) should be measured regularly, plotted on the length- or height-for-age curves, and the percentile and/or SDS should be calculated (Appendix 2, Table 32). Growth retardation is common in CKD.[2,3,12,27,28] The impact of CKD on growth depends on both the degree of kidney impairment and age of the child. Normal growth can be divided into 3 phases: infancy (dominated by nutrition), childhood (dominated by growth hormone), and puberty (dominated by sex hormones).[13] The infancy phase normally is replaced by the childhood pattern between 6 and 12 months of age. In CKD, onset of the childhood phase frequently is delayed until 2 to 3 years of age or interrupted by a transient resumption of the infancy pattern.[13] CKD also results in a delay in the onset of pubertal growth, as well as a shorter pubertal growth spurt.[29] Together, these alterations to the normal pattern of growth may lead to severe short stature. The typical CKD growth pattern is characterized by decreased growth velocity during infancy, followed by normal growth velocity during childhood and impaired growth velocity again during adolescence.[16] However, growth velocity also may be low during the childhood phase in children with CKD stages 4 or 5.[3,30] Numerous factors may influence growth in CKD, including acidosis,[31] disturbances in the growth hormone axis,[32] and poor nutritional intake.[2] Nutritional intake has its greatest influence during the infancy phase of growth.[16]

Length (infants) should be measured by using a length board, and height (older children), by using a wall-mounted stadiometer, preferably by the same well-trained person at each assessment. Calculating the SDS or plotting the child's height on the normal growth chart to determine the percentile allows comparison with healthy children. In 2000, the CDC published revised North American growth reference charts for infants and children up to 20 years of age (Figs 11 to 14).[33] In 2006, the WHO released new growth standards for children from birth to 5 years of age (Figs 1 to 10).[34] These growth *standards* are distinguished from the CDC *reference* charts in 2 important ways. First, the children contributing to the WHO Growth Standards were specifically

selected to represent children growing under ideal conditions: they had nonsmoking mothers, were from areas of high socioeconomic status, and received regular pediatric health care, including immunizations. A subset of 882 infants, all breastfed for at least 4 months, provided longitudinal data for 24 months. Second, the study population was of broad ethnic diversity; participants were recruited from Brazil, Ghana, India, Norway, Oman, and the United States. Importantly, ethnicity had very little impact on growth, indicating that the growth standards reflect a reasonable expectation for growth regardless of ethnicity; only 3% of the variability in growth within the population could be attributed to country of origin.[34]

Because the WHO Growth Standards represent ideal growth and ideal growth should be the goal for children with CKD, the WHO Growth Standards should be used as the reference for children from birth to 2 years. Differences between the CDC reference curves and the WHO Growth Standards are minimal after 2 years. For this reason and because the switch is made from length to height measurement at 2 years, 2 years appears to be a reasonable age to make the transition from the WHO Growth Standards to the CDC reference curves (www.rcpch.ac.uk/doc.aspx?id_Resource=2862; last accessed October 23, 2008).

It may be useful to consider the genetic height potential of the child when assessing adequacy of growth. Although the exact contribution of heredity cannot be calculated, an estimate of a child's adult height potential can be made by calculating midparental height adjusted for the sex of the child. Midparental height is calculated as follows (see Appendix 2, Table 33 for an online calculator):

- Girls: 5 inches (13 cm) is subtracted from the father's height and averaged with the mother's height;
- Boys: 5 inches (13 cm) is added to the mother's height and averaged with the father's height.

The midparental height is plotted on the growth chart (of the same gender as the child) at 20 years of age. For both girls and boys, 3.5 inches (8.5 cm) on either side of this calculated value (target height) represents the 3rd to 97th percentiles for anticipated adult height.[35] The 5 inches (13 cm) represents the average difference in height of men and women; thus, the child grows, on average, to the midparental height percentile.

Adequate growth is a good indication of adequate nutrition over the long term. However, acute weight loss may be severe and alterations in body composition may be substantial before linear growth is impaired. Growth usually continues at a normal rate in malnourished children until significant wasting occurs.[36] For this reason, additional measures of nutritional status are advised.

Length or Height Velocity-for-Age Percentile or SDS

The growth velocity (change in height per unit of time) can be determined by recording serial height measurements. In children younger than 2 years, the change in length percentile and/or SDS will give an idea of growth velocity (a negative change indicates poor growth; a positive change may represent catch-up growth). Calculation of growth velocity percentile and/or SDS for children younger than 2 years can be done by using data from the 2006 WHO Growth Standards. Height velocity percentile and/or SDS can be calculated for children older than 2 years by using reference data from the Fels Longitudinal Study.[37] It is important to recognize that height velocity cannot be accurately assessed for intervals shorter than 6 months in those older than 2 years. However, more frequent height measurements allow a running look at growth and give a general impression of its adequacy.

Estimated Dry Weight and Weight-for-Age Percentile or SDS

Euvolemic weight should be determined regularly. The weight should be plotted on the weight-for-age curves, and the percentile and/or SDS should be calculated. Weight is an important part of any nutritional assessment. In CKD, it is important to ensure that weight is measured in a euvolemic state. This generally is referred to as "dry weight" because fluid overload is common in those with CKD stage 5. Children with chronic nephrotic syndrome also may have fluid overload, even at milder stages of CKD. Fluid overload will influence not just weight, but also may affect other anthropometric measures, such as

arm circumference and skinfold thicknesses.[38,39] Volume depletion also may be present in some conditions resulting in pediatric CKD (dysplasia, obstructive nephropathy, and cystinosis). It is equally important that the euvolemic weight be considered in these cases. 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 midweek postdialysis weight and the combination of noninvasive blood volume monitoring and the postdialytic vascular compartment refilling rate are used for evaluation purposes in an HD patient.[40] The weight at a monthly visit (minus dialysis fluid in the peritoneal cavity) is used for the child on PD therapy. The estimated dry weight is challenging to evaluate 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. Hypertension that resolves with dialysis can be indicative of excess fluid weight. Other responses to dialytic fluid removal, such as cramping or hypotension, may also give clues about the fluid status of the patient. Decreased serum sodium and albumin levels may be markers of overhydration. Rapid weight gain in the absence of a significant increase in energy intake or decrease in physical activity must be evaluated critically before it is assumed to be dry weight gain.

After the dry weight has been determined, it should be used to calculate the BMI and determine the weight-for-age percentile and/or SDS (or be plotted on the weight-for-age curves). As noted in the section on height, the 2006 WHO Growth Standards should be used as the reference for children up to 2 years; the 2000 CDC growth charts should be used for children older than 2 years. It is important to recognize that the weight-for-age SDS is not particularly useful in isolation—weight-for-age will be low in growth-retarded children. Rather, it should be interpreted in the context of the height-for-age SDS.

BMI-for-Height-Age Percentile or SDS

It is suggested that BMI be determined each time height and weight are measured. BMI should be plotted on the sex-specific BMI-for-age curves, and the percentile and/or SDS should be calculated. BMI is an accepted and easily calculated method of evaluating weight relative to height. However, BMI, calculated as weight (kg) divided by height (m) squared is not completely independent of either age or height. This is explained in part by age-related changes in body proportions and in part by mathematics: a 1-dimensional measure (height) will predict a 3-dimensional measure (increasing weight represents body growth in 3 dimensions) to the third power, not the second power.[41] The solution has been to express BMI relative to age in developing children.[42] In this relation, age functions as a surrogate for both height and maturation. Because height, age, and maturation are highly correlated in healthy children, this approach works reasonably well. Sex-specific BMI-for-age reference data permit calculation of BMI-for-age *z* scores or percentiles, allowing meaningful and consistent interpretation of BMI in normal children regardless of age. In children with kidney disease, in whom growth retardation and delayed maturation are common, this approach has limitations. Expressing BMI relative to chronological age in a child with growth and/or maturational delay will result in inappropriate underestimation of his or her BMI compared with peers of similar height and developmental age. To avoid this problem, it may preferable to express BMI relative to height-age in children with CKD—that is, the age at which the child's height would be on the 50th percentile.[38,523] This approach ensures that children with CKD are compared with the most appropriate reference group: those of similar height and maturation.

Height-age is believed to provide a reasonable surrogate for maturation in most children (ie, the age at which a child would be at the 50th percentile for height likely is close to the age at which most healthy children would have a similar level of sexual/physical development). Similarly, in children with short stature, expressing BMI relative to height-age will minimize errors that may occur as a result of the correlation between BMI-for-age and height-for-age. However, caution must be used in applying this approach to children outside the pubertal or peripubertal period, for whom the correlation between height-age and maturation is less clear. BMI relative to chronological age may be more logical in some

cases, particularly when sexual maturation is complete.

Although the weight-for-height index is a meaningful measure during early and midchildhood, BMI has the advantage of being applicable throughout the lifespan, from infancy to adulthood, and is becoming the standard method of assessing weight relative to height.[43] While BMI-for-age charts are now available from birth onwards, clinical experience in using and interpreting BMI before 24 months of age is limited, as are data on its association with current or future morbidity and for this reason, BMI is suggested rather than weight-for-height index after the age of 2 years.

The CDC defines underweight as a BMI-for-age less than the 5th percentile (www.cdc.gov/nccdphp/dnpa/growthcharts/training/modules/module1/text/page5a.htm; last accessed February 1, 2008).[44] A BMI-for-age greater than or equal to the 85th percentile is considered overweight, and greater than the 95th percentile, obese.[45] The WHO definitions of underweight differ somewhat from those used by the CDC. A BMI-for-age SDS of −2.0 (BMI-for-age ~ < 3rd percentile) recently has been proposed as a cutoff to define underweight or "thinness" in children. This definition is attractive because it corresponds to the cutoff for grade 2 thinness in adults (BMI, 17 kg/m^2).[43] However, no high-quality studies are available linking BMI less than a certain cutoff to poor outcomes in the general population. Therefore, no evidence-based definitions of undernutrition or "thinness" exist. Furthermore, the applicability of such definitions to the CKD population is unknown. Two large studies of adult HD patients demonstrated an inverse relationship between BMI and mortality risk, with no clear BMI threshold above which the risk stabilized or began to increase; mortality risk continued to decrease even as BMI increased to greater than 30 kg/m^2.[46,47] A smaller study of adult HD patients suggested increased mortality risk with BMI less than 17 and BMI greater than 23 kg/m^2 compared with those with BMI between 17.0 and 18.9 kg/m^2.[48] In children with stage 5 CKD, a U-shaped association was demonstrated between BMI-for-age SDS and mortality risk. Children with a BMI SDS either greater or less than 0.50 had a greater risk of mortality than those with a BMI SDS of 0.5; each 1.0-SD unit difference in BMI SDS was associated with a 6% greater risk of mortality.[49] It is important to recognize that this study only demonstrated an association between BMI and mortality, but could not establish a causal relationship. Furthermore, the additional mortality risk associated with BMI SDS greater or less than 0.5 was small.

Interpretability of BMI may be limited in the CKD population due to fluid overload. Clearly, any excess fluid will artificially increase BMI. Fluid overload representing 10% of the body weight will result in a BMI SDS approximately 0.5 to 1.0 SD units greater than what it would be at dry weight. Therefore, efforts should be made to use only a true dry weight when calculating BMI.

High-quality reference values for BMI relative to age are now available throughout childhood. The 2000 CDC revised growth charts include sex-specific BMI-for-age curves for children and adolescents between 2 and 20 years of age.[33] These curves, developed using a North American population, provide a contemporary BMI reference that recognizes the dependence of BMI on age and allow calculation of BMI-for-age SDS and percentiles. The 2006 WHO Growth Standards also include BMI standards for children from birth to 5 years of age (www.who.int/childgrowth/standards/technical_report/en/index.html; last accessed October 23, 2008).[34] Together, the WHO Growth Standards and the CDC growth charts provide reference values for BMI from birth to adulthood. As for length and height measures, BMI should be compared with the WHO Growth Standards up to 2 years of age and with the CDC growth charts thereafter (www.rcpch.ac.uk/doc.aspx?id_Resource=2862; last accessed October 23, 2008).

Head Circumference-for-Age Percentile or SDS

Head circumference should be measured regularly in children 3 years and younger. Head circumference should be plotted on the head circumference-for-age curves. Poor head growth is well documented in children with CKD,[50,51] with infants at highest risk. Although no studies have specifically related head circumference to nutritional status in CKD, regular measurements of head circumference in conjunction with intermittent developmental assessments are an important part of routine pediatric CKD care. The 2007

WHO Growth Standards should be used as a reference.[52]

Normalized Protein Catabolic Rate

PEM may have profound effects on growth and development and may be associated with increased risk of morbidity and mortality.

Protein catabolic rate (PCR) has been studied as an objective measure of DPI in stable patients receiving maintenance HD. PCR can be normalized to a patient's weight (nPCR); nPCR initially was studied in the 1980s as a marker of DPI in pediatric HD patients assumed to be in stable nitrogen balance.[53] Calculation of nPCR is based upon the increase in blood urea nitrogen (BUN) level from the end of 1 HD treatment to the beginning of the next treatment to calculate the urea generation rate (G; mg/min). nPCR originally was calculated by using formal urea kinetic modeling in association with Kt/V calculations.[54] Recent pediatric data demonstrate that algebraic formulas yield nearly identical nPCR results compared with formal urea kinetic modeling.[55] The algebraic nPCR calculation is as follows:

$$G\,(mg/min) = [(C2 \times V2) - (C1 \times V1)]/t$$

where C1 is postdialysis BUN (mg/dL), C2 is predialysis BUN (mg/dL), V1 is postdialysis total-body water (dL; V1 = 5.8 dL/kg × postdialysis weight in kg), V2 is predialysis total-body water (dL; V2 = 5.8 dL/kg × predialysis weight in kg), and t is time (minutes) from the end of the dialysis treatment to the beginning of the following treatment.

Then, nPCR is calculated by using the modified Borah equation[56]:

$$nPCR = 5.43 \times estG/V1 + 0.17$$

where V1 is total-body water (L) postdialysis (0.58 × weight in kg).

Data from adult studies demonstrate that the pre- and postdialysis BUN levels from the same treatment can be used to calculate nPCR; additional blood sampling from the next treatment is not necessary.[57] Recent pediatric data demonstrated increases in nPCR in malnourished children on HD therapy who received IDPN. In these studies, higher nPCR was associated with subsequent weight gain, whereas lower nPCR predicted future weight loss in adolescents.[58,59]

Comparison of nPCR versus serum albumin level in an entire single-center population, irrespective of nutrition status, showed that nPCR less than 1 g/kg/d of protein predicted a sustained weight loss of at least 2% per month for 3 consecutive months in adolescent and young adult–aged patients,[60] whereas serum albumin levels could not. In younger pediatric HD patients, neither nPCR nor serum albumin level was effective in predicting weight loss. This potentially could be explained by: (1) better nutritional status in infants and toddlers who are more likely to be tube fed, (2) a greater contribution of unmeasured urine urea clearance, (3) differences in protein catabolism, and/or (4) different growth rates in younger children compared with older children. It is also possible that because nPCR was derived in adult patients receiving HD, nPCR may be a valid measure only for patients of adult age or size.

Although no data exist to guide recommended optimal nPCR measurement frequency in HD patients, the same data needed for Kt/V calculation allow for nPCR calculation without additional blood sampling. Thus, nPCR can be monitored monthly along with Kt/V to follow up trends for a particular patient and provide an objective measure of protein intake.[61] The K/DOQI Adult Nutrition Guidelines recommend monthly assessment of nPCR for maintenance HD patients.[62] It is suggested that nPCR level be targeted to the age-specific protein intake guidelines noted in Recommendation 5.

In a manner similar to the evaluation of nPCR in patients receiving HD, it is recommended that the DPI of adults receiving PD be estimated several times per year by determination of the protein equivalent of nitrogen appearance (PNA).[63] This is calculated by measuring the urea nitrogen content of urine and dialysate, which represents the total nitrogen appearance (TNA), and multiplying that value by 6.25 (there are ~6.25 g of protein per 1 g of nitrogen).[64] Although limited data for this subject are available in pediatrics and the assessment is not regularly carried out in pediatric dialysis centers, Mendley and Majkowski[65] defined the relationship between urea nitrogen and TNA in children undergoing PD as follows:

$$\text{TNA (g/d)} = 1.03\ (\text{urea nitrogen appearance}) + 0.02\ (\text{weight in kg}) + 0.56\ (\text{for subjects age 0 to 5 years})\ \text{or}\ 0.98\ (\text{for subjects age 6 to 15 years})$$

Patient age was taken into consideration because of its relationship to dialysate protein loss.

Edefonti et al[66] later reported that incorporating dialysate protein nitrogen and body surface area (BSA) in the formula could improve the prediction of TNA. Their recommended formula is as follows:

$$\text{TNA (g/d)} = 0.03 + 1.138\ \text{urea-N}_{\text{urine}} + 0.99\ \text{urea-N}_{\text{dialysate}} + 1.18\ \text{BSA} + 0.965\ \text{protein-N}_{\text{dialysate}}$$

Limitations of PNA are that it is valid only when the patient is not anabolic or catabolic, the value changes rapidly when DPI is altered and thus may not reflect usual protein intake, and it should be normalized for patient size, although the best parameter to use has not been determined. In adults, normalization to ideal weight is recommended.

Other Measures Considered

Serum albumin: Serum albumin was recommended in the 2000 K/DOQI Nutrition Guidelines as a marker of nutritional status. Hypoalbuminemia is a common finding in those with CKD and consistently has been associated with increased mortality in both adults[46,67-69] and children with CKD.[70] Because PEM may lead to hypoalbuminemia, serum albumin level generally has been considered a useful index of nutritional status. However, important limitations have been identified with respect to the ability of serum albumin level to function as a reliable marker of malnutrition in the setting of CKD.[38,71-77] Serum albumin is depressed in the setting of both systemic inflammation and volume-overload states.[73,74] In the absence of inflammatory markers, hypoalbuminemia is not predictive of increased mortality.[77] Given the association of hypoalbuminemia with mortality, it remains an important component of the general evaluation of patients with CKD. However, the value of albumin as a marker of nutritional status is questionable. Hypoalbuminemia should lead to careful assessment of volume status and protein loss and to investigation for causes of systemic inflammation.

Mid-arm anthropometry: Mid-arm circumference (MAC) and triceps skinfold thickness (TSF) previously were recommended as part of the nutritional assessment in pediatric CKD.[62] TSF was considered to reflect total fat mass, and the combination of TSF and MAC were used to calculate the mid-arm muscle circumference (MAMC) and mid-arm muscle area (MAMA), which are purported to reflect total muscle mass. *These measures are no longer recommended as a part of routine assessment*. There are 4 main problems with the use of these measures.

First, it is difficult to obtain reliable measurements, particularly in patients with CKD. Skinfold thickness measurement is extremely operator dependent and lacks precision, except in very experienced hands.[78] In children with CKD, the presence of fluid overload may result in overestimates and poor reliability of skinfold thickness.[38] MAC is easier to reliably measure than TSF, but is even more susceptible to overestimation due to fluid overload.[38,39]

Second, it is not clear that MAMC and MAMA are accurate reflections of total muscle mass, even in otherwise healthy individuals.[38] The relationship between total muscle mass and MAMC or MAMA is even less clear in those with CKD. Abnormal regional distribution of lean tissue in patients with CKD[79] may result in a breakdown in the relationship between MAMC or MAMA and total muscle mass. Furthermore, the potential errors associated with TSF and MAC due to fluid overload and distorted fat and lean distribution may be compounded when they are combined in equations to calculate MAMC and MAMA. Arm measures failed to reliably detect decreased lean mass as measured by using in vivo neutron activation analysis in at least 1 study of adult HD patients.[80]

Third, deficits in these parameters have never been described convincingly in children with CKD. Although arm measures have been reported to be low relative to age in prior studies of children with CKD, there is little evidence that deficits exist when appropriate adjustments were made for short stature. Given that children with CKD are often short for age, proportionally smaller arm circumferences and skinfold thicknesses are expected. Arm measures would be expressed more appropriately relative to height or height-age. When this has been done, deficits

have been rare. In only 1 pediatric study in which TSF was adjusted appropriately for height were significant deficits in TSF seen—and only in younger children.[12] The mean TSF-for-height-age z score was high at +0.9 in a study of 56 children with CKD.[5] There is growing evidence that TSF and total fat mass are high relative to height in the CKD population. Mean total fat mass (determined by using dual-energy X-ray absorptiometry [DXA]) for height-age z score was +1.1 in 50 children with CKD stages 3 to 5.[11] One study of PD patients found mean MAC-for-height-age z scores of −1.1 in 12 children younger than 10 years and −0.1 in 12 children older than 10 years.[12] However, another study of 56 children with CKD stages 3 to 5 found a mean MAC-for-height-age z score of +0.4.[5]

Finally, few studies have investigated the link between TSF, MAC, MAMC, or MAMA and outcome in the CKD population. MAMC failed to be identified as an independent predictor of mortality in a 3-year longitudinal study of 128 adult HD patients.[68]

Dual-energy X-ray absorptiometry (DXA): A whole-body DXA scan provides excellent estimates of fat mass and lean mass.[81] The main limitation of DXA in patients with CKD is that it is unable to distinguish normally hydrated from overhydrated lean tissue; thus, it may overestimate lean mass in volume-overloaded subjects. DXA has been used extensively for body-composition assessment in adults with CKD and in several small studies of children with CKD.[11,82-86] Although deficits in lean mass relative to height-age have been demonstrated in children with CKD,[11] there are insufficient data to support a recommendation for regular DXA scans in children with CKD. The added value of a DXA scan over such a simple and inexpensive measure as BMI has yet to be proved. Significant advantages associated with the extra information provided by DXA would need to be clearly demonstrated to justify the expense.

Bioelectrical impedance analysis (BIA): BIA allows estimation of body fluid compartment volumes, which may then be used to make inferences about body composition.[87] However, despite extensive BIA studies, investigators have been unsuccessful at developing broadly applicable BIA methods that function well on the individual level.[88-93] Margins of error are so large as to render results of dubious clinical value. Abnormalities in volume status probably are the biggest problem limiting the interpretability of BIA measures in children with CKD. All BIA measures, including impedance and phase angle,[94-96] will change when either fluid status, fat mass, or lean mass changes. However, it is impossible to distinguish which change has occurred based on BIA measures.

Single-frequency whole-body BIA has been used in an effort to predict total-body water in children receiving maintenance dialysis.[93] The BIA-derived total-body water estimates were compared with total-body water measured by means of isotope dilution (gold standard). Although the group mean total-body water measured by using bioimpedance was within 170 mL of that measured by using isotope dilution, limits of agreement were wide (±17% of the true value). This means that an individual subject with a true total-body water volume of 30 L could be estimated to have a total-body volume as high as 35.1 L or as low as 24.9 L by using BIA.

Multiple-frequency BIA (bioimpedance spectroscopy) allows direct estimation of both extracellular fluid (ECF) and intracellular fluid volumes,[97] although estimates of ECF volumes are more accurate.[98] A small study of children with mild-to-moderate chronic renal insufficiency used whole-body bioimpedance spectroscopy to successfully estimate ECF volume within 6% of that measured by using isotope dilution.[91] Bioimpedance spectroscopy is a promising technique, particularly for estimating ECF, but it has not yet been adequately validated in children or adults with CKD.

Whole-body BIA has significant limitations when abnormalities in fluid distribution exist. The technique is insensitive to large changes in fluid volume in the trunk and very sensitive to small changes in the limbs.[99] To avoid this problem, a segmental bioimpedance technique has been developed in which each of 5 body segments (2 arms, 2 legs, and trunk) are measured separately.[99] In an effort to avoid overrepresentation of the limbs and underrepresentation of the trunk in the final total-volume calculation, impedance from each segment is given appropriate weight; this accounts for the different contributions of each segment to total resistance.[99] This technique may be particularly useful in fluid-

overloaded persons. However, it has not been validated in children.

A final potential application of BIA is to help determine whether an individual is euvolemic. Although promising techniques have been developed in this regard,[100,101] these methods have not yet been tested in children.

Multiparameter nutritional assessment scales: Because no single parameter has been found that will identify all patients at nutritional risk, multiparameter indices of nutritional status have been developed in attempts to improve accuracy. Multi-item measures may increase reliability, scope, and precision compared with 1 individual objective measure.

One such index was developed specifically for children on PD therapy.[102,103] Anthropometric and bioimpedance measures were combined to generate a score; however, the means by which the parameters were combined to arrive at a final score has limited justification and many of the component measures are highly correlated. Furthermore, the score is heavily influenced by single-frequency BIA measurements, which are of questionable value. The method does not appear practical for routine clinical practice.

Subjective Global Assessment (SGA), a method of nutritional assessment using clinical judgment rather than objective measures, has been widely used to assess nutritional status of adults with CKD[104] for both clinical and research purposes. The clinician performing SGA considers 5 features of a medical-nutrition history (weight loss, dietary intake, gastrointestinal symptoms, functional capacity, and metabolic stress) and 4 features of a physical examination (subcutaneous fat loss, muscle wasting, edema, and ascites) to assign the patient an overall rating of well nourished, moderately malnourished, or severely malnourished without adhering to any kind of rigid scoring system.[105,106] An SGA specifically for the pediatric population recently has been developed and validated in children undergoing major surgery.[107] Applicability of this pediatric Subjective Global Nutrition Assessment (SGNA) in children with CKD is currently being studied.

Frequency of Assessment

1.3: It is suggested that the frequency of monitoring nutritional and growth parameters in all children with CKD stages 2 to 5 and 5D be based on the child's age and stage of CKD. (C) In general, it is suggested that assessments be performed at least twice as frequently as they would be performed in a healthy child of the same age. (C) Infants and children with polyuria, evidence of growth delay, decreasing or low BMI, comorbidities influencing growth or nutrient intake, or recent acute changes in medical status or dietary intake may warrant more frequent evaluation. (C)

The frequency with which a nutritional evaluation should be conducted depends on both the age of the child and the severity of CKD (Table 1). Current recommendations for measurement of growth parameters in *healthy* infants and children vary slightly by country. In general, 2 assessments are recommended in the first month, then monthly until 2 months of age, every 2 months until 6 months of age, every 3 months until 18 months of age, every 6 months until 2 years of age, and then yearly thereafter.[108,109]

Given that nutritional intake and growth may be impaired even with mild CKD in infants—and that these improve with nutritional supplementation[17,18,110,111]—it is suggested that growth parameters be monitored at least twice as frequently in infants with moderate CKD as is recommended for healthy infants. More frequent evaluations are required in infants with severe CKD (stages 4 to 5 and 5D). Early recognition of growth delay in infancy is crucial because growth failure in this critical period is extremely difficult to catch up later.[16,30] Any evidence of retarded growth in an infant should prompt detailed dietary assessment and intervention.

In older children, the impact of CKD on growth and body fat and lean stores appears to depend to a large degree on the severity of CKD. A "dose-response" relationship between glomerular filtration rate (GFR) and BMI-for-age *z* score was noted in 1 study, with lower GFR associated with lower mean BMI-for-age *z* score.[28] Again, given the risks of growth retardation in children with CKD, assessment of growth parameters is suggested to be performed at a minimum of every 6 months in children with CKD stages 2 to 3, ie, at least twice as often as recommended for healthy children. For children with more advanced CKD (stages 4 to 5 and 5D), more frequent evaluation may be warranted due to the greater risk of abnormalities.

Every effort should be made to conduct nutritional status assessments when the child is euvolemic.

These recommendations represent the minimum intervals for assessment. More frequent evaluation may be warranted in children with evidence of growth delay, decreasing or low BMI, any comorbidities potentially influencing growth or nutrient intake, or recent acute changes in medical status or dietary intake. Three-day food records at intervals more frequent than every 3 to 6 months are not required for infants or children with good appetites, grossly adequate dietary intakes, and adequate weight gain. More frequent records are indicated when there is concern about the adequacy of a child's intake or overconsumption of 1 or more nutrients.

COMPARISON TO OTHER GUIDELINES

The Caring for Australasians with Renal Impairment (CARI) CKD Guidelines recommend assessment of dietary intake, height/length, weight, head circumference, and BMI at 1- to 3-month intervals and suggest that determination of SDS for the anthropometric measures is preferable to simply plotting on the percentile curve. They also suggest expressing BMI relative to height-age rather than chronological age. MAC and TSF are not recommended by CARI due to a lack of evidence supporting their use. The use of nPCR is not advocated for in the CARI nutrition guidelines, although these guidelines were established before many of the recent studies cited were published.

The European ad hoc Committee on Assessment of Growth and Nutritional Status in Peritoneal Dialysis recommends a nutritional assessment, including height/length, weight, head circumference, MAC, and BMI, at a minimum interval of every month in children younger than 5 years and every 2 months for older children. TSF is not recommended due to poor reliability. They suggest assessment of dietary intake at least every 6 months and more frequently in infants. Caution is advised in interpreting serum albumin levels due to their poor reliability in indicating undernutrition. DXA is considered a nonessential measurement tool; it is suggested no more often than yearly. BIA also is considered nonessential since concerns with interpretability of BIA measures are raised. It is suggested that BIA be used only in combination with other assessment methods.

The 2006 update of the KDOQI Pediatric HD Adequacy Guidelines recommends monthly nPCR assessment.[63]

LIMITATIONS

Two main limitations with prior studies were identified. Many failed to distinguish older children from infants and very young children, in whom the impact of nutrition on growth and body composition may be quite different. Many prior studies also failed to account for CKD-related short stature when describing body composition, expressing measures relative to age rather than height. This resulted in overestimation of deficits in weight, fat and lean masses, and arm measures.

RESEARCH RECOMMENDATIONS

- Validity of 3-day diet records and 24-hour recalls in the CKD population in whom underreporting of restricted foods may be common.
- Identification of clinically relevant biomarkers for—and clinical predictors of—CKD-related protein-energy wasting.
- Determination of the prevalence of protein-energy wasting in pediatric CKD and how this relates to severity of CKD.
- Predictive value of BMI SDS in identifying protein-energy wasting.
- Identification of simple clinical markers of protein-energy wasting.
- Identification of objective methods of determining volume status.
- Further study of nPCR is warranted to identify nPCR values reflecting adequate protein intake for different pediatric patient age groups.
- The normalized PNA (nPNA) should be studied as an objective measure of protein intake for children receiving maintenance PD.
- Further work to develop and validate multiparameter nutritional assessment scales, such as the SGA, is warranted.

RECOMMENDATION 2: GROWTH

INTRODUCTION

Growth failure and linear height deficit are the most visible complications of CKD in children and are associated with serious medical and psychological comorbidities.

Early nutritional intervention and the prevention and treatment of metabolic deficits are key components in the preservation of growth in a child with CKD. In children who demonstrate poor growth despite these measures, the addition of rhGH therapy can be beneficial.

2.1 Identification and treatment of existing nutritional deficiencies and metabolic abnormalities should be aggressively pursued in children with CKD stages 2 to 5 and 5D, short stature (height SDS < −1.88 or height-for-age < 3rd percentile), and potential for linear growth. ***(A)***

2.2 The serum bicarbonate level should be corrected to at least the lower limit of normal (22 mmol/L) in children with CKD stages 2 to 5 and 5D. ***(B)***

2.3 rhGH therapy should be considered in children with CKD stages 2 to 5 and 5D, short stature (height SDS < −1.88 or height-for-age < 3rd percentile), and potential for linear growth if growth failure (height velocity-for-age SDS < −1.88 or height velocity-for-age < 3rd percentile) persists beyond 3 months despite treatment of nutritional deficiencies and metabolic abnormalities. ***(B)***

RATIONALE

2.1: Identification and treatment of existing nutritional deficiencies and metabolic abnormalities should be aggressively pursued in children with CKD stages 2 to 5 and 5D, short stature (height SDS < −1.88 or height-for-age < 3rd percentile), and potential for linear growth. (A)

A variety of factors can contribute to the poor growth seen in children with CKD.[112] Interventions to normalize inadequate protein and calorie intake, water and electrolyte losses in those with polyuric and salt-wasting conditions, metabolic acidosis (see Recommendation 2.2), renal osteodystrophy, and resistance to hormones mediating growth must be aggressively managed.

Protein-Energy Malnutrition

Caloric deficiency and abnormal protein metabolism may have an important role in growth impairment, particularly in infants and younger children.[113] Reduced caloric intake may be a result of anorexia, emotional distress, altered taste sensation, or nausea and vomiting. Prior studies provided evidence that energy intake significantly correlated with growth velocity in children with CKD that developed during infancy, such that normal growth occurred if energy intake exceeded 80% of recommended values, whereas it would be expected to cease if intake decreased to less than 40%.[114] Early nutritional interventions, including tube feeding in infants, and prevention and treatment of metabolic deficits of CKD are fundamental measures for preventing severe stunting in the first 2 years of life.[111,115] Studies also have shown that nutritional supplementation in malnourished children with CKD can result in improved growth.[18,111,116] Finally, there is recent evidence that frequent (daily) HD is associated with enhanced nutrition and a normal height velocity.[117]

Salt Wasting

Infants with renal dysplasia typically exhibit the most severe height deficits, which may reflect the age at onset of kidney disease, degree of tubular abnormality inherent in the condition, and the resultant loss of sodium and other substances important for growth.[118] Thus, salt supplementation for a polyuric infant with CKD who is growing poorly may be therapeutic.[111,119,120]

Renal Osteodystrophy

Growth can be adversely affected by renal osteodystrophy. Renal osteodystrophy represents a range of disorders, from secondary hyperparathyroidism and high-turnover bone disease to low-turnover osteomalacia and adynamic bone disease.[118] Secondary hyperparathyroidism may cause growth failure by modulating genes involved in endochondral bone formation and altering the architecture of the growth plate. A key component of the management of high-turnover bone disease is control of serum phosphorus

level. Dietary and medication therapy are designed to target a normal serum phosphorus level for age. The prevention/correction of adynamic bone disease requires close monitoring of dietary calcium intake and vitamin D therapy with a goal of maintaining serum calcium level in the normal range.[121]

Corticosteroids

The use of corticosteroids can lead to suppression of growth in children with CKD by their effect on the integrity of the somatotropic hormone axis.[122] The action of corticosteroids is at various levels of the axis and involves suppression of pituitary growth hormone release by stimulating hypothalamic somatostatin tone, downregulation of hepatic growth hormone receptors, inhibition of insulin-like growth factor (IGF) bioactivity, alteration of the IGF-binding protein serum profile, and a direct suppressive effect on local growth factor and tissue matrix production.[123] Discontinuing or modifying the dose of corticosteroids is in turn desirable from the perspective of growth as long as the patient's medical condition that prompted the use of the corticosteroids is not exacerbated.

2.2: Serum bicarbonate level should be corrected to at least the lower limit of normal (22 mmol/L) in children with CKD stages 2 to 5 and 5D. (B)

CKD-induced acidosis impedes statural growth through a variety of mechanisms, which lead to both endogenous growth hormone and rhGH resistance. Optimal growth in children with CKD will be achieved with acid-base status normalization.

Metabolic acidosis develops in adult patients with CKD stages 4 to 5.[25,26] Metabolic acidosis may impede statural growth through a number of growth factor–specific mechanisms, including reduction in thyroid hormone levels and blunting of IGF response to rhGH, which has been demonstrated in healthy adult patients after long-term acid loading.[124,125] Animal data also suggest an acidosis-induced human growth hormone–IGF-1 axis impairment[118] by decreasing pulsatile growth hormone secretion,[126] hepatic IGF-1 and growth hormone receptor messenger RNA (mRNA) production,[127] and IGF-1 expression at the level of the chondrocyte.[128] Metabolic acidosis also can impede growth through mechanisms not specific to growth factor impairment, such as increased protein catabolism,[129,130] increased calcium efflux from bone,[131,132] and decreased albumin synthesis.[133]

No data exist to evaluate the efficacy of isolated acidosis correction on growth failure in children with CKD, likely because growth retardation in children with CKD is multifactorial.[112] However, data show a profound growth improvement in children with isolated renal tubular acidosis treated with alkali therapy.[134,135] Because these studies showed that maximal height was inversely related to the duration of acidosis before therapy, oral alkali therapy should be initiated when persistent acidosis is observed in children with CKD. Oral alkali can be prescribed in the form of sodium bicarbonate or sodium citrate preparations, but citrate preparations should not be prescribed to patients receiving aluminum-based phosphorus binders because citrate enhances enteral aluminum absorption.

In children on dialysis therapy who have persistent acidosis, a trial of increased dialysis dose and/or a higher bicarbonate bath concentration can be considered to correct acidosis. Although no studies evaluated the effect of increasing dialysis dose in patients with persistent acidosis, 1 pediatric study demonstrated better growth rates in children receiving continuous ambulatory PD (CAPD) versus continuous cycler-assisted PD (CCPD) versus HD that may have been explained partially by better uremic control and acidosis correction by using CAPD.[136]

2.3: rhGH therapy should be considered in children with CKD stages 2 to 5 and 5D, short stature (height SDS < −1.88 or height-for-age < 3rd percentile), and potential for linear growth if growth failure (height velocity-for-age SDS < −1.88 or height velocity-for-age < 3rd percentile) persists beyond 3 months despite treatment of nutritional deficiencies and metabolic abnormalities. (B)

The growth hormone–IGF-1 axis is an important regulator of growth and metabolism, and substantial abnormalities in the axis have been identified in children with CKD, all of which result in growth hormone resistance. These abnormalities include decreased expression of the growth hormone receptor, impaired signal transduction of the growth hormone receptor, decreased production of IGF-1, and decreased

activity of IGF by inhibitory IGF-binding proteins.[112,123,137] Despite the presence of these inhibitory factors, the use of rhGH regularly results in improved height velocity in children with CKD.[112,137-141]

Use in CKD Stages 2 to 5

Clinical trials have demonstrated the safety and efficacy of rhGH therapy in promoting linear growth in children with CKD.[112,142] Fifteen randomized clinical trials examining rhGH versus placebo have demonstrated improvement in height SDS, height velocity, and height velocity SDS, with the most dramatic response occurring in the first year of treatment followed by a progressively reduced effect thereafter. The target height deficit at the initiation of therapy and duration of treatment are the most important predictors of cumulative height gain.[143] Long-term rhGH therapy in children with CKD has been shown to result in catch-up growth, and many patients achieve a final height within the normal range.[32,143-146]

Hokken-Koelega et al[145] found that treatment during puberty was associated with a sustained improvement in height SDS without deleterious effects on GFR and bone maturation. Treatment showed no significant increase in the incidence of malignancy, slipped capital femoral epiphysis, avascular necrosis, glucose intolerance, pancreatitis, progressive deterioration in renal function, fluid retention, or incidence of benign intracranial hypertension.[112] In a recent analysis of data contained in an international growth database of children with CKD, Nissel et al[143] revealed that the increment in height SDS during the first year of rhGH treatment was greatest in patients who were prepubertal and experienced a normal onset of puberty and those who had early puberty.

Use in Dialysis Patients

Clinical studies support the efficacy of rhGH therapy in patients requiring kidney replacement therapy. Whereas children receiving dialysis experience an increase in growth with rhGH therapy, the response is less than that of patients with earlier stages of CKD, thus emphasizing the need to initiate rhGH therapy at a young age and/or early in the evolution of CKD to maximize the achievement of growth potential.[32,143,144]

Use in Transplant Patients

Poor growth outcomes after kidney transplantation are associated with corticosteroid use, persistent CKD, and abnormalities of the growth hormone–IGF-1 axis. The use of rhGH after transplantation does lead to catch-up growth, and Fine et al[147] demonstrated that final height was superior in rhGH-treated kidney transplant patients compared with controls, with no adverse effect on allograft function. In most cases, initiation of rhGH therapy has been delayed until 1 year or more after kidney transplantation.[147]

COMPARISON TO OTHER GUIDELINES

- The CARI CKD Guidelines recommend that rhGH therapy be offered to short children (height $<$ 25th percentile for chronological age, height velocity $<$ 25th percentile for bone age) with CKD stages 2 to 5 and 5D.
- The European Pediatric Peritoneal Dialysis Working Group recommends that rhGH be considered in PD patients with growth potential only after nutritional parameters, with acidosis, hyperphosphatemia, and secondary hyperparathyroidism have been corrected.
- The CARI CKD Guidelines also recommend normalization of serum bicarbonate level to greater than 22 mmol/L in patients with CKD.

LIMITATIONS

- The lack of randomized controlled trials in children on dialysis therapy and after transplantation is an obstacle to our understanding of whom to treat with rhGH and what dose to use to achieve the best possible growth.
- Because CKD-related growth failure and the nature of acidosis are often multifactorial, few studies will be able to address the acidosis-related contributions directly. It would be unethical to prospectively randomly assign children to an acidosis arm given the known adverse effects of acidosis.

RESEARCH RECOMMENDATIONS

- Evaluations of rhGH dosing regimens that are titrated to the level of IGF-1.

- Study of non–growth-related benefits of rhGH therapy in children, such as psychosocial and quality-of-life benefits, bone development, neurodevelopment, and cardiovascular benefits.
- Evaluation of methods to overcome the poor use of rhGH in children with CKD and poor growth.[148]
- Study of the pathophysiological factors contributing to poorer response to rhGH in children on dialysis therapy compared with children before dialysis therapy.
- Further study of the impact of frequent HD on growth, with or without the use of rhGH.
- Studies of the effect of CKD-related acidosis and its treatment will need to assess children who are acidotic at baseline because it would be unethical to randomly assign children to an acidosis arm prospectively. The clinical and animal model data cited argue for correction of or controlling for the presence of acidosis in any study assessing growth outcomes in pediatric patients with CKD. Recent preliminary data for more frequent or intensive HD demonstrate improved growth profiles[149,150] that could be explained in part by improved acid-base status. Such studies should be expanded in the future.

RECOMMENDATION 3: NUTRITIONAL MANAGEMENT AND COUNSELING

INTRODUCTION

Malnutrition, growth delay, and nutrition-related metabolic abnormalities are common in children with CKD and are associated with a greater risk of morbidity and mortality. Numerous studies of infants and young children have documented energy intakes less than 80% of recommendations,[9,151,152] with reversal of both weight loss and poor growth when nutritional therapy is provided to meet recommendations. Although other factors are involved, nutritional care and therapy are essential to prevent or correct these disturbances and are vital components of the multidisciplinary management of children with CKD. Individualized nutrition care plans require frequent modification according to changes in the child's age, development, residual kidney function, and mode of kidney replacement therapy.

3.1 Nutrition counseling based on an individualized assessment and plan of care should be considered for children with CKD stages 2 to 5 and 5D and their caregivers. ***(B)***

3.2 Nutritional intervention that is individualized according to results of the nutritional assessment and with consideration of the child's age, development, food preferences, cultural beliefs, and psychosocial status should be considered for children with CKD stages 2 to 5 and 5D. ***(B)***

3.3 Frequent reevaluation and modification of the nutrition plan of care are suggested for children with CKD stages 2 to 5 and 5D. ***(C)*** **More frequent review is indicated for infants and children with advanced stages of CKD, relevant comorbidities influencing growth or nutrient intake, and evidence of inadequate intake or malnutrition or if acute illness or adverse events occur that may negatively impact on the nutritional status.** ***(C)***

3.4 Nutritional management coordinated by a dietitian who ideally has expertise in pediatric and renal nutrition is suggested for children with CKD stages 2 to 5 and 5D. ***(C)*** **It is suggested that nutritional management be a collaborative effort involving the child, caregiver, dietitian, and other members of the multidisciplinary pediatric nephrology team (ie, nurses, social workers, therapists, and nephrologists).** ***(C)***

RATIONALE

3.1: Nutrition counseling based on an individualized assessment and plan of care should be considered for children with CKD stages 2 to 5 and 5D and their caregivers. (B)

Children with CKD frequently have poor appetites and require modification of dietary nutrient intake to maintain optimal nutrition, growth, and development. Studies have shown that the caloric intake of infants and young children with CKD is frequently less than 80% of recommended intake,[9,151,152] and that low intakes and decreased rates of weight gain and growth may occur early in those with CKD and worsen with increasing severity of CKD.[9,28,153] Correction of nutritional deficits through enhanced nutrition in the form of oral supplements and/or tube feeding achieves catch-up weight gain for all and catch-up linear growth for infants and young children.[17,18,111,150,154-156] Alterations to fluid or dietary intake of protein, carbohydrate and/or fat, phosphorus, sodium, potassium, or calcium may be required. Vitamin, mineral, or trace element supplements also may be needed.

Nutrition counseling is performed based on the nutritional assessment and nutrition prescription and is recommended on a frequent basis because of the dynamic nature of a child's growth, food preferences, development, medical condition, and level of independence. Intensive counseling should occur at the time of initial presentation; when undesirable changes in appetite, weight gain, linear growth, blood work, blood pressure, or fluid balance occur; or when the method of kidney replacement therapy is altered. Dietary counseling should be positive in nature, providing information about foods the child can eat to replace foods that they must limit or avoid. Family members and primary caregivers should be involved in the education process to be sure

the child has appropriate foods available and to provide consistent support for recommended food and fluid modifications, as well as encouragement for nutrient consumption. Counseling must be targeted at the appropriate education level of the child and family member.

Evidence from studies using dietary intervention indicates that frequent nutrition counseling results in adherence and improved outcomes in the general pediatric population[157-159]; however, there are limited studies of the CKD population. A randomized controlled trial of individualized nutritional counseling and frequent follow-up in adults with CKD stages 4 or 5 showed positive changes in energy intake, nutritional status according to SGA, and body cell mass in the intervention group compared with the control group.[160]

3.2: Nutritional intervention that is individualized according to results of the nutritional assessment and with consideration of the child's age development, food preferences, cultural beliefs, and psychosocial status should be considered for children with CKD stages 2 to 5 and 5D. (B)

Indications for nutritional intervention include:

- impaired ability to ingest or tolerate oral feedings,[1]
- increased metabolic requirements,[1]
- documented inadequate provision or tolerance of nutrients,[1]
- acute weight loss of 10% or more,[1]
- a BMI value less than 5th percentile for height-age (underweight) or greater than 85th percentile (overweight),
- inadequate weight gain, length/height more than 2 SDs below the mean (<3rd percentile), or a significant decrease in usual growth percentile,
- abnormalities in nutrition-related biochemistries.

Neonates should also be considered at nutritional risk if they are preterm or have:

- low birth weight (<2,500 g) even in the absence of gastrointestinal, pulmonary, or cardiac disorders,
- a birth weight *z* score less than −2 SDs (<3rd percentile) for gestational age,[1]
- polyuria and inability to concentrate urine.

In addition to providing fuel for the body to function, food and beverages have an important role in family and social life and induce feelings of satisfaction, pleasure, and comfort. Promoting quality of life and patient satisfaction is a critical component of effective health care; therefore, diet and fluid restrictions should be individualized and imposed only when clearly needed. They should be kept as liberal as possible to achieve recommended energy and protein intakes and optimal weight gain and growth. Restrictions can be adjusted based on responses in relevant parameters. Children who are polyuric, have residual kidney function, or are on daily dialysis therapy[149] typically require less stringent restrictions.

Promoting satisfaction with a prescribed diet is an important component of effective nutrition intervention. Many factors are involved in satisfaction with and adherence to prescribed diets, including the complexity of the diets and differences between the patient's typical eating pattern and the prescribed one. An eating pattern that incorporates personal, ethnic, and cultural food preferences and gives satisfaction and pleasure while meeting prescribed medical recommendations is likely to support long-term maintenance of dietary changes.[161] The Modification of Diet in Renal Disease (MDRD) Study of adults with CKD measured patient satisfaction with modified protein and phosphorus eating patterns and the relationship of satisfaction to adherence.[162] Results showed that satisfaction decreased as the magnitude of diet changes increased, and that patient adherence to diet modification was related to their satisfaction with diet. In a study of adult Hispanic patients on HD therapy, knowledge of the renal diet, food-frequency consumption, socioeconomic status, family support, and attitudes toward the renal diet were identified as factors that influenced dietary adherence.[163] Patient education provided in the patient's native language also was an important element promoting adherence.

3.3: Frequent reevaluation and modification of the nutrition plan of care is suggested for children with CKD stages 2 to 5 and 5D. (C) More frequent review is indicated for infants and children with advanced stages of CKD, relevant comorbidities influencing growth or nutrient intake, evidence of inadequate intake

or malnutrition, or if acute illness or adverse events occur that may negatively impact on the nutritional status. (C)

The nutrition plan of care synthesizes information obtained from the nutritional assessment to determine short- and long-term goals from which the nutrition prescription and plan for individualized nutritional therapy is developed. The plan of care is developed in collaboration with the child and caregivers and shared with the multidisciplinary team. The nutrition care plan should be reviewed often with the child and all caregivers to keep them informed and improve adherence. Conditions that dictate more frequent evaluation of the nutrition plan of care include young age; unfavorable changes in anthropometric measures, oral intake, gastrointestinal function, nutrient-related laboratory values, or fluid or blood pressure status; indication of nonadherence with recommendations; prolonged or large doses of glucocorticosteroids; change in psychosocial situation; or when placement of an enteral feeding tube is under consideration. In these cases, updates to the care plan monthly or more often may be necessary.

Studies reporting stabilization or improvement in growth parameters with nutritional care and therapy have involved a multidisciplinary approach with frequent assessments and counseling by pediatric renal dietitians, many of which occurred at least monthly.[17,18,149,150,156,164,165] In a prospective longitudinal study to estimate the amount of dietetic care necessary to support and achieve adequate nutritional intake for growth in children (n = 13; age, 0.2 to 8.5 years) on long-term PD therapy with or without tube feeding, all direct and indirect contacts by the dietitian were recorded over a 3-year period.[164] During this time, mean weight SDS and BMI SDS improved (weight SDS, −1.32 to −0.73; BMI SDS, −0.91 to 0.17; $P = 0.03$). The mean number of dietetic contacts per patient per month was greater for children younger than 5 years (n = 5; 5.9 ± 1.9) compared with the older children (n = 8; 3.1 ± 1.6). The majority of all contacts (82%) were with children with feeding tubes (n = 8).

In the MDRD Study,[166] a variety of counseling strategies and sustained monthly support from dietitians helped prevent relapse and stimulated study participants' ability to improve their application of skills over time.[167] This was demonstrated in the follow-up period by the ability of the patients on the low-protein and very-low-protein diets to adhere to modifications and decrease their protein intake further over time.

3.4: Nutritional management coordinated by a dietitian who ideally has expertise in pediatric and renal nutrition is suggested for children with CKD stages 2 to 5 and 5D. (C) It is suggested that nutritional management be a collaborative effort involving the child, caregiver, dietitian, and other members of the multidisciplinary pediatric nephrology team (ie, nurses, social workers, therapists, and nephrologists). (C)

A registered dietitian should be a central and integral part of dietary management. Registered dietitians are proficient in the assessment and ongoing evaluation of the patient's nutrition status and development of the diet prescription and nutrition care plan. The pediatric population requires a registered dietitian skilled in the evaluation of growth and the physical, developmental, educational, and social needs of children. At a minimum, registered dietitians should be responsible for assessing the child's nutritional status; developing the nutrition plan of care; providing culturally sensitive education and counseling at the appropriate age level for patients, family members, and/or caregivers; making recommendations for implementing and adjusting oral, enteral, and parenteral nutrition; monitoring the patient's progress, including adherence to the nutrition prescription and documentation of these services.

Early involvement of occupational or speech therapists and pediatric psychologists or psychiatrists who specialize in feeding problems is invaluable for managing chewing/swallowing/food-refusal issues in toddlers, avoiding oral hypersensitivity in tube-fed infants, and enabling the smooth transition from tube feeding to complete oral feeds after transplantation.[17,154,168,169]

Nonadherence to dietary modifications is a recurring problem for children, especially in children lacking family support or adolescents rebelling against parental supervision. However, there has been limited study of dietary compliance in this population. In 2 prospective studies, adherence to a low-sodium diet was poor[165] and a decrease in use of nutritional supplements was

observed during a 2-year period despite intensive counseling to continue their use.[156] A program for the maintenance of special diets based on a token system of reinforcement was successful in effecting improved dietary behaviors related to intradialytic weight gain and excessive dietary protein and potassium intake in 4 children (aged 11 to 18 years) on HD therapy with longstanding compliance issues.[170] Social workers, child life therapists, and nurses can provide additional coping strategies to children and families to help them deal with the frustrations and burdens around feeding problems, diet restrictions, and nutritional support and improve their ability to adhere to new regimens. Pharmacists can work with children and families to find the most acceptable liquid or solid form of such medications as phosphate binders, iron supplements, renal multivitamins, and gastrointestinal motility agents and help them develop medication schedules that fit their feeding schedule and lifestyle and result in optimal drug effectiveness.

The financial burden of dietary manipulation and nutritional supplementation can be excessive for some families, and social workers can identify sources of funding and facilitate funding applications for eligible families. As examples, the daily cost to a family of providing an additional 250 calories through commercial carbohydrate modules (glucose polymers) is approximately $2.00, and the cost of providing 100% of nutritional needs to a 3-year-old child through G-tube feeding using a commercial adult renal feeding product is about $14.30.

Collaboration and good communication among all members of a family-centered team best suit the needs of the child and family and work toward achieving the ideal outcomes for the child.[156,165,171]

COMPARISON TO OTHER GUIDELINES

- The 2005 CARI Guidelines on Nutrition and Growth in Kidney Disease state that nutritional assessment and counseling is regarded as mandatory in the management of children with CKD and suggest that nutritional assessment and counseling by a pediatric renal dietitian should take place at 1- to 3-month intervals.[172]
- The American Heart Association Scientific Statement on cardiovascular risk reduction in high-risk pediatric patients, including those with CKD, recommends initial rigorous age-appropriate diet counseling by a dietitian followed by specific diet/weight follow-up every 2 to 4 weeks for 6 months.[173]

LIMITATIONS

Whereas it is assumed that consistent promotion of the benefits of dietary modification and provision of practical information and emotional support to children and their families can positively influence adherence and clinical outcomes and minimize stress around nutritional issues, there have been no high-quality studies to demonstrate such results in children with CKD.

RESEARCH RECOMMENDATIONS

- The effect of intensive and frequent dietary counseling for nutritional intake, nutritional status, quality of life, and occurrence of nutrition-related morbidities should be evaluated at various stages of CKD to identify how early in the progression of CKD nutrition intervention should occur and aid in determining adequate allocation of pediatric renal dietitians within programs.
- Studies are needed to evaluate strategies to enhance dietary adherence, with particular emphasis on the adolescent age group.

RECOMMENDATION 4: ENERGY REQUIREMENTS AND THERAPY

INTRODUCTION

Poor energy intake is common in children with CKD stages 2 to 5 and 5D due to reduced appetite and vomiting. Early intervention is critical with the introduction of tube feeds if energy requirements cannot be met by the oral route alone. A smaller percentage of children have excessive energy intake, and dietary intervention and lifestyle changes are needed to address the short- and long-term complications of overweight and obesity.

4.1 Energy requirements for children with CKD stages 2 to 5 and 5D should be considered to be 100% of the EER for chronological age, individually adjusted for PAL and body size (ie, BMI). ***(B)*** **Further adjustment to energy intake is suggested based upon the response in rate of weight gain or loss.** ***(B)***

4.2 Supplemental nutritional support should be considered when the usual intake of a child with CKD stages 2 to 5 or 5D fails to meet his or her energy requirements and the child is not achieving expected rates of weight gain and/or growth for age. ***(B)***

4.3 Oral intake of an energy-dense diet and commercial nutritional supplements should be considered the preferred route for supplemental nutritional support for children with CKD stages 2 to 5 and 5D. ***(B)*** **When energy requirements cannot be met with oral supplementation, tube feeding should be considered.** ***(B)***

4.4 A trial of IDPN to augment inadequate nutritional intake is suggested for malnourished children (BMI-for-height-age < 5th percentile) receiving maintenance HD who are unable to meet their nutritional requirements through oral and tube feeding. ***(C)***

4.5 A balance of calories from carbohydrate and unsaturated fats within the physiological ranges recommended as the AMDR of the DRI is suggested when prescribing oral, enteral, or parenteral energy supplementation to children with CKD stages 2 to 5 and 5D. ***(C)***

4.6 Dietary and lifestyle changes are suggested to achieve weight control in overweight or obese children with CKD stages 2 to 5 and 5D. ***(C)***

RATIONALE

4.1: Energy requirements for children with CKD stages 2 to 5 and 5D should be considered to be 100% of the EER for chronological age, individually adjusted for PAL and body size (ie, BMI). Further adjustment to energy intake is suggested based upon the response in rate of weight gain or loss. (B)

In children with CKD (excluding CKD stage 5), spontaneous energy intake decreases with deteriorating kidney function,[28] but there is no evidence that children with CKD have different energy requirements than those for healthy children. In a recent study of 25 children and adolescents with CKD stage 5 on HD therapy, resting energy expenditure measured by using indirect calorimetry was the same as for healthy age-matched controls when adjusted for lean body mass.[174] In 65 children aged 2 to 16 years with conservatively managed CKD (GFR < 75 mL/min/1.73 m^2), regular dietetic advice with particular attention to optimizing energy intake with or without the use of supplements maintained or significantly increased the height SDS with an energy intake maintained within the normal range.[156] In 35 children younger than 5 years with CKD stages 4 to 5, significant weight gain and accelerated linear growth was clearly demonstrated in those starting enteral feeding at age younger than 2 years; improved weight gain and maintenance of growth was observed in those starting enteral feeds at age 2 to 5 years without exceeding normal energy requirements.[18] The findings are similar to an earlier study of 22 children age 0.2 to 10 years on long-term dialysis therapy in which there was significant improvement in both height and weight SDS with an energy intake within the normal range.[154] Improved linear growth also has been demonstrated in 12 prepubertal or early pubertal children on HD therapy with increased time on dialysis and close monitoring of nutritional

Table 2. Equations to Estimate Energy Requirements for Children at Healthy Weights

Age	Estimated Energy Requirement (EER) (kcal/d) = Total Energy Expenditure + Energy Deposition
0-3 mo	EER = [89 × weight (kg) − 100] + 175
4-6 mo	EER = [89 × weight (kg) − 100] + 56
7-12 mo	EER = [89 × weight (kg) − 100] + 22
13-35 mo	EER = [89 × weight (kg) − 100] + 20
3-8 y	Boys: EER = 88.5 − 61.9 × age (y) + PA × [26.7 × weight (kg) + 903 × height (m)] + 20
	Girls: EER = 135.3 − 30.8 × age (y) + PA × [10 × weight (kg) + 934 × height (m)] + 20
9-18 y	Boys: EER = 88.5 − 61.9 × age (y) + PA × [26.7 × weight (kg) + 903 × height (m)] + 25
	Girls: EER = 135.3 − 30.8 × age (y) + PA × [10 × weight (kg) + 934 × height (m)] + 25

Source: ref 175.
See Appendix 2.

intake. This was achieved with an intake of 90.6% of the recommended energy intake.[150] The importance of caloric intake has also been shown in 31 prepubertal children on dialysis therapy treated with growth hormone, with a positive correlation between energy intake and growth velocity.[26]

All children with CKD stages 2 to 5 and 5D should have regular dietary assessments, with the frequency dependent on the degree of renal impairment to ensure EER for age, sex, and PAL (Tables 2 to 4; Appendix 2, Table 34 for online calculator) are achieved. If children younger than 3 years with a length- or height-for-age less than −1.88 SDS fail to achieve expected weight gain and growth when receiving EER (Table 2) based on chronological age, estimated requirements may be modified by using height-age.

As in the general public, the incidence of childhood obesity in those with CKD is increasing. National registry data for pediatric dialysis or transplant patients showed a significantly higher mortality rate at the upper and lower extremes of BMI-for-age.[49] Pretransplantation obesity is associated with decreased long-term renal allograft survival.[176] Prevention and treatment of obesity in patients with CKD is also important to reduce the risk of hyperlipidemia. Fat mass is less metabolically active than lean mass; therefore, energy requirements for overweight or obese children are lower and can be estimated by using equations specific for children heavier than a healthy weight (Table 3).

In infancy, feeds should be of breast milk or a whey-based infant formula with a low renal solute load if needed. Weaning solids should be introduced at the same time as recommended for healthy children. In children, high-energy foods and drinks are recommended as part of a controlled intake, with nutritional supplements or nutritionally complete feeds introduced if necessary. Calculated energy requirements are estimates, and some children will require more or less for normal growth; therefore, all dietary prescriptions should be individualized.

Early intervention to try to prevent the development of oral hypersensitivity and food-aversive behavior often is incorporated into the feeding plan and includes the correct timing for introduction of solids with gradual inclusion of new tastes and lumpier textures, messy play and food exploration, prohibition of force feeding with self-feeding behavior promoted, and sitting with the family at meal times.

Other members of the multidisciplinary team with expertise in infant feeding issues—eg, infant psychologists and speech, language, and occupational therapists—may be important in improving the outcome for normal feeding. However, overemphasis on maintaining the oral route to achieve an adequate nutritional intake may be counterproductive because symptoms may be

Table 3. Equations to Estimate Energy Requirements for Children Ages 3 to 18 Years Who Are Overweight

Age	Weight Maintenance Total Energy Expenditure (TEE) in Overweight Children
3-18 y	Boys: TEE = 114 − [50.9 × age (y)] + PA × [19.5 × weight (kg) + 1161.4 × height (m)]
	Girls: TEE = 389 − [41.2 × age (y)] + PA × [15.0 × weight (kg) + 701.6 × height (m)]

Source: ref 175.

Table 4. Physical Activity Coefficients for Determination of Energy Requirements in Children Ages 3 to 18 Years

	Level of Physical Activity			
Gender	Sedentary	Low Active	Active	Very Active
	Typical activities of daily living (ADL) only	ADL + 30-60 min of daily moderate activity (eg, walking at 5-7 km/h)	ADL + ≥60 min of daily moderate activity	ADL + ≥60 min of daily moderate activity + an additional 60 min of vigorous activity *or* 120 min of moderate activity
Boys	1.0	1.13	1.26	1.42
Girls	1.0	1.16	1.31	1.56

Source: Health Canada: http://www.hc-sc.gc.ca/fn-an/alt_formats/hpfb-dgpsa/pdf/nutrition/dri_tables-eng.pdf. Reproduced with the permission of the Minister of Public Works and Government Services Canada, 2008.

exacerbated by inappropriate expectations and the critical period of intervention to ensure normal nutrition dependent growth may be missed.

In children with CKD stage 5D on PD therapy, variable glucose absorption takes place from the dialysis fluid depending on the mode of dialysis, dialysate glucose concentration, and peritoneal membrane capacity. There are 2 adult studies documenting the caloric impact from dialysis fluid glucose.[177,178] One formula using both PD modality and peritoneal equilibration test (PET) transport characteristics was shown to closely approximate measured glucose absorption, but has not been evaluated in children.[177] In a pediatric study of 31 children older than 3 years on ambulatory PD therapy, the mean energy intake derived from peritoneal glucose absorption was 9 kcal/kg/d.[152] Kaiser et al[136] demonstrated better growth rates in children receiving CAPD versus CCPD versus HD that may have been partially explained by increased glucose absorption associated with CAPD. Because many children on PD therapy are underweight, the prescribed energy intake in those with CKD stage 5D should exclude the estimated calorie absorption from the dialysate because this may compromise the nutritional quality of the diet. However, some children—and particularly infants on PD therapy—gain weight at a faster rate than normal despite oral and/or enteral energy intakes that are lower than the average requirements. Reduced physical activity and increased exposure to dialysate glucose for fluid removal may be explanations, and in these cases, the calorie contribution from PD fluid should be taken into account when estimating energy requirements.

4.2: Supplemental nutritional support should be considered when the usual intake of a child with CKD stages 2 to 5 or 5D fails to meet his or her energy requirements and the child is not achieving expected rates of weight gain and/or growth for age. (B)

4.3: Oral intake of an energy-dense diet and commercial nutritional supplements should be considered the preferred route for supplemental nutritional support for children with CKD stages 2 to 5 and 5D. (B) When energy requirements cannot be met with oral supplementation, tube feeding should be considered. (B)

Energy requirements in infants and children include the energy needed for tissue deposition, with satisfactory growth a sensitive indicator of whether energy requirements are being met, particularly in infancy.[179] Poor energy intake and vomiting in children with CKD therefore will have an adverse effect on growth. Because short stature at dialysis therapy initiation is a marker for poor outcome in children initiating dialysis therapy, early intervention with intensive nutritional support may be critical to outcome.[180] Because calculated energy requirements are estimates, all dietary prescriptions should be individualized because some children will require more or less for normal growth. Formulas and enteral feedings may be concentrated and/or supplemented with a commercial glucose polymer powder and/or a liquid fat. Energy-dense feeds may be needed in children with CKD stage 5 with oligoanuria (see Tables 2 to 4 for EER; Appendix 2, Table 34, for resources to calculate EER; and Appendix 3, Table 36, for information for feeds and supplements).

However, both poor appetite and vomiting are common in infants and children with CKD and have a negative impact on the aim of achieving the dietary prescription. Poor appetite is multifactorial in origin and includes a thirst for water rather than feed in those with polyuric CKD, the administration of multiple unpleasant medications, and a preference for salty rather than energy-dense sweetened foods. The accumulation of appetite-regulating cytokines and hormones has been implicated in the cause of both this lack of spontaneous appetite and early satiety and provides a physiological explanation for the difficulties faced by caregivers in delivering the dietary prescription.[181,182] Gastroesophageal reflux was demonstrated in 73% of infants with chronic kidney failure, with poor feed intake and vomiting[183] and disordered gastric motility, delayed gastric emptying, and gastroesophageal reflux in 12 symptomatic children in association with increased polypeptide hormone levels.[184]

Symptoms of vomiting, irritability, and discomfort suggestive of gastroesophageal reflux initially should be managed conservatively by concentrating feeds to reduce feed volume and minimizing seated and supine positions after feeds because there is some evidence of benefit in infants without CKD.[185,186] Although there are no published data about the use of prokinetic agents (eg, metoclopramide, a dopamine receptor antagonist; domperidone, a peripheral D_2 dopamine receptor antagonist) or gastric acid suppressants (H_2 receptor blockers or proton pump inhibitors) in children with CKD, their use may be helpful. If symptoms persist, anatomic abnormalities should be excluded radiologically, but the role of routine pH studies and tests of gastric emptying in those with CKD is not established. A fundoplication may be indicated for intractable vomiting and can be performed after a gastrostomy is placed.

When poor appetite and vomiting preclude a nutritionally adequate intake, tube feeding commonly is implemented. Although registry data from the North American Pediatric Renal Transplant Cooperative Study (NAPRTCS) for the use of supplemental tube feeds in children younger than 6 years at the start of dialysis therapy showed no improvement in linear growth, follow-up was for only a year and no information was available for calorie intake.[187] However, in single-center studies, tube feeding has been shown to facilitate weight gain and growth. Significant weight gain and catch-up growth were achieved in 35 children with CKD stages 4 to 5 and age younger than 5 years if tube feeding was started before the age of 2 years. Loss of nutrition from vomiting is variable and hard to assess; however, the improved weight gain observed in this study over 2 years with enteral feeding and without an increase in energy intake for age suggests that vomiting can be reduced by slow delivery of feeds.[18] In a large study of 101 infants presenting with CKD who were younger than 6 months and had a GFR less than 20 mL/min/1.73 m^2 or CKD stage 5 within 2 years, 81% of the 81 survivors were tube fed and achieved a mean height SDS within the normal range by 1 year, with continued improvement thereafter.[17] In 12 infants starting PD therapy at younger than 1 year and on PD therapy for at least a year in association with enteral feeding, height, weight, and occipital head circumference SDS all improved significantly by 1 year, with continuing improvement in weight and occipital head circumference into the second year.[188] Coleman et al[154] included older children in their study of tube feeding using gastrostomy buttons in 22 children (0.2 to 10.3 years old) on long-term dialysis therapy. Although growth data did not distinguish between those starting gastrostomy feeding before ($n = 16$) or after the age of 5 years ($n = 6$), mean height and weight SDS increased significantly by 18 months. However Ramage et al,[189] in a study of 15 children on PD therapy and gastrostomy fed, subdivided growth outcome into those age younger than 2.5 years ($n = 8$) and those older than 2.5 years ($n = 7$) at the start of tube feeding. There was no further decrease in height SDS in either group, with significant weight gain in both age groups by 12 months.[189] Therefore, tube feeding should be considered for infants and children younger than 3 years who do not meet their EER orally despite dietary intervention and who are underweight or growth retarded (weight or length/height < -1.88 SDS) or failing to achieve normal rates of weight gain or growth. Although there are limited data about the use of tube feeding in children older than 3 years, this approach should be considered in the individual child with intake inadequate to maintain expected weight gain to prevent malnu-

trition, which increases the risk of infection, reduces stamina and cognition, and compromises long-term survival.[70] However, treatment with growth hormone may be indicated if growth failure persists despite meeting nutritional requirements, particularly after early childhood, because there is currently minimal evidence that improved nutrition alone can facilitate catch-up growth.

The method of tube-feed delivery and feed composition will depend on age, the presence or absence of vomiting, nutrient requirements, mineral and electrolyte imbalances, and the assessed intake that can be achieved orally. Infants may require only boluses of the balance of their feeding after oral feeds (ie, top-up boluses), but some may need the full prescription to be given by tube, which can then be delivered by pump as an overnight feed, with the rate adjusted as tolerated with additional daytime boluses (see Appendix 4, Table 38 for information about introducing and advancing enteral feeds). Older children may benefit from having the majority of their feed overnight to encourage hunger and oral intake during the day and so they can be free to undertake normal daytime activities without the pressure to meet all their requirements while at school or socializing.

Dello Strogolo et al[168] reported persistent feeding dysfunction in 8 of 12 infants with a GFR less than 35 mL/min/1.73 m^2 who were managed with nasogastric tube feeds for at least 9 months. Therefore, it is important that tube-fed infants and children be encouraged to continue some oral intake or have continued oral stimulation, eg, sucking on a pacifier and/or positive nonthreatening contact with food. Other studies are more encouraging. In 5 infants on PD therapy and nasogastric feeding with persistent food refusal, intensive behavior therapy by a multidisciplinary team enabled the infants to convert to full oral feeding.[190] Although there are concerns that tube feeding will further reduce oral intake, Ledermann et al[18] showed in children aged 0 to 2 years that the percentage of energy derived from the tube feed did not change over 2 years despite an increase in the absolute energy intake with age, confirming improved oral intake. The long-term outlook for normal feeding after transplantation is excellent, with reports of successful transitioning of almost all tube-fed children to oral diet and fluids within 10 months if children with significant comorbidity are excluded.[169,191]

Although the preferred method of tube feeding is by means of gastrostomy, nasogastric tubes may be used long term or as a temporary measure, particularly for infants weighing less than 4 kg or infants/children presenting with CKD stage 5 needing immediate PD therapy. Repeated replacement due to vomiting with subsequent aversive behavior and the psychosocial problems associated with the visibility of the tube are averted by the use of gastrostomies. Gastrostomies may be placed either percutaneously (radiologically or endoscopically) or by using an open procedure. Minor complications are well documented for both approaches, particularly exit-site erythema and infections. Migration of the retention disk and enterocolic fistulae can present as significant late complications of percutaneous placement, although the latter may be avoided by radiological placement because the bowel is outlined with contrast. Gastrocutaneous fistulae may need surgical closure after gastrostomy button removal. A percutaneously placed gastrostomy should be replaced every 18 to 24 months by either the same size gastrostomy tube or, if the track is adequate, a button gastrostomy according to the child's and family's preference.[192,193] Ideally, placement of a gastrostomy tube should occur before PD catheter placement. The placement of a percutaneous gastrostomy while on PD therapy should be discouraged because the risk of severe peritonitis and PD failure is high; conversely, an open Stamm gastrostomy, initially with a catheter and subsequently replaced by a button device, can be performed safely in children on PD therapy with suitable precautions (eg, antibiotic and antifungal coverage and time off PD therapy after placement). There is no evidence of an increased incidence of bacterial or fungal peritonitis with an established gastrostomy.[155,194,195]

A fundoplication may be performed with the gastrostomy or after initial gastrostomy placement if severe vomiting persists despite medical and nutritional management, but temporary HD therapy may be required.[155,196] A Stamm gastrostomy can be created at the same time as PD catheter placement without additional complications.[154]

The use of gastrojejunal tubes has been described by Geary and Chait,[110] but the expected reduction in vomiting was not observed and the need for continuous feed delivery reduces the practical application.

Other approaches may improve the nutritional status. In adult maintenance HD patients, increasing dialysis frequency to 6 times/wk improved both biochemical markers and weight gain.[197] A recent report of increased growth velocity in 5 children with intensified daily HD allowed a "free" diet raises the possibility that nutritional status improves with a higher dialysis dose.[149] Although the appetite stimulant megestrol acetate has been used in adults on HD therapy,[198,199] there are significant side effects and no published studies or case reports of the use of appetite stimulants or anabolic agents in children with CKD.

The 3½- to 4-hour HD session, which characteristically occurs thrice weekly, may offer an opportune time to provide oral nutritional supplementation, provided the patient is tolerant of the nutrient intake during the session. Although this is a common practice in Europe, the experience in many other centers has been less positive, prompting a philosophy against the allowance of oral intake during HD in adult and even pediatric centers alike.[200-203] The most frequent adverse outcome noted when meals have been provided is hypotension, presumably the result of either decreased cardiac output secondary to splanchnic sequestration of blood or through a decrease in splanchnic resistance leading to a reduction in systemic vascular resistance.[204,205] A decrease in relative blood volume also has been documented.[206] However, more recently, a prospective study of 85 adults receiving maintenance HD revealed the nutritional benefit and patient tolerance of an oral supplement provided during the HD session.[207] In a subsequent retrospective study of 126 stable adult HD patients, there also was no evidence of an association between oral intake during HD and intradialytic hypotension, although the prescribed dry weight was not achieved in a substantial percentage of patients with high oral intake.[208] It is distinctly possible that the fewer comorbidities that characterize pediatric versus adult patients receiving HD are associated with decreased risk of postprandial complications. However, evidence supporting this hypothesis is not yet available and mandates close monitoring of vital signs in any patient who receives nutritional supplementation during an HD session.

4.4: A trial of IDPN to augment inadequate nutritional intake is suggested for malnourished children (BMI-for-height-age < 5th percentile) receiving maintenance HD who are unable to meet their nutritional requirements through oral and tube feeding. (C)

Malnutrition, short stature, and low BMI are independent risk factors for mortality in adult and pediatric patients.[49,70,209] Data from adult patients receiving maintenance HD show that anorexia is an independent risk factor for death 12 months later.[210] Children receiving maintenance dialysis report high rates of depression,[211] poor adjustment to diagnosis and lower socioeconomic status,[212] and lower health-related quality of life[213-215] than healthy controls and therefore are at risk of anorexia-induced malnutrition. One pediatric center reports that psychosocial/malnutrition-related causes account for the most frequent reason for HD patient hospitalization.[58] Advanced CKD stages are often associated with anorexia and gastrointestinal disorders, which may inhibit the ability to maintain adequate nutritional status through the oral and/or enteral route. IDPN can be provided to augment inadequate nutritional intake in a small select group of children who are malnourished and unable to meet their requirements through oral and tube feeding.

Pilot pediatric data from small cohorts suggest that IDPN can be efficacious to augment inadequate oral and/or enteral nutrition in malnourished children, leading to improvements in BMI in children with organic,[58,59,216] but not psychosocial,[59] causes of malnutrition. Optimal IDPN solution composition is unknown; however, a typical IDPN prescription contains amino acids in amounts to meet estimated daily protein requirements, as well as dextrose and 20% or 30% lipid components to increase the caloric impact of the IDPN. Substrate infusion rates are adjusted upward as tolerated to enhance caloric intake while preventing or managing hyperglycemia and hyperlipidemia (Table 5).

Although data assessing IDPN efficacy in adult HD patients have not shown a clear benefit of IDPN to reduce mortality,[217,218] such data may

Table 5. Nutrient Content or Infusion Rates of IDPN Reported From Small Pediatric Cohorts

Parameter/Nutrient	Goldstein 2002 (n = 3)	Orellana 2005 (n = 9)	Krause 2002 (n = 4)
Age (y)	17-25	17-26	4-18
Protein, g/kg/treatment	1.3	1.3	0.5-1.5
Dextrose, mg/kg/min	5-9	5-9	18-46
Fat, g/kg/h	not reported	≤0.2-0.3	≤0.2
kcal/kg/treatment	not reported	11 kcal/kg from protein + dextrose; not reported for lipids	27-53

not be applicable to children, for whom adequate nutrition is requisite for normal growth and development.

IDPN is administered continuously during the entire course of the HD treatment and should be infused in the venous limb of the HD circuit to prevent clearance of amino acids and trace elements. More than two-thirds of the infused amino acids are retained, and the fluid used to deliver IDPN is removed through ultrafiltration. Trace element solutions can be added to provide zinc, copper, selenium, manganese, and chromium. Table 6 lists the potential adverse events associated with IDPN and a recommended monitoring schedule. Postinfusion hypoglycemia or symptoms suggestive of refeeding syndrome (eg, hypokalemia, hypophosphatemia, and hypomagnesemia) have been seen rarely in children on IDPN therapy.

In the absence of pediatric criteria, discontinuation criteria for adults may provide guidance.[217,219] Suggested criteria include clinical evidence of improving nutrition as evidenced by increased dry weight and an increase in oral intake to meet energy and protein requirements. Additional criteria for discontinuation include no improvement in nutritional status after 4 to 6 months of IDPN or complications or intolerance of IDPN therapy.[219]

IDPN provision can require substantial resources and should be used only when adequate financial and personnel resources are available. IDPN should not be promoted as a sole nutrition source; it should be used to augment other sources. If the combination of oral and/or enteral intake and IDPN is unable to meet energy and protein requirements, daily total or partial parenteral nutrition is indicated.

4.5: A balance of calories from carbohydrate and unsaturated fats within the physiological ranges recommended as the AMDR of the DRI is suggested when prescribing oral, enteral, or parenteral energy supplementation to children with CKD stages 2 to 5 and 5D. (C)

Fats, carbohydrates, and proteins can substitute for one another to some extent to meet the body's energy needs. Uneven distribution of calories from each of the macronutrients may be

Table 6. Potential Adverse Occurrences with IDPN

Component	Adverse Occurrence(s)	Monitoring Schedule	Response to Adverse Event
Protein	None		
Carbohydrate	Hyperglycemia (>350 mg/dL)	Serum glucose before HD, 1 hour into HD and at the end of HD • First week of IDPN • Week after change in dextrose rate • Symptomatic patient	• Decrease dextrose rate by 2 mg/kg/min • Add insulin to IDPN
Fat	Hyperlipidemia (50% rise in pre-HD TG level between 2 treatments)	• Serum TG levels before first and second treatment using lipids	• Discontinue lipids
	Hypersensitivity (egg allergy)	• During the first administration of intravenous lipids, a test dose of 0.5 mL/min for the first 30 min of infusion.	• Discontinue lipids

associated with inadequacy of certain nutrients and increased risk of such chronic diseases as coronary heart disease, obesity, and diabetes. Cardiovascular disease (CVD) is the leading cause of morbidity and death in the pediatric CKD population.[220,221] Upper extremes of BMI-for-age are associated with higher mortality rates in children on dialysis therapy and decreased long-term allograft survival and higher mortality rates in pediatric transplant patients. Although large-scale studies of risk-factor outcomes for those with CVD have not been performed in adults or children with CKD, the high mortality rate supports the need for risk-factor reduction early in the course of CKD to reduce long-term exposure to cardiovascular insult and improve outcomes. To achieve the best risk reduction, it appears that dietary strategies should aim to prevent or minimize increased triglyceride (TG) and cholesterol levels and avoid conditions—such as obesity—that contribute to dyslipidemia.

It often is necessary to supplement an infant's formula or a child's diet with fat and carbohydrate to provide optimal calories, especially when the child is fluid restricted. In the general population, low or high proportions of calories from carbohydrate or fat are associated with nutrient inadequacies (eg, fat-soluble vitamins) and/or chronic diseases, including heart disease, obesity, and diabetes.[175]

Macronutrients are related to heart disease and obesity in many ways. Excess energy intake results directly in obesity, which increases the risk of heart disease. High intake of dietary cholesterol, saturated fat, or *trans* fatty acids can increase total and low-density lipoprotein (LDL) cholesterol levels in the blood whereas monounsaturated and polyunsaturated fatty acids a decrease total and LDL blood cholesterol levels. High intakes of n-3 polyunsaturated fatty acids (omega-3 fatty acids [n-3 FA], docosahexanoic acid [DHA], and eicosapentanoic acid [EPA]) are associated with decreasing TG levels and a decreased risk of heart disease. High carbohydrate (ie, simple sugars) and low fat intakes tend to increase plasma TG levels and decrease high-density lipoprotein (HDL) cholesterol levels, with a carbohydrate source of monosaccharides (especially fructose) causing a more extreme effect. Hypertriglyceridemia also has been associated with enhanced glucose uptake in children on PD therapy. Dietary fiber, particularly naturally occurring viscous fiber, reduces total and LDL cholesterol levels, and high intakes have been associated with reduced rates of CVD.

As noted previously, CVD is the leading cause of morbidity and mortality in children with CKD, accounting for approximately 25% of total deaths.[220,221] These rates are 1,000 times higher than the national pediatric cardiovascular death rate.[220] CVD in children with CKD is associated with traditional (dyslipidemia, hypertension, obesity, physical inactivity, and genetics) and nontraditional factors (uremia, uremia-related anemia, prothrombogenic factors, inflammation, fluid overload, left ventricular hypertrophy, increased homocysteine levels, and vascular calcification).[220] Children with CKD have been identified as being in the highest risk category for pediatric CVD.[173]

Dyslipidemia occurs relatively early in the progression of CKD (ie, GFR, 30 to 59 mL/min/1.73 m^2) and increases in prevalence as kidney function deteriorates.[222] In children and adolescents on PD therapy, reported rates of dyslipidemia range from 29% to 87%.[223] Hypertriglyceridemia and hypercholesterolemia have been reported in 90% and 69% of children with CKD stage 5, respectively.[224] Dyslipidemia in pediatric CKD manifests primarily as increased levels of serum TG, contained predominantly in very LDLs (VLDLs) of hepatic origin.[225] This occurs in combination with high levels of VLDL and intermediate-density lipoproteins (IDLs), low levels of HDL particles, and normal or modestly increased levels of total and LDL cholesterol.[226,227] Sometimes referred to as atherogenic dyslipidemia, the metabolic abnormalities underlying it are complex.[227] Hypertriglyceridemia is an independent contributor to the development of CVD[228-232] and may also accelerate progression of CKD to CKD stage 5, dialysis, and transplantation.[233-235]

Recommended ranges for a healthy distribution of calories from protein, fat, and carbohydrate for the general pediatric population have been established by the DRI.[175] These AMDR (Table 7) are based on evidence that consumption greater or less than these ranges may be associated with nutrient inadequacy and increased risk of developing such chronic diseases as coronary heart disease, obesity, diabetes, and/or

Table 7. Acceptable Macronutrient Distribution Ranges

Macronutrient	Children 1-3 y	Children 4-18 y
Carbohydrate	45%-65%	45%-65%
Fat	30%-40%	25%-35%
Protein	5%-20%	10%-30%

Source: Health Canada: http://www.hc-sc.gc.ca/fn-an/alt_formats/hpfb-dgpsa/pdf/nutrition/dri_tables-eng.pdf. Reproduced with the permission of the Minister of Public Works and Government Services Canada, 2008.

cancer. There is no information to suggest that dietary advice regarding macronutrient distribution in children with CKD should be different from that in the general population; therefore, it seems prudent to maintain a distribution of calories similar to that recommended by the AMDR for children with CKD stages 2 to 5 and 5D.

The DRI provide further recommendations for specific types of carbohydrate and fat to avoid or limit for the purpose of chronic disease risk reduction (Table 8). Given the high risk of CVD in children with CKD, it is recommended that children and their caregivers be counseled to use sources of unsaturated fat rather than saturated or *trans* fats and, as much as possible, to choose complex carbohydrates instead of simple sugars.

Calorically dense formulas frequently are prescribed for infants; however, there are no AMDR for those younger than 1 year. Therefore, when advancing the caloric density of formula, the distribution of protein, fat, and carbohydrate should be kept consistent with the base formula,[236] which must adhere to strict standards (7% to 12% protein, 40% to 54% fat, and 36% to 56% carbohydrate; www.codexalimentarius.net; last accessed March 30, 2008). Infants and young children need a somewhat greater proportion of fat in their diets to meet energy needs. Protein and electrolyte issues typically predict whether the energy density of an infant's formula can be concentrated (ie, more formula concentrate and less water) or increased by the addition of modular components of carbohydrates (eg, powder or liquid forms of tasteless glucose polymers) and/or fat (eg, ordinary oil used at home, emulsified oil, or medium-chain TG; Appendix 3, Table 36). When uremia, hyperkalemia, hyperphosphatemia, or formula osmolarity prevent concentrating formulas, additions of carbohydrate and/or fat are indicated. Fat additions to formula should be in the form of heart-healthy unsaturated fats, such as canola, olive, or corn oil. Providing enteral feedings containing glucose polymers and oil emulsions in a balanced profile of fat and carbohydrate to children with CKD managed conservatively (n = 5) or by using PD (n = 5) did not enhance hyperlipidemia compared with 37 children who were not tube fed.[237]

Children with CKD stages 2 to 5 and 5D and dyslipidemia have been identified as a high-risk population for CVD.[173] Table 9 lists more precise recommendations for stricter lowering of total dietary fat, cholesterol, and *trans* and saturated fats directed to toddlers, children, and adolescents with dyslipidemia and CKD stage 5, 5D, or a kidney transplant.

The K/DOQI Dyslipidemia Guidelines' recommendations, endorsed by the K/DOQI Cardiovascular Guidelines, recommend that the dietary and lifestyle recommendations made for adults are also appropriate for postpubertal children and adolescents with CKD (Table 11), but that prepubertal children should follow recommendations from the National Cholesterol Expert Panel in Children and Adolescents (NCEP-C).[238] Since then, a consensus statement on dietary recommendations for children and adolescents from the American Heart Association (AHA),[239] endorsed by the American Academy of Pediatrics, provides more current guidance than the NCEP-C recommendations for working with children and adolescents with CKD (Tables 9 and 10), recognizing that dietary modifications to increase calories or restrict potassium and/or phosphorus in-

Table 8. Additional Recommendations on Specific Types of Fat and Carbohydrate

Macronutrient	Recommendation
Dietary cholesterol	As low as possible while consuming a nutritionally adequate diet
Trans fatty acids	As low as possible while consuming a nutritionally adequate diet
Saturated fatty acids	As low as possible while consuming a nutritionally adequate diet
Added sugars	Limit to a maximal intake of no more than 25% of total energy

Source: Health Canada: http://www.hc-sc.gc.ca/fn-an/alt_formats/hpfb-dgpsa/pdf/nutrition/dri_tables-eng.pdf. Reproduced with the permission of the Minister of Public Works and Government Services Canada, 2008.

Table 9. Dietary Treatment Recommendations for Children with Dyslipidemia and CKD Stages 5, 5D, and Kidney Transplant

Macronutrient	Serum LDL-C >100 mg/dL	Serum TG >150 mg/dL
Energy		If associated with excess weight, energy balance + activity recommendations for weight loss
Dietary fat	<30% of calories	Low
Dietary cholesterol	<200 mg/d	
Trans fatty acids	Avoid	
Saturated fatty acids	<7% of calories	
Carbohydrate		Low simple carbohydrate

Source: Kavey et al.[173]

take make macronutrient modifications more challenging to achieve.

The extent to which the macronutrient content of the diet should be manipulated must consider the child's nutritional status and other dietary mineral and/or electrolyte restrictions. The first priority for nutritional care is meeting energy, protein, and micronutrient requirements to achieve optimal growth for individual children. If a child is well nourished, adding dietary modifications for dyslipidemia prevention or management can be safely undertaken. Studies of the general pediatric population have shown that dietary fat restriction to 30% of total caloric intake is safe and, in particular, free of adverse effects on growth, development, or nutrition.[240,241]

Renal diet restrictions to control uremia (protein) and mineral and electrolyte abnormalities limit the variety and palatability of the diet, and additional (dyslipidemia) restrictions can be overwhelming and may reduce caloric intake further. In light of this, dietary intervention for treatment of dyslipidemia is not recommended for undernourished children with CKD[220,223]; however, such simple changes as a switch to heart-healthy fats can be implemented easily.

4.6: Dietary and lifestyle changes are suggested to achieve weight control in overweight or obese children with CKD stages 2 to 5 and 5D. (C)

Childhood obesity is an international public health problem reaching epidemic proportions. A review of data from the US Renal Data System for more than 1,900 pediatric dialysis or transplant patients showed that mortality rates were significantly higher at the upper and lower extremes of BMI-for-age.[49] Pretransplantation obesity and increased BMI-for-age after transplantation are associated with decreased long-term renal allograft survival.[176] Prevention and treatment of obesity in patients with CKD is also important to reduce the risk of hyperlipidemia.[242]

A multiorganization scientific statement on cardiovascular risk reduction in high-risk pediatric patients made the following recommendations for high-risk children, including those with

Table 10. Tips to Implement AHA Pediatric Dietary Guidelines for Prevention or Treatment of Dyslipidemia and CVD in Prepubertal Children

Reduce added sugars, including sugar-sweetened drinks and juices.
Use canola, soybean, corn, or safflower oils, or other unsaturated oils, in place of solid fats during food preparation.
Use fresh, frozen, and canned vegetables and fruits, and serve at every meal; be careful with added sauces and sugar.
Introduce and regularly serve fish as an entrée.
Remove the skin from poultry before eating.
Use only lean cuts of meat and reduced-fat meat products.
Limit high-calorie sauces such as Alfredo, cream sauces, cheese sauces, and hollandaise.
Eat whole-grain breads and cereals rather than refined products.
Eat more legumes (beans) and tofu in place of meat for some entrees.
Read food labels—especially for breads, breakfast cereals, and prepared foods—for content, and choose high-fiber, low-salt/low-sugar alternatives.

Source: Gidding et al.[239]

Table 11. Dietary Modifications to Lower Serum Cholesterol and Triglycerides for Adolescents with CKD

Food Choices	Choose	Decrease
Eggs (cholesterol <200 mg/d)	• Limit to 2 eggs per week, or use 2 egg whites in place of 1 egg, or use cholesterol-free egg substitutes regularly	• Egg yolks and whole eggs (often hidden ingredients in cookies, cakes, desserts)
Meat, poultry, and alternatives	• Lean meat products, well trimmed of fat • Poultry without skin • Fish, shellfish • Low-fat tofu; tempeh; soy protein products	• High-fat meals (sausage, bacon, organ meats such as liver, sweetbreads, brain) • Sandwich-style meals such as ham, "cold cuts," processed meats
Fish, shellfish	• Fish or shellfish, baked or broiled without additional fat	• Avoid consuming bones of fish (sardines, anchovies, fish heads, etc) due to phosphorus content
Fats and oils (saturated fat <7% total kcal) (total fat 25%-35% total kcal)	• Unsaturated oils—safflower, sunflower, corn, soybean, cottonseed, canola, olive, peanut • Margarine—made from any of the oils above, especially soft and liquid forms • Salad dressings—made from any of the oils above	• Hydrogenated and partially hydrogenated fats • Coconut, palm kernel, palm oil, coconut and coconut milk products • Butter, lard, shortening sold in cans, bacon fat, stick margarine • Dressing made with egg yolk, cheese, sour cream, or milk
Breads and grains (dietary fiber goal of >20 g/d may be difficult with fluid restriction; focus on viscous/soluble fiber)	• Breads without toppings or cheese ingredients • Cereals: oat, wheat, corn, multigrain • Pasta, rice • Crackers—low-fat animal crackers, unsalted soda crackers and bread sticks, melba toast • Homemade breads made with recommended fats and oils	• Breads of high-fat content such as croissants, flaky dinner rolls • Granolas that contain coconut or hydrogenated fats • High-fat crackers (more than 3 g of fat per serving on label) • Commercially baked pastries and biscuits
Fruits and vegetables	• Choices within CKD diet parameters in fresh, frozen, or low-sodium canned forms	• Fried fruits or vegetables or served with butter or cream sauces; avocado
Sweets (may be restricted in diabetics or presence of high TG)	• Sweets: sugar, syrup, honey, jam, preserves, candy made without fat (hard candy) • Frozen desserts: low-fat and nonfat sherbet, sorbet, fruit ice • Cookies, cakes, and pies made with egg whites or egg substitutes or recommended fats; angel food cake; fig and other fruit bar cookies • Nondairy regular and frozen whipped toppings in moderation	• Candy made with chocolate, cream, butter, frostings • Ice cream and regular frozen desserts • Commercially baked cookies, cakes, cream and regular pies • Commercially fried pastries such as doughnuts • Whipped cream

Note: Diet decisions should be made in consultation with a nephrology dietitian to adapt food choices to the patient's individual medical and nutritional condition. Careful selection of foods within each category will be necessary to stay within phosphorus, potassium, and sodium restrictions.

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CKD stages 5 and 5D and kidney transplant recipients with a BMI greater than the 95th percentile. Step 1 treatment: (a) age-appropriate reduced-calorie training for child and family; (b) specific diet/weight follow-up every 4 to 6 months, repeated BMI calculation at 6 months; and (c) activity counseling with a goal of 1 hour or more of active play per day and screen time limited to 1 hour or less per day. Step 2 treatment if follow-up BMI remains greater than the 95th percentile: weight-loss program referral plus consider referral for exercise testing and recommendations from exercise specialist appropriate for cardiac status.[173] Interventional strategies for

treatment of child and adolescent overweight and obesity in the non-CKD population[45] may be helpful.

Fiber

The AI for total fiber is based on daily caloric intake, and for all children 1 year and older is 14 g/1,000 kcal/d. To normalize cholesterol levels and reduce the risk of cardiovascular heart disease, an increase in soluble fiber intake is recommended as an addition to reductions in saturated fatty acid and cholesterol intake.[239,241] Fiber also can aid laxation and promote satiety, which can reduce energy intake and the risk of overweight.

Dietary fiber is found in most fruits, vegetables, legumes, and whole grains, which are foods restricted in low-potassium and low-phosphorus diets; therefore, meeting daily fiber recommendations for healthy children is more challenging for children with CKD who have limited intake of these foods due to low-potassium and/or low-phosphorus diet restrictions. Appendix 3, Table 37 lists some foods containing 1.9 g or greater of fiber per serving and includes their potassium and phosphorus content to guide advice about increasing fiber intake for individual children. High-fiber foods with extremely high potassium and/or phosphorus content have been omitted. Tasteless mineral- and electrolyte-free powdered forms of fiber (eg, Unifiber®, Benefiber®) are available to add to meals or drinks if children are unable to meet their fiber intake by diet. High-fiber diets require additional fluid intake, which may not be possible for oliguric or anuric patients with strict fluid restriction.

Omega-3 Fatty Acids (n-3 FA)

Approximately 75% of children with CKD have hypertriglyceridemia, for which there is no effective therapy. Both primary and secondary prevention studies provide strong evidence that consumption of fish and fish oils rich in the n-3 FAs EPA and DHA reduce all-cause mortality and various CVD outcomes in adults.[243,244] By far, the strongest most consistent evidence of the cardioprotective benefits of n-3 FA is for the lowering of serum TG levels that is dose dependent and similar in various (adult) populations.[244,245] Adults with CKD who were treated with n-3 FA for 8 weeks had significant decreases in TG levels ranging from 20% to 50% compared with controls.[246-248] Pediatric data for the TG-lowering effect of n-3 FA are limited to several pre/post studies.[249,250] Eighteen children (7 to 18 years old) on dialysis therapy experienced a 27% decrease in TG levels from 236 ± 31 to 171 ± 21 mg/dL after 8 weeks of EPA plus DHA supplementation.[251] In a trial of n-3 FA and alternate-day prednisone on progression of disease in children and young adults (age, 7.4 to 39.7 years) with immunoglobulin A (IgA) nephropathy, a 17% decrease in TG level was observed after 2 years of therapy with 3.36 g/d of EPA plus DHA.[252]

EPA and DHA can be synthesized in vivo through the elongation and desaturation of α-linolenic acid; however, this process occurs slowly and is inefficient. Therefore, EPA and DHA, found almost exclusively in fish and marine sources, must be provided in the diet; the highest sources are fatty fish (eg, tuna, mackerel, trout, salmon, herring, sardines, and anchovies).[253] Adults on dialysis therapy consume fish in amounts far less than recommendations and have lower tissue EPA plus DHA stores compared with healthy people.[254] The higher mercury content of certain fatty fish (shark, swordfish, marlin, orange roughy, king mackerel, escolar [snake mackerel], tilefish, and albacore or "white" tuna) has led various regulatory bodies to issue recommendations about the maximum intake of these fish for young children, who are considered to be more susceptible than adults to the adverse health effects of methylmercury.

Several safety concerns around the use of n-3 FA have been raised, including prolonged bleeding times, worsening glycemic control in patients with diabetes, small increases in LDL cholesterol levels, and environmental contaminants in fish-oil products. Despite these concerns, n-3 FAs have been found to be extremely safe by both Health Canada and the US Food and Drug Administration.

At this time, there is insufficient evidence to recommend routine use of n-3 FAs to treat hypertriglyceridemia in children with CKD.

COMPARISON TO OTHER GUIDELINES

- CARI CKD Guidelines: similar suggestions for energy intake and tube feeding, but no firm guidelines.
- European Pediatric Peritoneal Dialysis Working Group: similar recommendations for energy intake for PD and enteral feeding patients, but less detail.

LIMITATIONS

- No controlled trials; mainly small observational and interventional studies.
- Studies of IDPN have the following issues that plague most pediatric CKD studies: (1) small sample size, (2) single-center populations, and (3) no control group or randomization scheme for comparison.
- The absence of prospective studies in the pediatric HD population on the intake of food is a major limitation. Whereas studies of adult patients are available, differences in the cardiovascular status of children and adults with CKD and on dialysis therapy make it difficult to extrapolate the adult experience to children.
- The vast majority of research has focused on the effects and management of undernutrition in children with CKD, and not overnutrition. There are no studies examining the effect of varying macronutrient content on serum markers of dyslipidemia or long-term cardiovascular outcomes in children with CKD.

RESEARCH RECOMMENDATIONS

- Determination of energy requirements at different stages of CKD and with different methods of kidney replacement therapy.
- The role of enteral feeding in the older child and adolescent in preventing the development of protein-energy wasting syndrome.
- Research should be directed to further delineation of the role and dose of IDPN to treat and/or prevent malnutrition in specific pediatric HD populations, including those receiving more frequent HD.
- Research should be conducted to evaluate the tolerance of pediatric HD patients to intradialytic oral nutritional supplementation. The quantitative contribution of the dialysis-based nutrition to the daily caloric and protein intake and its impact on overall patient well-being also should be assessed.
- Research should be conducted to better delineate:
  - the risks and benefits of treatments such as n-3 FA/fish-oil supplementation and plant stanols in children with CKD and dyslipidemia.
  - the impact of dietary and lifestyle factors on managing overweight/obesity in children with CKD and whether weight management has an impact on progression of kidney disease, morbidity, and mortality.

RECOMMENDATION 5: PROTEIN REQUIREMENTS AND THERAPY

INTRODUCTION

The recommendation for protein intake in children with CKD has to consider maintenance of growth and an adequate nutritional status, but also the intrinsic link of DPI and phosphorus load. The growing evidence for a major impact of phosphorus overload on cardiovascular morbidity in children and adults with CKD provides a rationale to avoid excessive protein intake in this population. At a given level of quantitative protein intake, the phosphorus content and bioavailability of the protein sources, the quality of protein, and the metabolic environment are important additional factors to consider in the dietary protein prescription.

5.1 It is suggested to maintain dietary protein intake at 100% to 140% of the DRI for ideal body weight in children with CKD stage 3 and at 100% to 120% of the DRI in children with CKD stages 4 to 5. ***(C)***

5.2 In children with CKD stage 5D, it is suggested to maintain dietary protein intake at 100% of the DRI for ideal body weight plus an allowance for dialytic protein and amino acid losses. ***(C)***

5.3 The use of protein supplements to augment inadequate oral and/or enteral protein intake should be considered when children with CKD stages 2 to 5 and 5D are unable to meet their protein requirements through food and fluids alone. ***(B)***

RATIONALE

5.1: It is suggested to maintain dietary protein intake at 100% to 140% of the DRI for ideal body weight in children with CKD stage 3 and at 100% to 120% of the DRI in children with CKD stages 4 to 5. (C)

Progressive CKD is generally associated with a reduction in spontaneous dietary intake of both protein and energy. In a study comparing 50 children with CKD stages 3 to 4 with healthy controls, protein intake was found to be 33% lower and energy intake was 10% lower in patients with CKD.[255] However, whereas spontaneous energy intake tends to be critically low, eg, less than 80% to 85% of the RDA, DPI in those with CKD is far in excess of the average requirements, typically 150% to 200% of the RDA.[9,255,256]

The efficacy of low-protein diets in reducing the rate of CKD progression has been assessed in randomized prospective trials in both adult and pediatric patients. In the MDRD trial, no significant beneficial effect of decreasing DPI from 1.3 to either 0.58 or 0.3 g/kg/d, supplemented with essential keto acids, could be demonstrated; subtle signs of a suboptimal nutritional status were noted with these diets.[257] In a pediatric trial involving 191 children with CKD stages 3 to 4, a reduction in protein intake aiming at 100% (0.8 to 1.1 g/kg ideal body weight [defined as the weight at the same percentile as the child's height percentile for the same age and sex]) and achieving 120% of the dietary intake recommended by WHO did not alter the rate of CKD progression compared with a cohort with ad libitum protein intake (mean, 181% of RDA).[256,258] The reduction in protein intake, with maintenance of energy intake at greater than 80% of the RDA in both groups, did not affect statural growth, weight gain, body composition, or serum albumin levels within the observation period of 2 to 3 years.

Hence, although there is no evidence for a nephroprotective effect of dietary protein restriction, protein intake can be restricted safely to 0.8 to 1.1 g/kg/d in children with CKD. Because dietary protein restriction reduces the accumulation of nitrogenous waste products and facilitates lowering dietary phosphorus intake, it appears appropriate to gradually lower DPI toward 100% of the DRI in children advancing from CKD stage 3 to stage 5. This should delay the onset of signs and symptoms of uremia, although it should be noted that in the pediatric trial cited, the time of initiation of kidney replacement therapy was not delayed significantly in the low-protein cohort. Moreover, implementation and maintenance of a strict low-protein diet requires a major lifestyle change that may not be acceptable to many families. Hence, moderate protein restriction aiming at 100% to 140% of the DRI in CKD stage 3 and 100% to 120% of the DRI in CKD stages 4 to 5 may be a reasonable compromise in most cases (Table 12).

Table 12. Recommended Dietary Protein Intake in Children with CKD Stages 3 to 5 and 5D

	DRI				
Age	DRI (g/kg/d)	Recommended for CKD Stage 3 (g/kg/d) (100%-140% DRI)	Recommended for CKD Stages 4-5 (g/kg/d) (100%-120% DRI)	Recommended for HD (g/kg/d)*	Recommended for PD (g/kg/d)†
0-6 mo	1.5	1.5-2.1	1.5-1.8	1.6	1.8
7-12 mo	1.2	1.2-1.7	1.2-1.5	1.3	1.5
1-3 y	1.05	1.05-1.5	1.05-1.25	1.15	1.3
4-13 y	0.95	0.95-1.35	0.95-1.15	1.05	1.1
14-18 y	0.85	0.85-1.2	0.85-1.05	0.95	1.0

*DRI + 0.1 g/kg/d to compensate for dialytic losses.
†DRI + 0.15-0.3 g/kg/d depending on patient age to compensate for peritoneal losses.

These protein recommendations refer to a stable child and assume that energy intake is adequate (ie, it meets 100% of estimated requirements). Inadequate caloric intake results in the inefficient use of dietary protein as a calorie source, with increased generation of urea. Ensuring caloric needs are met is an important step in assessing protein requirements and modifying protein intake.

Protein requirements may be increased in patients with proteinuria and during recovery from intercurrent illness. Modification of protein recommendations also may be necessary in obese or stunted children. Obese individuals have a greater percentage of body fat, which is much less metabolically active than lean mass. Therefore, it is believed that basing protein (and energy) requirements of obese individuals on their actual weight may overestimate requirements. Conversely, using ideal body weight for an obese person does not take into account the increase in body protein needed for structural support of extra fat tissue. Therefore, a common practice is to estimate protein requirements of obese individuals based on an "adjusted" weight (ie, adjusted weight = ideal weight for height + 25% × [actual weight − ideal weight], where 25% represents the percentage of body fat tissue that is metabolically active) rather than their actual body weight.[259] This formula is based on physiological theory rather than scientific evidence. In young children (ie, age <3 years) or stunted children (ie, length- or height-for-age < −1.88 SDS), protein requirements initially should be estimated by using chronological age, but may be reestimated by using height age if there are indications of inadequate protein intake (see Recommendation 5.3).

5.2: In children with CKD stage 5D, it is suggested to maintain dietary protein intake at 100% of the DRI for ideal body weight plus an allowance for dialytic protein and amino acid losses. (C)

Our recommendations for DPI in dialyzed children differ from previous adult and pediatric guidelines based on several lines of reasoning.

First, the Food and Nutrition Board of the Institute of Medicine of the National Academy of Sciences in 2002 replaced the RDA of 1989 with DRI values for the intake of nutrients by Americans and Canadians. For protein, the DRI values are lower than the RDA across all age groups.[175]

Second, previous recommendations for dialyzed patients were based on the concept that in addition to replacements for dialytic amino acid and protein losses, at least 0.3 to 0.4 g/kg of dietary protein should be added to the intake recommended for healthy subjects.[62] The evidence base for this notion is weak and primarily based on adult literature.

The widespread notion that dialysis induces generalized protein catabolism through generalized protein degradation resulting from cytokine release induced by exposure to bioincompatible membranes (in HD) or dialysis fluids (in PD) has not been universally confirmed by metabolic studies. Net protein "catabolism" seems to be limited to the dialytic removal of amino acids and/or protein and a slightly reduced protein synthesis during HD sessions. Whole-body protein breakdown is not increased.[260]

Observational studies showing a correlation between high protein intake and better outcomes in adult dialysis patients[261,262] do not prove that a high-protein intake by itself stimulates tissue anabolism. Reviews of nitrogen-balance studies performed in adult dialysis patients with different protein intakes[56,263-270] conclude that HD patients are in neutral nitrogen balance with a protein intake as low as 0.75 to 0.87 g/kg/d, and PD patients, with 0.9 to 1.0 g/kg/d. A single nitrogen-balance study has been performed in dialyzed children.[152] In 31 pediatric patients receiving automated PD, the investigators observed a positive correlation between nitrogen balance and DPI and concluded that DPI should be at least 144% of RDA. However, nitrogen balance also positively correlated with total energy intake, and no multivariate analysis was performed to address whether energy intake, protein intake, or both were independent effectors of nitrogen balance.

A single randomized prospective study in adults[271] and several trials in children have addressed the effect of selectively increasing amino acid supply in patients on PD therapy. Despite increases in amino acid and dietary protein intake, no significant beneficial effects on nutritional status and longitudinal growth in children were achieved by this intervention, whereas urea concentrations frequently increased.[272-276] These results are compatible with the interpretation that it is not possible to induce tissue anabolism by selectively increasing protein and amino acid ingestion except in subjects with subnormal baseline protein intake. If more protein is ingested than needed for metabolic purposes, all the excess is oxidized and results in accumulation of nitrogenous-containing end products.

Third, although evidence for beneficial effects of a high DPI is lacking, there is growing concern that it may even be harmful to dialyzed children. In a DXA study of body composition in 20 children on long-term PD therapy and a mean DPI of 144% of the RDA, protein intake inversely correlated with bone mineral density, bone mineral content, and fat-free mass, and also with plasma bicarbonate level, suggesting that a high protein intake may cause tissue catabolism and bone loss through aggravating metabolic acidosis.[277]

Finally, the most convincing argument for limiting DPI in dialyzed children is derived from the solid evidence for a key etiologic role of dietary phosphorus load in the pathogenesis of dialysis-associated calcifying arteriopathy in pediatric and adult patients. Several studies of children and adults with childhood-onset CKD stage 5 have demonstrated correlations between serum phosphorus levels and cumulative phosphate-binder requirements and arteriopathy,[278-282] which, in turn, is linked to the excessive cardiovascular mortality of patients with CKD.[283,284]

There is a nearly linear relationship between protein and phosphorus intake,[285] which determines a frequent association of high protein in the diet with hyperphosphatemia.[286] Whereas hyperphosphatemia is a powerful independent predictor of mortality on dialysis therapy,[287] evidence for any benefit from high-protein diets is lacking.[288] Hence, it appears mandatory to limit protein intake to the safe levels known to ensure adequate growth and nutrition in healthy children.

The adverse impact of hyperphosphatemia on cardiovascular, bone, and endocrine function in children with CKD mandates the preferential selection of protein sources that are relatively low in phosphorus. The lowest amount of phosphorus in proportion to the quantity and quality of protein comes from animal-flesh proteins (average, 11 mg of phosphorus per 1 g of protein), whereas eggs, dairy products, legumes, and lentils have higher phosphorus-protein ratios (average, 20 mg of phosphorus per 1 g of protein; Table 13). Complexity is added by the variable digestibility of dietary protein and bioavailability of dietary phosphorus. Protein digestibility from animal proteins is 95%, whereas protein digestibility from plant proteins (85%) and mixed meals (85% to 95%) is lower. Whereas phosphorus in animal meat is stored as organic phosphates in intracellular compartments that are easily hydrolyzed and readily absorbed, 75% of phosphorus in plants is in the form of phytic acid. Because humans do not express the degrading enzyme phytase, the bioavailability of phosphorus from plant-derived food is very low. Phosphorus availability from animal products is greater than 70%, whereas availability from plant products (50%) and mixed meals (50% to 70%) is lower. Hence, despite their higher specific

Table 13. Average Ratio of Phosphorus to Protein Content in Various Protein-Rich Foods

Food Category	Ratio of mg Phosphorus to g Protein	Ratio Adjusted for Digestion/ Absorption
Egg white	1.4	1
Meat	9	6
Tofu	12	7
Egg	14	10
Legumes	17	10
Lentils	20	12
Nuts	25	15
Milk	29	21
Seeds	50	29

Note: Mathematical estimations based on protein digestibility-corrected amino acid scores (PDCAA) and data on estimated phosphorus bioavailability.

phosphorus content, some plant sources of protein may actually result in a lower rate of phosphorus uptake per mass of protein than meat-based foods (see Appendix 3, Table 35).[289] If healthy humans are administered an equivalent amount of either animal or plant protein, urinary phosphorus excretion is higher with the meat-based diet.[290] Moreover, meat products are frequently "enhanced" by the addition of phosphate salts; these additions may markedly increase the total phosphorus load. Hence, a mixed composition of dietary protein with a strong contribution of vegetable protein rich in phytic acid should be encouraged.

Although dialyzed children require larger amounts of protein per unit of body weight than adults to grow in size and lean body mass, this demand is fully accounted for by the age-adjusted pediatric DRI. Hence, the only additional dietary protein requirement justified by evidence is the replacement of dialytic nitrogen losses. In those on long-term PD therapy, daily peritoneal protein losses decrease with age across childhood from an average of 0.28 g/kg in the first year of life to less than 0.1 g/kg in adolescents.[292] Peritoneal amino acid losses add approximately one-third to the nitrogen lost with protein, resulting in an total additional dietary protein requirement ranging from 0.15 to 0.35 mg/kg, depending on patient age (see Table 12).

Peritoneal permeability for protein shows large interindividual variation, but appears to be relatively constant within subjects. Transperitoneal protein transport correlated with small-molecule transport rates; the peritoneal transporter status as assessed by using the PET provides some indication of the level of peritoneal protein losses. High peritoneal transporters tend to have low serum albumin levels; these patients may be at need for increased dietary protein supply. Because dialytic protein concentrations can be measured easily, consideration should be given to regular monitoring of peritoneal protein excretion and individual adaptation of the dietary protein prescription according to actual peritoneal losses.

Amino acid and protein losses during HD vary according to dialyzer membrane characteristics and reuse. Losses have not been quantified in children. In adults, an average of 8 to 10 g of amino acids and less than 1 to 3 g of protein are lost per HD session.[288,293,293a,293b] On the basis of 3 HD sessions per week for a 70 kg adult, this equates to 0.08 g/kg/day.† Assuming that dialytic amino acid losses are in linear relationship to urea kinetics, children can be expected to have similar or slightly higher amino acid losses than adults. An added DPI of 0.1 g/kg/d should be appropriate to compensate for pediatric hemodialytic losses (see Table 12). Under all conditions, at least 50% of dietary protein intake should be of high biological value‡ to protect body protein and mimimize urea generation.

In patients undergoing intensified HD modalities, in particular, extended nocturnal HD, the removal of nitrogenous waste products and phosphorus is almost doubled, frequently resulting in a need for phosphorus substitution.[294] Appetite and spontaneous dietary energy and protein intake reportedly increase in these patients. The

† (13 g AA and protein ×3 sessions)÷ 7 days per week ÷ 70 kg = 0.08 g/kg/d.

‡ protein containing the 9 essential amino acids in a proportion similar to that required by humans has high biological value. When one or more essential amino acids are scarce, the protein is said to have low biological value. Animal sources of protein (eg, meat, poultry, fish, eggs, milk, cheese, yogurt) provide high biological value protein. Protein found in plants, legumes, grains, nuts, seeds and vegetables are of low biological value.

excellent nitrogen and phosphorus clearances achieved with intensified treatment schedules and the concomitantly increased amino acid losses permit and require liberalization of DPI.

These recommendations for DPI refer to dialyzed children in stable clinical condition. Protein requirements may be increased in patients with proteinuria, during and after peritonitis episodes, and during recovery from intercurrent illness.

5.3: The use of protein supplements to augment inadequate oral and/or enteral protein intake should be considered when children with CKD stages 2 to 5 and 5D are unable to meet their protein requirements through food and fluids alone. (B)

Occasionally, protein intake may be inadequate in children with CKD because of anorexia, chewing problems, or the need for very stringent phosphorus restriction. Suggested signs of inadequate protein intake include abnormally low serum urea levels, an undesirable downward trend in nPCR for adolescents on HD therapy (see Recommendation 1, nPCR), and/or documentation of low protein intake by using food records, food questionnaires, or diet recall. Powdered protein modules (Appendix 3; Table 36) can be added to expressed breast milk, infant formula, beverages, pureed foods, or other moist foods to boost their protein content, and minced or chopped meat, chicken, fish, egg, tofu, or skim milk powder can be added to soups, pasta, or casseroles. Liquid protein-rich renal supplements (Appendix 3) can also be used orally or enterally to boost protein intake.

COMPARISON TO OTHER RECOMMENDATIONS

The CARI CKD Guidelines recommend that children have a protein intake equivalent to or greater than those recommended by the Food and Agriculture Organization, WHO, and United Nations University for healthy children.

LIMITATIONS

- The assumption that restricting protein intake may lower dietary phosphorus load and thereby contribute to better cardiovascular outcomes in children with CKD has not been substantiated by clinical trial evidence to date.
- The bioavailability of phosphorus in many protein-containing foods is unknown or highly variable. Moreover, the effects of selecting dietary protein sources according to phosphorus content and bioavailability may be overridden by hidden phosphorus sources in processed foods.

RESEARCH RECOMMENDATIONS

- Controlled prospective studies are required to compare the long-term effects of different levels of DPI on growth, nutritional status, serum phosphorus levels, and cardiovascular morphology and function in children with CKD stages 2 to 5 and on dialysis therapy.
- Phosphorus bioavailability studies in humans for various dietary protein sources are needed to provide comprehensive evidence-based identification of preferred dietary protein sources.
- In children on PD therapy, amino acid–containing dialysis solutions are available that permit the provision of nitrogen carriers without any phosphate load. Whereas the use of 1 bag of amino acid fluid per day did not consistently improve the nutritional status of children on CAPD therapy, recent short-term studies have suggested an anabolizing effect of combined peritoneal administration of glucose and amino acids in children and adults on automated PD (APD) therapy.[295-297] This concept requires further exploration in long-term randomized clinical trials. Longitudinal growth and nutritional status, as well as indicators of PD efficacy and safety, should be studied.

RECOMMENDATION 6: VITAMIN AND TRACE ELEMENT REQUIREMENTS AND THERAPY

INTRODUCTION

Patients with CKD and those on dialysis therapy are at risk of vitamin and mineral deficiencies as a result of abnormal renal metabolism, inadequate intake/poor gastrointestinal absorption, and dialysis-related losses. The provision of adequate quantities of these nutrients is essential because of their importance to growth and development in children.

6.1 The provision of a dietary intake consisting of at least 100% of the DRI for thiamin (B_1), riboflavin (B_2), niacin (B_3), pantothenic acid (B_5), pyridoxine (B_6), biotin (B_8), cobalamin (B_{12}), ascorbic acid (C), retinol (A), α-tocopherol (E), vitamin K, folic acid, copper, and zinc should be considered for children with CKD stages 2 to 5 and 5D. ***(B)***

6.2 It is suggested that supplementation of vitamins and trace elements be provided to children with CKD stages 2 to 5 if dietary intake alone does not meet 100% of the DRI or if clinical evidence of a deficiency, possibly confirmed by low blood levels of the vitamin or trace element, is present. ***(C)***

6.3 It is suggested that children with CKD stage 5D receive a water-soluble vitamin supplement. ***(C)***

RATIONALE

6.1: The provision of a dietary intake consisting of at least 100% of the DRI for thiamin (B_1), riboflavin (B_2), niacin (B_3), pantothenic acid (B_5), pyridoxine (B_6), biotin (B_8), cobalamin (B_{12}), ascorbic acid (C), retinol (A), α-tocopherol (E), vitamin K, folic acid, copper, and zinc should be considered for children with CKD stages 2 to 5 and 5D. (B)

Little information exists about the vitamin and trace element needs specific to children with CKD and those on dialysis therapy. However, in view of the important role of these nutrients as cofactors in a number of metabolic reactions, and recognizing that achieving the DRI should reduce the risk of developing a condition that is associated with the nutrient in question that has a negative functional outcome,[298,299] the practice has been to target 100% of the DRI as the goal for children with CKD stages 2 to 5 and on dialysis therapy (Table 14).

The B vitamins are essential for carbohydrate, protein, and fat metabolism; oxidation-reduction reactions; transamination and decarboxylation; glycolysis; and blood formation. Most *thiamin* in the body is present as thiamin pyrophosphate, which is a coenzyme for the oxidative decarboxylation of α-ketoacids. The metabolism of *riboflavin* resulting in functional flavoproteins is important because the flavoenzymes are important factors involved in oxidation-reduction reactions that are necessary for a variety of metabolic pathways, including energy production. *Pantothenic acid* is necessary for the synthesis of such compounds as fatty acids, cholesterol, and steroid hormones and for energy extraction during oxidation of amino acids. *Pyridoxine* is a coenzyme for nearly 100 enzymatic reactions and is essential for gluconeogenesis and niacin formation. *Biotin* has an important role in the metabolism of carbohydrates, fatty acids, and some amino acids. Finally, *cobalamin* has a key role in the metabolism of folic acid.

Ascorbic acid is involved in collagen synthesis through its role as a reversible reducing agent, whereas retinol is necessary for normal night vision. α-Tocopherol is the main antioxidant in biological membranes and vitamin K is a coenzyme for the posttranslational carboxylation of glutamate residues that ultimately influence the coagulation cascade. Folic acid is required for DNA synthesis, and copper functions as a cofactor in several physiologically important enzymes, such as lysyl oxidase, elastase, ceruloplasmin, and superoxide dismutase, as does zinc.

The DRIs were established by the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes of the Food and Nutrition Board, Institute of Medicine, National Academy of Sciences, as an expansion of the periodic RDA reports. Most studies examining vitamin status in children and adults with CKD occurred before the release of the DRI and hence report intake relative to the earlier RDA. The DRIs

Table 14. Dietary Reference Intake: Recommended Dietary Allowance and Adequate Intake

	Infants 0-6 mo	Infants 7-12 mo	Children 1-3 y	Children 4-8 y	Males 9-13 y	Males 14-18 y	Females 9-13 y	Females 14-18 y
Vitamin A (μg/d)	400	500	**300**	**400**	**600**	**900**	**600**	**700**
Vitamin C (mg/d)	40	50	**15**	**25**	**45**	**75**	**45**	**65**
Vitamin E (mg/d)	4	5	**6**	**7**	**11**	**15**	**11**	**15**
Vitamin K (μg/d)	2.0	2.5	30	55	60	75	60	75
Thiamin (mg/d)	0.2	0.3	**0.5**	**0.6**	**0.9**	**1.2**	**0.9**	**1.0**
Riboflavin (mg/d)	0.3	0.4	**0.5**	**0.6**	**0.9**	**1.3**	**0.9**	**1.0**
Niacin (mg/d; NE)	2*	4	**6**	**8**	**12**	**16**	**12**	**14**
Vitamin B_6 (mg/d)	0.1	0.3	**0.5**	**0.6**	**1.0**	**1.3**	**1.0**	**1.2**
Folate (μg/d)	65	80	**150**	**200**	**300**	**400**	**300**	**400**
Vitamin B_{12} (μg/d)	0.4	0.5	**0.9**	**1.2**	**1.8**	**2.4**	**1.8**	**2.4**
Pantothenic Acid (mg/d)	1.7	1.8	2	3	4	5	4	5
Biotin (μg/d)	5	6	8	12	20	25	20	25
Copper (μg/d)	200	220	**340**	**440**	**700**	**890**	**700**	**890**
Selenium (μg/d)	15	20	**20**	**30**	**40**	**55**	**40**	**55**
Zinc (mg/d)	2	**3**	**3**	**5**	**8**	**11**	**8**	**9**

Note: RDAs are in bold type; AIs are in ordinary type.

Source: Health Canada: http://www.hc-sc.gc.ca/fn-an/alt_formats/hpfb-dgpsa/pdf/nutrition/dri_tables-eng.pdf. Reprinted with the permission of the Minister of Public Works and Government Services, Canada, 2008.

*As preformed niacin, not niacin equivalents (NE) for this age group.

apply to the apparently healthy general population and are based on nutrient balance studies, biochemical measurement of tissue saturation or molecular function, and extrapolation from animal studies. Unfortunately, only limited data exist about the vitamin needs for infants and children, and there is no assurance that meeting the DRI will meet the needs of patients with kidney disease.

6.2: It is suggested that supplementation of vitamins and trace elements be provided to children with CKD stages 2 to 5 if dietary intake alone does not meet 100% of the DRI or if clinical evidence of a deficiency, possibly confirmed by low blood levels of the vitamin or trace element, is present. (C)

6.3: It is suggested that children with CKD stage 5D receive a water-soluble vitamin supplement. (C)

Children with CKD and those on dialysis therapy are at risk of alterations in vitamin and trace element levels or function as a result of decreased intake secondary to anorexia or dietary restrictions, increased degradation or clearance from blood, loss per dialysis, or interference with absorption, excretion, or metabolism (Tables 15 and 16).

Although limited, most data about the subject are derived from studies of adult populations. Whereas studies conducted in children receiving dialysis have documented dietary intake of most water-soluble vitamins, zinc, and copper that has been less than the RDA, the combination of dietary intake and supplemental intake has routinely met or exceeded the RDA.[300-303] In large part, this is due to the rarity of a vitamin and mineral supplement specifically formulated for infants and children on dialysis therapy and the resultant need to use one of the proprietary renal supplements available.[304-306] Caution should be exercised when using these supplements to not exceed the UL for the contents of the preparation when the intake of diet and supplement is combined (Tables 17 and 18). In older children and adolescents, daily vitamin supplementation is feasible without providing excessive vitamin intake. For smaller dosing in infants and toddlers, less frequent dosing (eg, every 2 to 3 days) or partial dosing (eg, half tablet) may be required if a liquid product or easily divisible tablet is not available. Children with healthy appetites for a variety of nutritious foods and children receiving the majority or all of their energy requirements from adult renal formulas generally meet 100% of the DRI for vitamins and trace elements and may not require vitamin supplementation.

Table 15. Physiological Effects and Sources of Vitamins

Name	Effects of Deficiency	Effects of Excess	Food Sources
Biotin	Seborrheic dermatitis, anorexia, nausea, pallor, alopecia, myalgias, paresthesias	Unknown	Liver, egg yolk, soybeans, milk, meat
Cyanocobalamin (vitamin B_{12})	Pemicious anemia; neurologic deterioration, methyl-malonic acidemia	Unknown	Animal foods only: meat, fish, poultry, cheese, milk, eggs, vitamin B_{12}-fortified soy milk
Folacin group of compounds	Megaloblastic anemia, impaired cellular immunity, irritability, paranoid behavior, neural tube defects in fetus of pregnant women	Masking of B_{12} deficiency symptoms in patients with pemicious anemia not receiving cyanocobalamin	Yeast, liver, leafy green vegetables, oranges, cantaloupe, seeds, fortified breads and cereals (grains)
Niacin (vitamin B_3)	Pellagra, dementia, diarrhea, dermatitis	Flushing, pruritis, liver abnormalities, hyperuricemia, decreased LDL and increased HDL cholesterol	Milk, eggs, poultry, meat, fish, whole grains, enriched cereal and grains
Pantothenic acid	Observed only with use of antagonists; depression, fatigue, hypotension, muscle weakness, abdominal pain	Unknown	Organ meats, yeast, egg yolk, fresh vegetables, whole grains, legumes
Pyridoxine (vitamin B_6)	Irritability, depression, dermatitis, glossitis, cheilosis, peripheral neuritis; in infants, irritability, convulsions, microcytic anemia	Neuropathy, photosensitivity	Liver, meat, whole grains, legumes, potatoes
Riboflavin (vitamin B_2)	Photophobia, cheilosis, glossitis, corneal vascularization, poor growth	Unknown	Meat, dairy products, eggs, green vegetables, whole grains, enriched breads and cereals
Thiamin (vitamin B_1)	Beriberi: neuritis, edema, cardiac failure, hoarseness, anorexia, restlessness, aphonia	Unknown	Enriched cereals and breads, lean pork, whole grains, legumes, in small amounts in most nutritious foods
Ascorbic acid (vitamin C)	Osmotic diarrhea, bleeding gums, perifollicular hemorrhage, frank scurvy	Massive doses predispose to kidney stones; nausea, abdominal pain; rebound scurvy when massive doses stopped	Papaya, citrus fruits, tomatoes, cabbage, potatoes, cantaloupe, strawberries
Retinol (vitamin A)	Night blindness, xerophthalmia, keratomalacia, poor bone growth, impaired resistance to infection, follicular hyperkeratosis	Hyperostosis, hepatomegaly, hepatic fibrosis, alopecia, increased cerebrospinal fluid pressure, hyper calcemia	Fortified milk, liver, egg, cheese, yellow fruits and vegetables (carotenoid precursors)
Vitamin E	Hemolytic anemia in premature infants; fat malabsorption causes deficiency; hyporeflexia, and spinocerebellar and retinal degeneration	Bleeding, impaired leukocyte function	Sardines, green and leafy vegetables, vegetable oils, wheat germ, whole grains, butter, liver, egg yolk
Vitamin K	Primary deficiency rare; hemorrhagic manifestations, possible effect on bone mineral density	Water-soluble analogs only: hyperbilirubinemia, hemolysis	Cow milk, green leafy vegetables, pork, liver

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Water-Soluble Vitamins

Thiamin (vitamin B_1)

Adult patients with CKD ingesting a low-protein diet have demonstrated borderline low thiamin levels.[307] In 1 study of children receiving dialysis, the spontaneous dietary intake was below the RDA in 28 of 30 patients.[301] Whereas a substantial quantity of thiamin is removed by HD, little appears to be lost by the peritoneal route in patients receiving chronic PD

Table 16. Physiological Effects and Sources of Trace Elements

Name	Effects of Deficiency	Effects of Excess	Food Sources
Zinc	Anorexia, hypogeusia, retarded growth, delayed sexual maturation, impaired wound healing, skin lesions	Few toxic effects; may aggravate marginal copper deficiency	Oysters, liver, meat, cheese, legumes, whole grains
Selenium	Cardiomyopathy, anemia, myositis	Irritation of mucous membranes, pallor, irritability, indigestion	Seafood, meat, whole grains
Copper	Sideroblastic anemia, retarded growth, osteoporosis, neutropenia, decreased pigmentation	Few toxic effects; Wilson disease, liver dysfunction	Shellfish, meat, legumes, nuts, cheese

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(CPD).[308,309] In most cases, the combination of dietary intake and daily supplement to equal the DRI will prevent deficiency. Thiamin stores can be assessed indirectly by means of erythrocyte transketolase activity or directly by means of high-performance liquid chromatography (HPLC).[310-312]

Riboflavin (vitamin B_2)

A low-protein diet may contain inadequate quantities of riboflavin,[312] and both Pereira et al[301] and Kriley and Warady[300] have documented spontaneous intake of riboflavin less than the RDA in children receiving dialysis. However, riboflavin deficiency is uncommon in patients being treated with HD or CPD and who receive a combined diet/supplement intake that meets or exceeds the DRI. Erythrocyte glutathione reductase activity is used to evaluate riboflavin status.[312]

Niacin (vitamin B_3)

There are limited data about the niacin status of patients with CKD, with or without the use of dialysis. The metabolic clearance of niacin is rapid, and thus it is believed that losses into dialysate are likely to be low. Prior studies have demonstrated the intake of niacin to be less than or equivalent to the RDA in patients prescribed a low-protein diet.[314] Whereas Pereira et al[301] found the spontaneous intake of niacin to be less than the RDA in 27 of 30 children receiving dialysis, the combined dietary and supplement intake exceeded the RDA in all cases. Thus, it is recommended that the DRI for niacin be provided per diet and/or supplement.

Table 17. Dietary Reference Intakes: Tolerable Upper Intake Levels

	Infants 0-6 mo	Infants 7-12 mo	Children 1-3 y	Children 4-8 y	Males/Females 9-13 y	Males/Females 14-18 y
Vitamin A (μg/d)	600	600	600	900	1,700	2,800
Vitamin C (mg/d)	ND	ND	400	650	1,200	1,800
Vitamin E (mg/d)	ND	ND	200	300	600	800
Vitamin K (μg/d)	ND	ND	ND	ND	ND	ND
Thiamin (mg/d)	ND	ND	ND	ND	ND	ND
Riboflavin (mg/d)	ND	ND	ND	ND	ND	ND
Niacin (mg/d; NE)	ND	ND	10	15	20	30
Vitamin B_6 (mg/d)	ND	ND	30	40	60	80
Folate (μg/d)	ND	ND	300	400	600	800
Vitamin B_{12} (μg/d)	ND	ND	ND	ND	ND	ND
Pantothenic Acid (mg/d)	ND	ND	ND	ND	ND	ND
Biotin (μg/d)	ND	ND	ND	ND	ND	ND
Copper (μg/d)	ND	ND	1,000	3,000	5,000	8,000
Selenium (μg/d)	45	60	90	150	280	400
Zinc (mg/d)	4	5	7	12	23	34

Abbreviation: ND, not determined.

Source: Health Canada: http://www.hc-sc.gc.ca/fn-an/alt_formats/hpfb_dgpsa/pdf/nutrition/dri_tables-eng.pdf. Reproduced with permission of the Minister of Public Works and Government Services, Canada, 2008.

Table 18. Multivitamin Comparisons*

Nutrient	Paediatric Dialyvit† (per tablet)	Ketovite‡ (per tablet)	Replavite & Hill-Vite (per tablet)	Dialyvite 800 with Zinc 15 (per tablet)	Nephrocap (per caplet)	Nephronex Caps (per caplet)	Liquid Nephronex (per 5 mL)	Strovite Forte Syrup (per 5 mL)
Vitamin A (μg)	—	—	—	—	—	—	—	400
Vitamin C (mg)	40	17	100	60	100	60	60	100
Vitamin D (μg)	—	—	—	—	—	—	—	3.3
Vitamin E (mg)	6	5	—	—	—	—	—	6.7
Vitamin K (μg)	20	500	—	—	—	—	—	—
Thiamin (mg)	0.8	1	1.5	1.5	1.5	1.5	1.5	5
Riboflavin (mg)	1	1	1.7	1.7	1.7	1.7	1.7	5.7
Niacin (mg)	12	3.3	20	20	20	20	20	33.3
Vitamin B_6 (mg)	2	0.3	10	10	10	10	10	6.7
Folic Acid (μg)	1,000	250	1,000	800	1,000	1,000	900	333
Vitamin B_{12} (μg)	1	—	6	6	6	10	10	6.7
Pantothenic Acid (mg)	6	0.4	10	10	5	10	10	8.3
Biotin (μg)	20	170	300	300	150	300	300	50
Copper (μg)	800	—	—	—	—	—	—	1,000
Zinc (mg)	8	—	—	15	—	—	—	5
Iron (mg)	—	—	—	—	—	—	—	3.3

*Representative but not all-inclusive list of vitamin preparations.

†Recommended dose for children 1-5 years old: half tablet daily; Recommended dose for children > 5 years old: 1 tablet daily.

‡Recommended dose: 3 tablets daily.

Pantothenic acid (vitamin B_5)

There are few data available about the status of pantothenic acid in adult patients with CKD or those receiving dialysis, and no data are available for children. However, the vitamin is removed by HD, and normal, low, and high levels have been found in adult dialysis patients.[315-317] Accordingly, patients on HD and CPD therapy likely should receive 100% of the DRI for this vitamin. Pantothenic acid levels are measured by means of radioimmunoassay.

Pyridoxine (vitamin B_6)

Low pyridoxine intake has been documented in a number of adult surveys of dialysis patients. In children, low intake of pyridoxine in children with CKD was reported by Foreman et al.[9] Stockberger et al[318] found intake to be lower than 59% of the RDA in 67% of children receiving CPD, and Pereira et al[301] noted intake less than the RDA in 26 of 30 pediatric dialysis patients. In a study of infants receiving CPD, Warady et al[303] documented dietary pyridoxine intake of only 60% RDA. There are also a host of medicines that can interfere with pyridoxine (and folic acid) metabolism (Table 19).

Low blood levels (measured as plasma pyridoxal-5-phosphate by means of HPLC) have been documented in HD and CPD patients, and dialysis removal of the nutrient likely contributes to the deficiency. A daily pyridoxine-HCl supplement of 10 mg has been recommended for adult HD and CPD patients because this is the lowest dose that has been proved to correct pyridoxine

Table 19. Medicines and Other Substances Interfering with Vitamin B_6 and Folic Acid Metabolism That May Contribute to Vitamin Deficiency

Vitamin B_6	Folic Acid
Isoniazide	Salicylazosulfapyridine
Hydralazine	Ethanol
Ipronlazide	Diphenylhydantoin
Penicillamine	Methotrexate
Oral contraceptives	Pyrimethamine
Cycloserine	Pentamidine
Thyroxine	Trimethoprim
Theophylline	Triamterene
Caffeine	Cycloserine
Ethanol	Mysoline
	Primidone
	Barbiturates
	Yeasts, beans

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deficiency. Lower supplemental doses, in addition to that provided by diet, likely would be sufficient in infants and young children based on the marked increase in blood level that has occurred with a 10-mg supplement in this population.[300] Supplements that equate to the RDA have previously been recommended.[302,319] Functional tests (eg, erythrocyte oxaloacetate transaminase) have been used to assess vitamin B_6 deficiency. As noted, direct measurement of total pyridoxine by means of HPLC also can be performed.

Biotin (vitamin B_8)

The intake of biotin has been estimated to be less than the RDA in adult patients with CKD prescribed with a low-protein diet.[316] In addition, intestinal absorption of biotin may be compromised in patients with CKD. The impact of HD on biotin status is poorly understood because both high and low blood levels have been reported.[320,321] Although there is no information regarding the influence of CPD on biotin losses and there is no information at all from children with kidney disorders, intake equal to the DRI should be provided per diet and/or supplement. Plasma biotin is measured by using microbiological assays.

Folic acid (vitamin B_9)

Litwin et al[321a] documented normal folic acid levels in 18 children with CKD and Pereira et al[301] found the dietary intake of folic acid to be greater than the RDA in 21 of 30 pediatric dialysis patients. Low folic acid levels have been reported in adult patients receiving CPD, with an average dialysis loss of 107 μg/d in 1 study.[322,323] Folic acid status (red blood cell and plasma) may be compromised by inhibitors of folic acid absorption (Table 19). Folic acid (along with vitamins B_6 and B_{12}) also has a key role in the handling of plasma homocysteine. Whereas some data have suggested that increased plasma homocysteine levels are a risk factor for CVD, other more recent studies have suggested otherwise.[324,325] Studies conducted in children have all demonstrated lowering of the plasma homocysteine level (the normal plasma concentration of homocysteine is ~5 to 10 μmol/L) following the provision of folic acid.[326-329] Thus, most children with CKD and those on dialysis therapy should receive the DRI, whereas adults are prescribed 1.0 mg/d.[330,331] If lowering plasma homocysteine level is the clinical goal, children with increased plasma homocysteine levels probably should receive 2.5 to 5.0 mg/d of folic acid.[305,310-313,315,317] However, in dialysis patients, administration of folate and vitamins B_6 and B_{12} has been reported to lower, but not normalize, plasma homocysteine levels.[332,333] Red blood cell folate levels are most indicative of body stores.[334] The reduced form of folic acid, tetrahydrofolate, may be measured by using a radioimmunologic technique.

Cobalamin (vitamin B_{12})

Most adult and pediatric patients with CKD and dialysis patients have been reported to have normal cobalamin levels, regardless of whether they receive a supplement.[300,303,309,322,323] Dietary intake also appears to meet or exceed the DRI in most, but not all, dialysis patients.[300,301,303,335] Serum vitamin B_{12} levels can be determined by using radioassay methods.

Ascorbic acid (vitamin C)

Decreased vitamin C levels have been reported in patients with CKD, as well as those receiving HD and CPD.[335-337] The low levels seen in dialysis patients are the result of low intake (eg, restricted intake of fruits) and dialysis losses.[301,322,335-337] In children, Pereira et al[301] found that 24 of 30 children received less than the RDA by diet alone. Warady et al[303] reported a negative mass transfer of 32 mg/d in children receiving APD, an amount compensated for by oral supplementation. However, in a study of infants receiving APD, Warady et al[303] reported dietary intake to be 140% of RDA, increasing to 180% of RDA with the addition of a 15-mg/d supplement. Excessive vitamin C intake (eg, 0.5 to 1 g/d in adults) can result in increased oxalate concentrations in plasma and soft tissues.[338,339] Thus, recommended combined dietary and supplement intake should not greatly exceed the DRI, with caution exercised when providing supplementation. Plasma ascorbic acid levels reflect dietary intake, and leukocytes levels estimate the body pool.

Fat-Soluble Vitamins

Retinol (vitamin A)

Vitamin A is not removed by dialysis, and elevated serum levels are present in patients with CKD and on dialysis therapy without supplementation.[300,302,303,309] Whereas retinol-binding protein (the transport protein for vitamin A) is catabolized in the renal tubules in individuals with normal kidney function, both vitamin A and retinol-binding protein accumulate when the GFR is reduced and there is impaired renal tubular activity.[340,341] Kriley and Warady[300] documented serum vitamin A levels in pediatric dialysis patients without supplements that were 3-fold greater than control patients. Because the risk of developing vitamin A toxicity is high when supplements with vitamin A are provided, total intake of vitamin A should be limited to the DRI, with supplementation rarely recommended and limited to those with very low dietary intake. Plasma vitamin A levels are measured by means of HPLC.

Vitamin K

There is no need for an intake of vitamin K greater than the DRI unless the patient is eating poorly and receiving long-term antibiotic therapy.[309,342,343] Plasma vitamin K levels are measured by means of liquid chromatography.

α-Tocopherol (vitamin E)

Plasma vitamin E levels in patients receiving HD have been reported as low, normal, and high.[344-346] No differences in levels were found comparing predialysis and postdialysis samples, and no α-tocopherol was found in dialysis effluent.[347,348] Studies of CPD patients have also reported both low and high levels of α-tocopherol.[335,349,350] Nevertheless, because of its ability to alleviate oxidative stress in patients at risk of CVD, patients with CKD and dialysis patients (aged $<$ 9 years) should receive the DRI of vitamin E.[351,352] Serum vitamin E levels are measured by means of HPLC.

Trace Elements

Copper

Dietary intake less than the DRI has been noted for copper in children receiving CPD.[353] Although copper excess is associated most commonly with CKD, low serum copper and ceruloplasmin levels also have been reported in children receiving HD.[303] Intake should be monitored every 4 to 6 months because supplementation to the DRI may be required in patients with particularly low dietary intake. Assessment of serum copper levels may be beneficial when clinical signs of overload or deficiency are present.

Selenium

Although selenium is normally excreted by the kidney and not removed by dialysis, low serum levels occur in patients with CKD or those receiving maintenance HD.[337,354] The selenium content of food is dependent on the selenium content of soil on which crops have grown or animals have grazed.[309] Selenium-dependent glutathione peroxidase activity in the blood, an integral component of the antioxidant defense, has also been found to be lower in patients with CKD than in healthy subjects, and the reduction worsens with increasing severity of disease. Supplementation of selenium in patients with CKD has resulted in a minimal increase in selenium-dependent glutathione peroxidase activity in patients with CKD, but not dialysis patients. Whereas routine supplementation is not recommended, patients should receive a daily dietary intake that meets the DRI.

Zinc

Low serum zinc levels result from removal by dialysis and poor intake. Intake less than the RDA has been documented in children receiving CPD.[353] Children and adults should receive the DRI for zinc, with supplementation reserved for treatment of clinical manifestations of zinc deficiency after laboratory confirmation.

COMPARISON TO OTHER GUIDELINES

- Vitamin and trace element intake recommendations are included in the European Best Practice Guideline on Nutrition.[309] However, those guidelines address the needs of only the adult HD population.
- The pediatric portion of the CARI CKD Guidelines recommends supplements of water-soluble vitamins for dialysis patients not receiving nutritional supplements. Supplements of vitamins A, B_{12}, and E are not recom-

mended because dietary intake routinely meets the DRI. The DRI for copper and zinc are recommended, with regular monitoring of serum zinc levels in patients receiving a low-protein diet.[334]

- The European Pediatric Peritoneal Dialysis Working Group recommends vitamin and trace mineral intake in accordance with reference nutrient intake.[319]

LIMITATIONS

The absence of studies in children with CKD and those on dialysis therapy that have assessed vitamin and trace element blood levels (1) before the institution of supplementation or after a wash-out period, and (2) after supplementation in a randomized manner with a control group for comparison. In addition, of the limited number of studies on the topic, most address dialysis and not predialysis patients with CKD, and all are based on single-center populations.

RESEARCH RECOMMENDATIONS

- Assess the selenium status of children with CKD stages 2 to 5 and 5D,
- Assess the vitamin and trace element needs of children with CKD and those on dialysis therapy by studying dietary intake and blood levels of these patients before and after supplementation,
- Assess the vitamin and trace element needs of patients receiving frequent HD,
- Further the development of a vitamin and trace element formulation designed to specifically meet the needs of pediatric patients.

RECOMMENDATION 7: BONE MINERAL AND VITAMIN D REQUIREMENTS AND THERAPY

7.1: Calcium

INTRODUCTION

The management of oral and/or enteral calcium intake in children with CKD is a challenging problem for physicians and dietitians. Whereas insufficient calcium supply may cause deficient mineralization of the skeleton, calcium overload may be associated with severe vascular morbidity.

7.1.1 In children with CKD stages 2 to 5 and 5D, it is suggested that the total oral and/or enteral calcium intake from nutritional sources and phosphate binders be in the range of 100% to 200% of the DRI for calcium for age. ***(C)***

RATIONALE

Adequate dietary calcium intake during childhood is necessary for skeletal development, including acquisition of an optimal peak bone mass during puberty.[355] Both insufficient and excessive oral and/or enteral calcium supply may occur in children with CKD. Intestinal calcium absorption is increasingly impaired in those with CKD as endogenous production of calcitriol (1,25-dihydroxyvitamin D; $1,25[OH]_2D$) decreases, but is readily stimulated by vitamin D therapy. Spontaneous calcium intake frequently is insufficient in adolescent patients in whom acceptance of high-calcium foods is limited and in children on phosphorus-restricted diets. The homeostatic mechanisms for regulating calcium balance are impaired most severely in children with CKD stage 5 and on dialysis therapy. Calcium absorption cannot be adjusted because of the kidney's inability to produce $1,25(OH)_2D$. Also, vitamin D receptor expression may be reduced.

However, therapy with high doses of active vitamin D sterols (eg, calcitriol, alfacalcidol) may boost intestinal calcium absorption. Oral and/or enteral treatment with calcium-containing phosphate binders and absorption from dialysis fluids with supraphysiological calcium content markedly enhance the calcium load. Increasing evidence suggests that the resulting strongly positive calcium balance is a major contributor to soft-tissue calcifications. Although it is impossible to accurately assess the actual absorption of calcium derived from diet and binders in this setting, it appears reasonable to limit total oral and/or enteral calcium ingestion.

Intake of 100% of the DRI for calcium is a reasonable starting point for children with CKD (Table 20). Although the safe limit of dietary calcium intake in children of different ages has not been defined by study evidence, it appears logical to scale maximal calcium intake relative to the age-specific DRI. The safe UL of dietary calcium intake in healthy individuals older than 1 year is 2,500 mg/d. For adults and children 9 years and older, this is approximately 2 times the DRI.

A number of measures are effective to improve low oral and/or enteral calcium intake and absorption: increased consumption of calcium-rich and/or calcium-fortified foods or tube feedings, supplementation with calcium-containing pharmacological agents between meals or bolus tube feedings, use of calcium-containing phosphorus binders for managing hyperphosphatemia, and supplementation with vitamin D.

If spontaneous intestinal calcium absorption is low, as typically observed in early stages of CKD, vitamin D should be supplemented to augment plasma $1,25(OH)_2D$ synthesis and maximize calcium absorption.

If plasma calcium levels and urinary calcium excretion remain low and dietary assessment suggests inadequate calcium intake, consumption of foods with high endogenous calcium

Table 20. Recommended Calcium Intake for Children with CKD Stages 2 to 5 and 5D

Age	DRI	Upper Limit (for healthy children)	Upper Limit for CKD Stages 2-5, 5D (Dietary + Phosphate Binders*)
0-6 mo	210	ND	≤420
7-12 mo	270	ND	≤540
1-3 y	500	2,500	≤1,000
4-8 y	800	2,500	≤1,600
9-18 y	1,300	2,500	≤2,500

Abbreviation: ND, not determined.

*Determined as 200% of the DRI, to a maximum of 2,500 mg elemental calcium.

Table 21. Calcium Content of Common Calcium-Based Binders or Supplements

Compound	Brand Name	Compound Content (mg)	% Calcium	Elemental Calcium (mg)	No. of Pills to Equal ~1,500 mg Elemental Calcium
Calcium Acetate	PhosLo™	667	25%	167	9
Calcium Carbonate	Children's Mylanta	400	40%	160	9
	Chooz™ (Gum)	500	40%	200	7.5
	TUMS™				
	TUMS EX™ (extra strength)	750	40%	300	5
	TUMS Ultra™	1,000	40%	400	3.75
	LiquiCal	1,200	40%	480	3
	CalciChew™	1,250	40%	500	3
	CalciMix™				
	Oscal 500™				
	TUMS 500™				
	Caltrate 600™	1,500	40%	600	2.5
	NephroCalci™				
Calcium Citrate	Citracal™	Not Recommended			
Calcium Acetate + Magnesium Carbonate	MagneBind™ 200	200 Magnesium carbonate		(Magnesium = 57 mg)	13
		450 Calcium acetate		113 mg	
	MagneBind™	300 Magnesium carbonate		(Magnesium = 85 mg)	20
		300 Calcium acetate		76 mg	

Adapted with permission.[121]

content (eg, milk, yogurt, cheese, Chinese cabbage, kale, and broccoli) and calcium-fortified food products should be encouraged. The bioavailability of calcium from milk and dairy products generally is high; however, the high phosphorus content of these products must be considered in children who require dietary phosphorus restriction. Some foods high in phytates, such as bran cereal, may have poor bioavailability of calcium.[356-358] Fortified products seem to provide calcium bioavailability comparable to milk.[359-361]

If dietary intake alone does not meet the DRI, use of oral and/or enteral calcium supplements should be considered (Table 21). Salts of calcium—gluconate (9% elemental calcium), lactate (13% elemental calcium), acetate (25% elemental calcium), or carbonate (40% elemental calcium)—are usually well tolerated by children of all ages. Calcium-containing phosphate binders can be applied easily and effectively in infants. Conversely, calcium chloride should be avoided as a supplement in patients with CKD due to the possible development of metabolic acidosis. Calcium citrate should not be given because citrate augments aluminum absorption.[362] Maximal absorption of calcium supplements is achieved when calcium salts are taken between meals and separate from iron supplements.[363,364]

As CKD progresses, increasing phosphate retention creates the need for oral and/or enteral phosphate-binder therapy. Calcium carbonate and calcium acetate are effective phosphate binders in children and should be used as first-choice therapy in patients with low dietary calcium intake.[365-370] Calcium carbonate and calcium acetate easily can be crushed, dissolved in formula milk, and administered through enteral tubes. However, hypercalcemic episodes occur in approximately 25% of patients, depending on the type and dose of the calcium-containing binder and the coadministration of active vitamin D sterols (eg, calcitriol and alfacalcidol). Calcium acetate has a higher specific phosphorus-binding efficacy than calcium carbonate[371] and causes fewer hypercalcemic episodes than calcium carbonate at a given phosphate-binder dose.[372-374] Hence, calcium carbonate should be preferred in children with insufficient dietary

calcium intake and no need for active vitamin D therapy, whereas calcium acetate is the preferable phosphate binder in children considered at moderate risk of calcium overload. In contrast to the use of calcium salts as supplements, calcium-containing phosphate binders should be taken with meals to obtain maximal phosphorus-binding efficacy and minimal intestinal absorption of free calcium. For calcium acetate, fecal excretion of phosphate has been shown to be higher when the phosphate binder is given with meals.[375]

The use of any calcium-containing phosphate binder should be limited by the maximally acceptable total oral and enteral calcium intake. For example, in a dialyzed 8-year-old with a typical spontaneous dietary calcium intake of 700 mg/d, a maximum of 900 mg of elemental calcium ingested as phosphate binders should be administered to stay within the recommended maximal total calcium intake of 1,600 mg (200% of the DRI). This would correspond to a prescription of 4 to 5 tablets containing 500 mg of calcium carbonate (200 mg of elemental calcium) or 5 tablets containing 667 mg of calcium acetate (167 mg of elemental calcium) per day. If dietary calcium intake is higher, calcium-containing phosphate-binder intake and/or dialysate calcium concentration need to be reduced, and the use of calcium-free phosphate binders should be considered. In a 1-year-old anuric child with an upper limit of 750 mg/d of calcium intake, a maximum of 875 mg of calcium carbonate (ie, 350 mg of elemental calcium) per day would be acceptable if dietary calcium intake is 400 mg.

These model calculations should be viewed as a general principle of dietary calcium prescription and may not always be applicable in clinical practice. Also, they do not consider confounding factors, such as treatment with active vitamin D sterols, which has been found to increase calcium absorption (reported to be 35% to 40% in those with CKD[377]) by 30%.[378] The dosage of calcium-based phosphate binders should be reduced in dialysis patients with low PTH levels because these patients commonly have low-turnover bone disease with a reduced capacity of the bone to incorporate a calcium load.[379]

To avoid the critical accumulation of calcium, oligoanuric children on dialysis therapy may require a further reduction in total oral and enteral calcium intake from nutritional sources and phosphate binders. In those with CKD stage 5, urinary calcium excretion—the major physiological elimination pathway—is severely impaired or absent. An anuric child receiving HD or PD with a neutral dialysate calcium concentration is incapable of disposing of any calcium exceeding the amounts required for bone formation by any mechanism other than soft-tissue precipitation. Hence, the upper limit of dietary calcium intake considered safe in healthy subjects may not be applicable to oligoanuric patients. In these children, further limitation of oral and enteral calcium intake from both dietary sources and calcium-containing phosphate binders should be considered, although evidence to support this further restriction is not yet available. Modification to decrease the calcium concentration in the dialysate is an additional therapeutic option to be considered in both HD and PD patients. Calcium balance during PD usually is negative with the use of 2.5 mEq/L calcium dialysate and positive with 3.0 to 3.5 mEq/L calcium dialysate.[380-384] Calcium balance during HD may be neutral or negative with the use of a 2.5-mEq/L calcium dialysate.[385,386] Dietary and pharmacological interventions should aim at avoiding both hypo- and hypercalcemic episodes.

COMPARISON TO OTHER GUIDELINES

These recommendations are in agreement with the K/DOQI Clinical Practice Guidelines for Bone Metabolism and Disease in Children with Chronic Kidney Disease in limiting total oral and enteral calcium intake to 200% or less of the DRI. These guidelines differ in that the pediatric K/DOQI Bone Metabolism and Disease guidelines are more liberal and allow up to 2 times the DRI for elemental calcium by calcium-based phosphate binders and a total intake of elemental calcium of up to 2,500 mg/d, regardless of age.

LIMITATIONS

- Neither the lower nor the upper limits of safety for calcium intake have been determined in children with different stages of CKD or oligoanuria.
- The effect of concomitant treatment with active vitamin D sterols on oral and enteral

calcium uptake is difficult to quantitate due to the multiplicity of factors involved.
- Newer non–calcium-containing phosphorus binders often are not available, and their cost may be prohibitive. Data for their safety in infants and children are limited.

RESEARCH RECOMMENDATIONS

- Short-term calcium balance studies and controlled long-term outcome studies are required in children receiving HD and PD to determine the relative roles of dietary calcium, calcium-containing phosphate binders, and dialysate calcium in the development of hypercalcemia, extraskeletal calcifications, CVD, adynamic bone disease, and bone fractures.
- Calcium balance between children with CKD with and without oligoanuria should be compared.
- The long-term safety of non–calcium-containing phosphate binders in infants and young children requires further investigation.

7.2: Vitamin D

INTRODUCTION

Recent clinical evidence suggests a high prevalence of vitamin D insufficiency in children and adults with CKD.

7.2.1 In children with CKD stages 2 to 5 and 5D, it is suggested that serum 25-hydroxyvitamin D levels be measured once per year. ***(C)***

7.2.2 If the serum level of 25-hydroxyvitamin D is less than 30 ng/mL (75 nmol/L), supplementation with vitamin D_2 (ergocalciferol) or vitamin D_3 (cholecalciferol) is suggested. ***(C)***

7.2.3 In the repletion phase, it is suggested that serum levels of corrected total calcium and phosphorus be measured at 1 month following initiation or change in dose of vitamin D and at least every 3 months thereafter. ***(C)***

7.2.4 When patients are replete with vitamin D, it is suggested to supplement vitamin D continuously and to monitor serum levels of 25-hydroxyvitamin D yearly. ***(C)***

RATIONALE

A decrease in serum calcidol (25-hydroxyvitamin D; 25[OH]D), the substrate for renal synthesis of $1,25(OH)_2D$, induces secondary hyperparathyroidism in individuals with normal kidney function[387,388] and may aggravate secondary hyperparathyroidism in patients with CKD.[389,390] The critical lower limit of the serum vitamin D concentration is not well defined. Serum concentrations show considerable seasonal and regional variation. Although severe manifestations of vitamin D deficiency, such as osteomalacia and hypocalcemia, are seen only with 25(OH)D concentrations less than 5 ng/mL (<12 nmol/L), levels less than 30 ng/mL (75 nmol/L) are suggestive of vitamin D "insufficiency" as manifested by hyperparathyroidism and increased risk of bone demineralization and hip fractures.[391,392] Supplementation with vitamin D, 800 IU/d, along with a modest dietary calcium supplement, reduced the hip fracture rate by 43% in a double-blinded placebo-controlled trial in elderly women.[393]

Vitamin D insufficiency is observed in a large proportion (typically 80% to 90%) of patients with CKD.[394,395] In a population-based study of patients hospitalized in New England, CKD was a major risk factor for low serum 25(OH)D levels.[396] Vitamin D insufficiency may be more relevant in those with CKD than in healthy individuals because, in contrast to healthy subjects in whom 25(OH)D is not rate limiting for calcitriol synthesis,[397] $1,25(OH)_2D$ levels correlated with 25(OH)D levels in patients with CKD.[394,395] This probably is explained by impaired compensatory upregulation of renal 1-α-hydroxylase and an increased contribution of strictly substrate-dependent extrarenal calcitriol synthesis in patients with impaired kidney function.[398,399]

Reasons for the high prevalence of low vitamin D levels in patients with CKD include their sedentary lifestyle with reduced exposure to sunlight, limited ingestion of foods rich in vitamin D (cod liver oil, fish, liver, egg yolk, fortified milk, and fortified margarine), reduced endogenous synthesis of vitamin D_3 in the skin in patients with uremia,[287] and urinary losses of 25(OH)D and vitamin D–binding protein in nephrotic patients.[400]

Table 22. Recommended Supplementation for Vitamin D Deficiency/Insufficiency in Children with CKD

Serum 25(OH)D (ng/mL)	Definition	Ergocalciferol (Vitamin D_2) or Cholecalciferol (Vitamin D_3) Dosing	Duration (mo)
<5	Severe vitamin D deficiency	8,000 IU/d orally or enterally × 4 wk or (50,000 IU/wk × 4 wk); then 4,000 IU/d or (50,000 IU twice per mo for 2 mo) × 2 mo	3
5-15	Mild vitamin D deficiency	4,000 IU/d orally or enterally × 12 wk or (50,000 IU every other wk, for 12 wk)	3
16-30	Vitamin D insufficiency	2,000 IU daily or (50,000 IU every 4 wk)	3

Note: Conversion factor for Serum 25(OH)D: ng/mL × 2.496 = nmol/L.
Adapted with permission.[121]

Even in patients with CKD stage 5D with little or no residual renal 1-α-hydroxylase activity, vitamin D deficiency is associated with more marked secondary hyperparathyroidism.[401] In anephric individuals, high doses of ergocalciferol (D_2) or alfacalcidol (25[OH]D) can increase serum calcitriol levels, pointing to a significant role of extrarenal 1-α-hydroxylase activity.[402-404] However, the role of 25(OH)D deficiency and its correction in patients on maintenance dialysis therapy is controversial because the ability to generate adequate levels of $1,25(OH)_2D$ is markedly reduced or absent. However, 25(OH)D has been claimed to exert specific effects on cell metabolism. 25(OH)D, but not $1,25(OH)_2D$, improved muscular function and phosphate content.[405]

In patients with CKD, nutritional vitamin D deficiency and insufficiency can be prevented or corrected by supplementation with vitamin D_3 (cholecalciferol) or vitamin D_2 (ergocalciferol). Cholecalciferol appears to have higher bioefficacy than ergocalciferol, although long-term comparative trials are lacking in humans.[406,407] The DRI for prevention of vitamin D deficiency in children and adolescents is 200 IU.[376] This value, published more than a decade ago, is 50% lower than the RDA that it replaced and, given increasing reports of vitamin D insufficiency in the general public, is controversial. The required daily vitamin D intake for patients of any age with CKD is unknown. In individuals with normal kidney function, the recommended upper limit of vitamin D is 1,000 IU/d in neonates and infants younger than 12 months and 2,000 IU/d for all other ages.[376] The equivalent of this dose can be achieved by administering 1 capsule (50,000 IU) once a month.[408] Daily doses of 10,000 IU of ergocalciferol have been administered in adult patients with advanced CKD for periods longer than 1 year with no evidence of vitamin D overload or renal toxicity.[409,410] Whereas signs of vitamin D intoxication would be the exception at doses recommended in this guideline, the development of hypercalcemia would be evidence of excessive dosing.

We recommend treating vitamin D deficiency and insufficiency, with the specific dosing regimen dependent on the severity of the disorder (Table 22). Smaller doses of vitamin D probably are sufficient in children younger than 1 year. When repletion (ie, serum 25[OH]D ≥ 30 ng/mL) has been accomplished, vitamin D homeostasis should be maintained by once-daily administration of 200 to 1,000 IU.

Calcitriol, alfacalcidol, or other synthetic active vitamin D analogs (eg, doxercalciferol and paracalcitol) should not be used to treat 25(OH)D deficiency.

COMPARISON TO OTHER GUIDELINES

Our recommendations are in line with the K/DOQI Clinical Practice Guidelines for Bone Metabolism and Disease in Children with CKD.

LIMITATIONS

The doses of ergocalciferol or cholecalciferol required to correct vitamin D insufficiency and to maintain normal vitamin D plasma levels have not been established in children with different stages of CKD.

RESEARCH RECOMMENDATIONS

- The dose-response relationship, as well as the comparative safety and efficacy, of different

administration intervals (daily versus monthly) of equivalent total doses of ergocalciferol or cholecalciferol should be studied across pediatric age groups.
- The effects of ergocalciferol and cholecalciferol supplementation on serum $1,25(OH)_2D$, PTH, calcium, and phosphorus levels and bone and cardiovascular end points should be studied in prospective controlled trials in children with different stages of CKD, including dialysis.
- The impact of various 25(OH)D treatment regimens on bone health of children with CKD.

7.3: Phosphorus

7.3.1 In children with CKD stages 3 to 5 and 5D, reducing dietary phosphorus intake to 100% of the DRI for age is suggested when the serum PTH concentration is above the target range for CKD stage and the serum phosphorus concentration is within the normal reference range for age. ***(C)***

7.3.2 In children with CKD stages 3 to 5 and 5D, reducing dietary phosphorus intake to 80% of the DRI for age is suggested when the serum PTH concentration is above the target range for CKD stage and the serum phosphorus concentration exceeds the normal reference range for age. ***(C)***

7.3.3 After initiation of dietary phosphorus restriction, it is suggested that serum phosphorus concentration be monitored at least every 3 months in children with CKD stages 3 to 4 and monthly in children with CKD stage 5 and 5D. ***(C)*** **In all CKD stages, it is suggested to avoid serum phosphorus concentrations both above and below the normal reference range for age.** ***(C)***

RATIONALE

Epidemiological studies of adult patients with CKD have demonstrated a positive association, albeit not a causal link, between hyperphosphatemia and morbidity and mortality independent of CKD stage. Although the benefits of lowering serum phosphorus level on patient-level clinical outcomes have not been demonstrated in prospective interventional studies, it is generally accepted and biologically plausible that increased serum phosphorus levels be avoided in patients with CKD stages 3 to 5 and 5D in an effort to control CKD-associated bone disease and CVD. Associations between hyperphosphatemia and CKD-associated vasculopathy have also been observed in children with CKD stage 5.[282,411]

Although serum phosphorus levels usually are not increased in the early stages of progressive CKD,[363,412-414] the dietary phosphorus load is an important determinant of the severity of hyperparathyroidism, even in those with mild renal insufficiency. In children and adults with CKD stage 3, dietary phosphorus restriction decreases increased PTH levels and increases $1,25(OH)_2D$ production, whereas dietary phosphorus intakes approximately twice the DRI for age aggravate hyperparathyroidism despite little or no change in serum phosphorus levels.[413,415,416] Also, bone biopsy studies showed marked improvement in bone resorption and defects in bone mineralization by using dietary phosphate restriction.[415] In 4 studies in children, dietary phosphate restriction did not lead to impaired statural growth.[256,417-419] Studies in adult and pediatric patients provided no evidence for any adverse effect of dietary phosphate restriction on nutritional status.[256,257,420-423] However, severe restriction of dietary phosphorus in children with moderate and severe CKD leading to subnormal serum phosphorus levels was associated with histological findings of worsening osteomalacia.[415]

Hence, a solid body of evidence suggests that moderate dietary phosphate restriction is beneficial with respect to the prevention and treatment of hyperparathyroidism and safe with respect to growth, nutrition, and bone mineralization. We recommend limiting dietary phosphorus intake to 100% of the DRI (Table 23) in normophosphatemic patients (using/not using phosphorus-lowering medications) if serum PTH concentration exceeds the target range (Table 24). Although similar PTH target ranges have been recommended by 2 Expert Work Groups,[121,424] the optimal range is controversial and may be lower than previously believed.[425] In CKD stages 4 and 5, when serum phosphorus levels increase to

Table 23. Recommended Maximum Oral and/or Enteral Phosphorus Intake for Children With CKD

Age	DRI (mg/d)	Recommended Phosphorus Intake (mg/d)	
		High PTH and Normal Phosphorus*	High PTH and High Phosphorus†
0-6 mo	100	≤100	≤80
7-12 mo	275	≤275	≤220
1-3 y	460	≤460	≤370
4-8 y	500	≤500	≤400
9-18 y	1,250	≤1,250	≤1,000

Source: Health Canada: http://www.hc-sc.gc.ca/fn-an/alt_formats/hpfb-dgpsa/pdf/nutrition/dri_tables-eng.pdf. Reproduced with the permission of the Minister of Public Works and Government Services Canada, 2008.

*≤ 100% of the DRI.

†≤ 80% of the DRI.

greater than the target normal range for age (Table 25) and hyperparathyroidism is already established, phosphorus restriction to approximately 80% of the DRI is recommended.

Higher physiological serum concentrations of calcium and phosphorus are observed in healthy infants and young children, presumably reflecting the increased requirements of these minerals by the rapidly growing skeleton. Rickets due to phosphorus deficiency occurs in preterm infants fed insufficient amounts of phosphorus and in infants and children with hypophosphatemia due to inherited disorders of renal phosphate transport.[426] Hence, when dietary phosphorus is restricted to control hyperphosphatemia and secondary hyperparathyroidism in children with CKD, subnormal serum phosphorus values should be avoided (Table 25).

The dietary prescription should aim at minimizing phosphate intake while ensuring an adequate protein intake. To achieve this aim, protein sources with low specific phosphorus content should be prescribed (see Table 13, Recommendation 5). Most food sources exhibit good phosphate bioavailability with the exception of plant seeds (beans, peas, cereals, and nuts) that contain phosphate in phytic acid.

Table 24. Target Range of Serum PTH by Stage of CKD

CKD Stage	GFR Range (mL/min/1.73m^2)	Target Serum PTH (pg/mL)
3	30-59	35-70
4	15-29	70-110
5, 5D	<15	200-300

Reprinted with permission.[121]

Table 25. Age-Specific Normal Ranges of Blood Ionized Calcium, Total Calcium and Phosphorus

Age	Ionized Calcium (mmol/L)	Calcium (mg/dL)	Phosphorus (mg/dL)
0-5 mo	1.22-1.40	8.7-11.3	5.2-8.4
6-12 mo	1.20-1.40	8.7-11.0	5.0-7.8
1-5 y	1.22-1.32	9.4-10.8	4.5-6.5
6-12 y	1.15-1.32	9.4-10.3	3.6-5.8
13-20 y	1.12-1.30	8.8-10.2	2.3-4.5

Adapted with permission[121]; Specker.[524]

Conversion factor for calcium and ionized calcium: mg/dL × 0.25 = mmol/L.

Conversion factor for phosphorus: mg/dL × 0.323 = mmol/L.

Milk and dairy products are a major source of dietary phosphorus. In young infants with CKD, phosphorus control can be achieved easily by using formulas with a low phosphorus content. It usually is feasible, and common clinical practice, to continue oral and/or enteral use of a low-phosphorus formula and delay the introduction of phosphorus-rich cow's milk until the age of 18 to 36 months.

Dietary phosphate restriction can be hindered by the inadvertent consumption of food containing phosphate additives, which can increase phosphorus intake up to 2-fold compared with unprocessed foods. This is a particular problem in patients with CKD who rely heavily on processed foods.[427,428]

Unfortunately, most available nutrient databases do not consider the impact of additives on total phosphorus content of foods. An exception is the USDA National Nutrient Database for Standard Reference, which lists more than 60 phosphate-containing food additives (www.ars.usda.gov/Main/site_main.htm?modecode=12-35-45-00; last accessed October 23, 2008).

The aspects mentioned illustrate that dietary modification of phosphorus intake is a complex and challenging task. Multiple pitfalls, including nonadherence in older children and adolescents, may result in inefficient lowering of phosphorus intake; conversely, overrestriction may lead to signs of phosphate deficiency, particularly in young infants. Hence, involvement of an experi-

enced pediatric dietitian is key to phosphorus management in children with CKD.

A recent randomized clinical trial assessed the efficacy of a low-phosphorus diet compared with additional treatment with different phosphate binders in adults with CKD stages 3 to 5. Coronary calcification increased in patients on the low-phosphorus diet alone, to a lesser extent in calcium carbonate-treated patients, and not at all in sevelamer-treated patients.[429] Notably, urinary phosphorus excretion did not decrease by the institution of the low-phosphorus diet alone and increased by 50% during the 2-year follow-up. These results highlight the difficulty of implementing and maintaining a phosphorus-restricted diet in clinical practice. Hence, dietary phosphate restriction should be considered an important, but not solitary, component in the management of uremic bone and vascular disease in association with vitamin D and phosphate-binder therapy and dialytic removal.

The link between hyperphosphatemia and patient mortality observed in adult studies[287,430-432] and the associations between serum phosphorus level and surrogate markers of vascular morbidity in adult and pediatric patients with CKD[282,433,434] provide a rationale to lower serum phosphorus levels pharmacologically if dietary phosphorus restriction is insufficient to maintain normophosphatemia. The current goal to target normal phosphorus levels is different from the allowance for slightly higher phosphorus values within the K/DOQI Pediatric Bone Guidelines.[121] Oral and enteral phosphate binders are effective in lowering serum phosphorus concentrations in children with CKD.[365-371] It should be noted that the association between bone and mineral metabolism disorders and cardiovascular risk and mortality are largely reported from either in vitro or retrospective cohort studies, which can prove association, but not cause and effect.

If total intestinal calcium load becomes excessive or hypercalcemia exists with the use of calcium-containing phosphate binders, these should be reduced in dose or replaced by calcium- and aluminium-free phosphate binders. The only calcium- and aluminum-free phosphate binder with proven efficacy and safety in children is sevelamer, which has been assessed in 2 randomized controlled clinical trials studying a total of 47 children. In 1 study, 29 hemodialyzed children were assigned to either sevelamer or calcium carbonate, and either calcitriol or doxercalciferol, as well. Although serum phosphorus levels were equally well controlled in the sevelamer and calcium-carbonate arms at the end of the 8-month study period, serum calcium and calcium-phosphorus ion product levels were significantly higher and hypercalcemia episodes were more frequent in the calcium-carbonate group, with no significant difference in serum PTH levels.[435] The second trial used a crossover design to compare sevelamer with calcium acetate in 18 children with CKD stages 3 to 4 or 5D during 8-week observation periods. Phosphorus and PTH control were similar with both treatments, whereas hypercalcemia occurred more frequently with calcium acetate. A decrease in LDL cholesterol levels by 34% and a greater incidence of metabolic acidosis were observed with sevelamer.[436]

Sevelamer is a resin that, in aqueous solution, attains a gel-like consistency and cannot be applied through feeding tubes without a high risk of tube blockage. However, it is possible to pretreat breast milk,[437] infant formula, and cow's milk[438] by dissolving sevelamer, waiting for precipitation, decanting, and feeding the supernatant of the processed fluid. This maneuver reduces phosphorus content by 80% to 90%.

Larger comparative trials in adults consistently observed lower serum calcium and higher PTH levels with sevelamer than with calcium-containing phosphate binders.[256,422,426-429,435-437,439-441] In adult patients with CKD stages 3 to 5 and 5D, randomized controlled trials have provided evidence that the use of sevelamer attenuates the progression of arterial calcifications compared with patients receiving calcium-based phosphate binders.[429,439-441]

Whereas neither cardiovascular nor all-cause mortality was reduced significantly by using sevelamer therapy in 1,068 patients completing the Dialysis Clinical Outcomes Revisited Study, the Renagel In New Dialysis Patients trial suggested a significant mortality reduction in incident dialysis patients receiving sevelamer for a median of 44 months.[439,440]

Lanthanum carbonate recently has become available as an alternative calcium- and alumi-

num-free binder with high affinity for phosphate and minimal intestinal absorption. In a randomized study in adult patients, lanthanum carbonate controlled plasma phosphate levels well and induced less adynamic bone disease than calcium carbonate.[442] However, no long-term data about the effect of lanthanum on the functions of liver and kidney and bone, in which lanthanum accumulates,[443] and its safety profile in children are available.

It should be emphasized that any phosphate-binder therapy introduces a major pill burden. The need to swallow several large tablets or capsules with each meal is a major physical and psychological challenge to many patients that can seriously compromise long-term adherence to this and other medications. Hence, phosphate-binder therapy should be individualized, realizing that in some patients, lowering of serum phosphate levels into the normal range may not be possible or may lead to an unacceptable decreased quality of life. In these cases, other options, such as intensified dialysis protocols, should be evaluated.

COMPARISON TO OTHER GUIDELINES

- With respect to dietary phosphorus restriction, our guidelines are similar to the current K/DOQI Pediatric Bone Guidelines[121] by our recommendation to lower dietary phosphorus intake to 100% of the DRI in children with an increased PTH level and normal serum phosphorus level for age and to less than 80% of the DRI in children with both an increased PTH level and increased serum phosphorus level for age.[355] Furthermore, whereas the indication for calcium-free phosphate binders is exclusively guided by serum calcium level, we also accept supramaximal total calcium intake as a reason to switch to calcium-free binders irrespective of serum calcium level.
- Our goal to target normal phosphorus levels is different from the allowance for slightly higher phosphorus values for children with CKD stages 5 and 5D within the K/DOQI Pediatric Bone Guidelines.
- The target PTH levels recommended here are similar to the European Guidelines for the prevention and treatment of renal osteodystrophy in children with chronic renal failure,[424] which recommend target PTH levels in the normal range for children with CKD stages 1 to 3 and 2 to 3 times normal for children with CKD stages 4 to 5 and 5D.

LIMITATIONS

- Whereas dietary phosphate restriction and phosphate-binder therapy exert a beneficial effect on secondary hyperparathyroidism, clinical trial evidence for an effect on such hard outcome end points as mortality, arterial calcifications, and hospitalization or fracture rates is lacking.
- Both dietary phosphate restriction and the pill burden and side effects associated with oral or enteral phosphate-binder use can be bothersome and a challenge to long-term prescription adherence.

RESEARCH RECOMMENDATIONS

- Randomized clinical trials are needed to assess the long-term impact of dietary phosphorus restriction on biochemical parameters, bone mineral density, linear growth, nutritional status, preservation of kidney function, and cardiovascular function in children across the age groups with CKD stages 2 to 4.
- Studies are needed to evaluate whether lowering serum phosphorus levels into the normal or low-normal range improves clinical outcomes in children with CKD stages 4 to 5 and 5D, including assessments of coronary artery calcification, intima-media thickness of large arteries, and arterial elasticity indices.
- Prospective comparative studies are needed to evaluate the efficacy and safety of different phosphate binders, including lanthanum carbonate, in children with CKD stages 4 to 5 and 5D. Possible end points include biochemical markers of bone and mineral metabolism, growth and nutritional status, and arterial morphology and function.

RECOMMENDATION 8: FLUID AND ELECTROLYTE REQUIREMENTS AND THERAPY

INTRODUCTION

Fluid and electrolyte requirements of individual children vary according to their primary kidney disease, degree of residual kidney function, and method of kidney replacement therapy. Supplementation or restriction of fluid, sodium, and potassium intake is individualized and influenced by the volume of urine output and the ability to concentrate urine, hydration status, and the presence or absence of hypertension or hyperkalemia. Dietary and other therapeutic lifestyle modifications are recommended as part of a comprehensive strategy to lower blood pressure and reduce CVD risk in those with CKD.[444]

8.1 Supplemental free water and sodium supplements should be considered for children with CKD stages 2 to 5 and 5D and polyuria to avoid chronic intravascular depletion and to promote optimal growth. (*B*)

8.2 Sodium supplements should be considered for all infants with CKD stage 5D on PD therapy. *(B)*

8.3 Restriction of sodium intake should be considered for children with CKD stages 2 to 5 and 5D who have hypertension (systolic and/or diastolic blood pressure ≥ 95th percentile) or prehypertension (systolic and/or diastolic blood pressure ≥ 90th percentile and < 95th percentile). *(B)*

8.4 Fluid intake should be restricted in children with CKD stages 3 to 5 and 5D who are oligoanuric to prevent the complications of fluid overload. *(A)*

8.5 Potassium intake should be limited for children with CKD stages 2 to 5 and 5D who have or are at risk of hyperkalemia. *(A)*

RATIONALE

8.1: Supplemental free water and sodium supplements should be considered for children with CKD stages 2 to 5 and 5D and polyuria to avoid chronic intravascular depletion and to promote optimal growth. (B)

The primary cause of CKD needs to be considered when initiating dietary modification of fluids and sodium. Although restriction of sodium and/or fluids is appropriate in children with CKD associated with sodium and water retention, the most common causes of CKD in children are associated with excessive loss of sodium and chloride. Infants and children with obstructive uropathy or renal dysplasia have polyuria, polydypsia, and difficulty conserving sodium chloride. These children develop a salt-wasting state and require salt supplementation.[119] In addition to its effect on extracellular volume, sodium depletion also adversely affects growth and nitrogen retention.[445] Sodium intake supports normal expansion of the ECF volume needed for muscle development and mineralization of bone.[446] Therefore, infants and children with polyuric salt-wasting forms of CKD who do not have their sodium and water losses corrected may experience vomiting, constipation, and significant growth retardation associated with chronic intravascular volume depletion and a negative sodium balance.[111] It is important to note that normal serum sodium levels do not rule out sodium depletion and the need for supplementation.

Individualized therapy can be accomplished by first prescribing at least the age-related DRI of sodium and chloride (Table 26).[119] In 2 small cohort studies, infants with polyuric salt-wasting CKD stages 3 to 5 who were given nutritional support with generous fluids and sodium supplements achieved better growth compared with published data for nonsupplemented infants with CKD. The dosage of sodium supplements used by the 2 studies varied between 2 to 4 mmol of sodium (Na)/100 mL formula added to 180 to 240 mL/kg/d of formula[111] and 1 to 5 mmol Na/kg body weight/d[120] and was adjusted according to blood biochemistry test results. The average dose used in the first study was Na, 3.2 ± 1.04 mmol/kg.[111] Nasogastric or gastrostomy tube feedings were used[111] or suggested for critical periods.[120]

Table 26. DRI for Healthy Children for Water, Sodium, Chloride and Potassium

	Total Water* (L/d)		Sodium† (mg/d)		Chloride (mg/d)		Potassium (mg/d)	
Age	AI	Upper Limit	AI	Upper Limit	AI	Upper Limit	AI	Upper Limit
0-6 mo	0.7	ND	120	ND	180	ND	400	ND
7-12 mo	0.8	ND	370	ND	570	ND	700	ND
1-3 y	1.3	ND	1,000	1,500	1,500	2,300	3,000	ND
4-8 y	1.7	ND	1,200	1,900	1,900	2,900	3,800	ND
9-13 y	2.4	ND	1,500	2,200	2,300	3,400	4,500	ND
14-18 y	3.3	ND	1,500	2,300	2,300	3,600	4,700	ND

Abbreviation: ND, not determined.

Source: Health Canada: http://www.hc-sc.gc.ca/fn-an/alt_formats/hpfb-dgpsa/pdf/nutrition/dri_tables-eng.pdf. Reproduced with the permission of the Minister of Public Works and Government Services Canada, 2008.

*Total water includes drinking water, water in beverages, and water that is part of food.

†Grams of sodium × 2.53 = grams of salt; 1 teaspoon salt = 2,300 mg sodium.

Sodium given as alkali therapy should be considered as part of the daily sodium allowance.[119]

Home preparation of sodium chloride supplements using table salt generally is not recommended due to potential errors in formulation that could result in hypo- or hypernatremia.[447]

8.2: Sodium supplements should be considered for all infants with CKD stage 5D on PD therapy. (B)

Infants on PD therapy are predisposed to substantial sodium losses, even when anuric. High ultrafiltration requirements per kilogram of body weight result in removal of significant amounts of sodium chloride. These losses cannot be replaced through the low sodium content of breast milk (160 mg/L or 7 mmol/L) or standard commercial infant formulas (160 to 185 mg/L or 7 to 8 mmol/L).[449] Consequences of hyponatremia include cerebral edema and blindness; therefore, neutral sodium balance must be maintained. Therapy should be individualized based on clinical symptoms, including hypotension, hyponatremia, and/or abnormal serum chloride levels. Sodium balance measurements, determined from dietary and medication intake and dialysate effluent losses, should be considered every 6 months concurrent with the measurement of dialysis adequacy. More frequent measurement is indicated after significant changes to the dialysis prescription or clinical status.

8.3: Restriction of sodium intake should be considered for children with CKD stages 2 to 5 and 5D who have hypertension (systolic and/or diastolic blood pressure ≥ 95th percentile) or prehypertension (systolic and/or diastolic blood pressure ≥ 90th percentile and < 95th percentile). (B)

When kidney function is impaired, ECF volume increases, edema occurs, and blood pressure increases. Hypertension is already common in the early stages of CKD, with 48% to 63% of children affected.[444,450] More than 50% of children on dialysis therapy have uncontrolled hypertension,[450,451] and an additional 20% have controlled hypertension.[63,451-454] Children with severe hypertension are at increased risk of hypertensive encephalopathy, seizures, cerebrovascular events, and congestive heart failure.[455] Less severe hypertension can contribute to progression of CKD. Therefore, dietary modification is encouraged for children and adolescents who have blood pressures in the prehypertensive range, as well as those with hypertension.[455]

A systematic review of pediatric clinical trials demonstrated that modest dietary sodium restriction reduces blood pressure in hypertensive children without CKD.[456] In dialysis patients, many observational and interventional studies of patients with CKD have shown that restricting sodium intake is an essential tool for volume and blood pressure control.[457-459] Aside from preventing acute complications of hypertension, optimal control of blood pressure reduces further kidney damage and modifies progression of disease.

The K/DOQI Clinical Guidelines for Hypertension,[444] CVD,[220] and Dialysis Adequacy[63] are all in agreement that dietary sodium restriction is an important component of a comprehensive strategy for volume and blood pressure control in adults and children with CKD. The earliest recommendation from the Hypertension Guidelines

was to limit daily sodium intake to less than 2,400 mg (<104 mmol).[444] The more recent Cardiovascular and Adequacy Guidelines have lowered the recommendation to less than 2,000 mg (<87 mmol) of sodium per day.[450,459] The most recent 2005 Dietary Guidelines for Americans older than 2 years[460] recommend that individuals with hypertension, blacks, and middle-aged and older adults aim to consume no more than 1,500 mg (65 mmol) of sodium per day. To provide more size-appropriate guidelines for infants and young children, based on a standard 60- to 70-kg adult, 1,500 to 2,400 mg/d of sodium would be the equivalent of sodium, 1 to 2 mmol/kg/d. This degree of restriction is reasonably consistent with the age-appropriate DRI for healthy children (Table 26).

The average daily intake of sodium in healthy children is far above recommended levels. In a national community health survey, 77% of children aged 1 to 3 years exceeded the recommended upper limit for sodium (1,500 mg/d), with a mean intake of 1,918 mg/d.[461] In children 4 to 8 years old, daily intake averaged 2,700 mg and 93% had consumed more than the recommended upper limit. For most of these children, adding salt at the table did not contribute to their high sodium intakes because 69% of those aged 1 to 3 years and 52% of those aged 4 to 8 years "never" added salt to their food. Salt intakes of adolescents exceeded recommended upper limits by 27% to 79%; the intake of males was significantly higher than that of females.

Sodium occurring naturally in food accounts for only about 10% of total intake, whereas salt added at the table or while cooking provides another 5% to 10% of total intake.[462] The majority (75%) of sodium in the diet comes from salt added by manufacturers during processing [462] to enhance flavor, control the growth of bacteria, provide certain functional characteristics, or act as a preservative. By weight, salt is composed of 40% sodium and 60% chloride. One teaspoon of salt contains about 2,300 mg of sodium.

Reduction of sodium intake can be achieved by replacing processed and canned foods with fresh foods; reading food labels to identify less salty foods; reducing salt added to foods at the table; in cooking, substituting fresh herbs and spices to flavor foods; and eating fast foods less often. The nutrition facts panel on food labels lists sodium content as actual amount (mg) and percent of the recommended daily value (% DV). Foods containing less than 140 mg or 5% DV are considered low in sodium,[460] and foods that have no more than 170 to 280 mg of sodium or 6% to 10% of the DV for sodium should be chosen. Salt substitutes, also referred to as light salts, typically replace all or some of the sodium with another mineral. Salt substitutes replacing Na chloride (NaCl) with potassium chloride (KCl) are contraindicated in children with hyperkalemia.

Certain medications (eg, antacids, laxatives, and nonsteroidal anti-inflammatory drugs) can be a significant source of sodium. Kayexalate® (sodium polystyrene sulfonate) contains 100 mg (4.3 mmol) of sodium per 100 g of powder. Where available, non–sodium-containing potassium binders (eg, calcium polystyrene sulfonate) should be used for children with severe hypertension and hyperkalemia.

Restriction of salt and fluid intake requires considerable patient motivation, which is often a problem in the adolescent population. The K/DOQI Hypertension Guidelines recommend dietary education by a dietitian every 3 months.[444] Patients used to a high-sodium intake may lose their appetite and become malnourished if sodium restriction is instituted too abruptly and too strictly.[63] In these patients, sodium restriction should be introduced gradually to provide time for taste adjustment. By cutting back gradually, most patients find that they do not miss the salt.

8.4: Fluid intake should be restricted in children with CKD stages 3 to 5 and 5D who are oligoanuric to prevent the complications of fluid overload. (A)

Children with oliguria or anuria need to limit their fluid intake to avoid associated complications of altered fluid status, including hypertension. Fluid restriction for oligoanuric children on HD therapy is also indicated, and an interdialytic increase above their "dry" weight (≤5% of their dry weight) is expected and desirable. Severe restriction of food (and fluid) intake by children for the purpose of avoiding extra HD sessions fosters malnutrition and should be discouraged.

Daily fluid restriction = insensible fluid losses (Table 27) + urine output + amount to replace additional losses (eg, vomiting, diarrhea, enterostomy output) − amount to be deficited.

Table 27. Insensible Fluid Losses

Age Group	Fluid Loss
Preterm infants	40 mL/kg/d
Neonates	20-30 mL/kg/d
Children and adolescents	20 mL/kg/d or 400 mL/m^2

To restrict fluid intake, children should be advised to reduce their intake of beverages, as well as foods that are liquid or semiliquid at room temperature (eg, ice, soup, Jell-O, ice cream, yogurt, pudding, and gravy). This can be achieved by drinking only when thirsty, taking small amounts throughout the day using small cups or glasses, quenching thirst by sucking on crushed ice, eating cold fruit, chewing gum, gargling or using breath sprays/sheets, and avoiding high-sodium or very sweet foods. About 80% of an individual's total water intake comes from drinking water and beverages and the other 20% is derived from food.[448] Many fruits and vegetables contain lots of water and can inconspicuously add to a child's fluid intake. These foods are not restricted routinely. The free water content of infant formulas (~90% by volume) and enteral feedings (70% to 85%) should be considered when formulating feeding regimens for fluid-restricted children (see Appendix 3, Table 36).

Attempts at fluid restriction may be futile if sodium is not restricted at the same time.[63] Reducing fluid intake alone is not practical most of the time because the increased ECF osmolality brought about by the excessive sodium ingestion will stimulate thirst, followed by further fluid ingestion and isotonic fluid gain.[63,463,464]

8.5: Potassium intake should be limited for children with CKD stages 2 to 5 and 5D who have or are at risk of hyperkalemia. (A)

Ninety-eight percent of the body's potassium is contained in cells, whereas only 2% is in the extracellular compartment. Potassium moves rapidly between the intra- and extracellular compartments to maintain normal serum levels. Because of the uneven distribution between compartments, small shifts can result in major changes in serum potassium concentrations. Maintaining a normal serum potassium concentration depends on these shifts, as well as excretion of potassium from the body. Intestinal excretion accounts for approximately 10% of potassium excretion, whereas the remainder is excreted in urine. Renal potassium excretion typically is maintained until GFR decreases to less than 10 to 15 mL/min/1.73 m^2. The risk of hyperkalemia is also increased by urinary obstruction, rhabdomyolysis, hemolysis (eg, blood transfusions and tumor lysis), acidosis, or treatment with potassium-sparing diuretics, angiotensin-converting enzyme inhibitors, or angiotensin receptor blockers.

Extracellular potassium influences muscle activity, especially the heart. Both hypokalemia and hyperkalemia cause alterations in all muscle function (skeletal, myocardial, and smooth muscle contractility) and cardiac arrhythmias. Hyperkalemia is common in patients with CKD stage 5 and, when severe, can rapidly lead to death from cardiac arrest or paralysis of muscles that control ventilation. Therefore, control of serum potassium is a critically important part of dietary management in patients with CKD.

When the kidney loses its ability to filter potassium (K), counseling children and caretakers to limit dietary potassium is critical to prevent and manage hyperkalemia. There are no data for the degree of dietary potassium restriction required for children with hyperkalemia. Suggested dietary management of hyperkalemia in adults limits intake to less than 2,000 to 3,000 mg (<50 to 75 mmol/d) of K daily.[444,465,466] Based on a 70-kg standard adult, this is the equivalent of less than 30 to 40 mg/kg/d (<0.8 to 1 mmol/kg/d). For infants and young children, 40 to 120 mg (1 to 3 mmol/kg/d) of K may be a reasonable place to start. Breast milk (mature) has the lowest potassium content (546 mg/L; 14 mmol/L) compared with standard commercial cow's milk-based infant formulas (700 to 740 mg/L; 18 to 19 mmol/L). Volumes of infant formula of 165 mL/kg or greater will exceed 120 mg (3 mmol) K/kg and may aggravate hyperkalemia. Children can lower potassium intake by restricting intake of such high-potassium foods as bananas, oranges, potatoes and potato chips, tomato products, legumes and lentils, yogurt, and chocolate.[460] The nutrition facts panel on food labels is not required to list potassium, but may provide potassium content as actual amount (mg) and % DV. Foods containing less than 100 mg or less than 3% DV are considered low in potassium. Foods containing 200 to 250 mg or greater than 6% DV are considered high in potassium (http://www.kidney.org/ATOZ/atoz

Item.cfm?id=103; http://www.kidney.org/Atoz/atozItem.cfm?id=148; last accessed November 12, 2008).[467] If potassium is not listed, it does not mean that the food does not contain potassium. Presoaking root vegetables, including potatoes, effectively lowers potassium content by 50% to 75%.[468,469]

Salt substitutes, also referred to as light salts, typically replace all or some of the sodium with another mineral, such as potassium or magnesium. Salt substitutes that contain potassium may cause hyperkalemia with life-threatening consequences in individuals with hyperkalemia or a tendency toward it.[470] Potassium-containing salt substitutes are inappropriate for people who need to limit both salt and potassium.

When hyperkalemia persists, despite strict adherence to dietary potassium restriction, nondietary causes of hyperkalemia—such as spurious values, hemolysis, metabolic acidosis, other exogenous potassium sources, constipation, inadequate dialysis, medications (angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, nonsteroidal anti-inflammatory agents, and potassium-sparing diuretics), and tissue destruction due to catabolism, infection, surgery, or chemotherapy—should be investigated further.[471,472]

Moderate to severe hyperkalemia may require treatment with a potassium binder. When oral, enteral, or rectal administration of potassium-binding resins is ineffective, undesirable, or not feasible, infant formula, enteral feedings, or other fluids can be pretreated to safely and effectively reduce their potassium content. Depending on the dosage of potassium binder used, this process lowers the potassium content of the feeding by 12% to 78%.[473-477] This process also may be indicated when there are concerns about obstruction of an enteral feeding tube. In addition to reducing potassium content, other reported changes associated with binder use include an increase or reduction in other nutrients, such as sodium and calcium.

Children on PD or frequent HD therapy (ie, >5 sessions/wk) rarely need dietary potassium restriction and may actually develop hypokalemia. Normokalemia may be achieved through counseling and frequent reinforcement of a high-potassium diet,[478] KCl supplements, or addition of potassium to the dialysate.

COMPARISON TO OTHER GUIDELINES

This guideline is in agreement with the following CARI CKD Guidelines[479]:

- Supplements of 4 to 7 mmol/kg/d of sodium chloride may be required to maximize growth in children with CKD and renal dysplasia.
- Sodium chloride supplements should be given to the limit of tolerance as indicated by increased blood pressure.
- When an infant requires high-sodium intake, a higher sodium renal milk formula (20 mmol/L), where available, may be preferable to a standard infant formula (7 mmol/L) or breast milk (6 mmol/L).

This guideline did not agree with the following suggestion in the CARI CKD Guidelines:

- Sodium chloride supplements may be added to a standard infant formula (1/4 metric teaspoon of table salt = 17 mmol).

No clinical guidelines were found for the degree of potassium restriction for children with or at risk of hyperkalemia. The CARI Guidelines for adults recommend a reduced potassium diet that limits intake to approximately 50 to 65 mmol (2,000 to 2,500 mg) of potassium daily.[480] The European Best Practice Guidelines on Nutrition for adults recommend a daily potassium intake of 50 to 70 mmol (1,950 to 2,730 mg) potassium daily or 1 mmol/kg ideal body weight for hyperkalemic predialysis patients.[309]

LIMITATIONS

There are no studies examining the effects of various levels of fluid, sodium, or potassium restriction on outcomes in children with CKD.

RESEARCH RECOMMENDATIONS

- Studies to determine the optimal level of sodium and potassium restriction to control blood pressure and hyperkalemia in children of different ages or body sizes are needed.
- Studies to identify the best counseling and motivational methods to improve dietary adherence to dietary restriction of fluid, sodium, and potassium are required.

RECOMMENDATION 9: CARNITINE

INTRODUCTION

Patients with CKD stage 5D and receiving HD have repeatedly been shown to have low levels of endogenous L-carnitine and elevated acylcarnitine levels. Whereas clinical symptoms compatible with carnitine deficiency can be evident in this patient population, there are limited data that provide evidence for successful therapeutic intervention with L-carnitine supplementation in HD patients.

9.1 In the opinion of the Work Group, there is currently insufficient evidence to suggest a role for carnitine therapy in children with CKD stage 5D.

RATIONALE

L-Carnitine is a biologically active amino acid derivative that has a key role in the regulation of fatty acid metabolism and adenosine triphosphate formation in multiple organs.[481] Total carnitine concentration includes both free and bound (ie, acylated) carnitine, which reflects levels in both serum and tissues, such as muscle, liver, and kidney. Total acylcarnitine levels are increased in patients with CKD stage 5D, with values as much as 4.6 times greater than in healthy subjects.[481] Carnitine deficiency is confirmed by measurements of plasma free and total carnitine with an acyl:free carnitine ratio greater than 0.4 (ie, [total − free carnitine] ÷ free carnitine) or a total serum carnitine value less than 40 μmol/L (Table 28).[482]

Patients who receive HD may be at risk of the development of carnitine deficiency as a result of loss of carnitine during the dialysis procedure, in addition to possible reductions in dietary intake and endogenous synthesis. In turn, patients on HD therapy have been documented to have low plasma and tissue L-carnitine levels.[481-484] Far less information pertaining to the relationship between dialysis and carnitine deficiency is available from the PD population.[485,486]

Table 28. Normal Serum Carnitine Levels (μmol/L)

	Serum Free Carnitine	Serum Total Carnitine
Neonates*	26-76	35-102
Children	41.4 ± 10.0†	56.2 ± 11.4†
Adolescent females†	39.3 ± 8.1	53.2 ± 8.9
Adolescent males†	39.6 ± 9.3	53.5 ± 10.5
Adult female*	19.3-53.9	28.1-66.4
Adult male*	34.8-69.5	44.2-79.3

Adapted with permission.[482]
*Data are presented as 95% CI.
†Data are presented as mean ± SD.

Carnitine deficiency can result in the development of anemia, cardiomyopathy, and muscle weakness, all symptoms that may be present in the dialysis population.[481,482,487,488] It is also associated with intradialytic hypotension in patients receiving HD. However, studies addressing the therapeutic use of supplemental L-carnitine in dialysis patients are few and have characteristically included small numbers of patients.[485,486,489,490] This has compromised any ability to generate definitive evidence supporting the role of regular supplemental L-carnitine in the treatment of these symptoms. Along these lines, the KDOQI Adult and Pediatric Work Group on Anemia Management conducted a thorough evaluation of the data particular to the treatment of anemia in patients with CKD and concluded there was insufficient evidence to recommend a role for carnitine in the treatment of anemia.[491] Most, but not all, of the few pediatric studies that have been conducted on the subject of carnitine deficiency in dialysis patients have provided evidence for an increase in plasma carnitine level after carnitine supplementation with no associated change in any symptoms.[485,486,489,490]

Although the Work Group cannot recommend the use of carnitine at this time, it does not want to discourage any therapeutic trial of carnitine if the clinical symptoms are suggestive of the disorder, especially when the evaluation provides laboratory evidence compatible with a diagnosis of carnitine deficiency. In a manner similar to that of an NKF Carnitine Consensus Conference and in line with the recommendation from the prior K/DOQI Pediatric Nutrition Guidelines, the Work Group believes that a trial may be indicated when all other causes for the symptoms in question have been excluded and the patient has been unresponsive to standard therapies.[487] Although carnitine supplementation has been provided through the intravenous and oral routes in pa-

tients with CKD, there have not been comparative studies of the 2 routes of therapy despite significant differences in their respective pharmacokinetics.[485,486,490] The bioavailability of oral L-carnitine in patients with CKD is unknown. In studies of healthy adults, the portion of oral L-carnitine that is not absorbed is converted to trimethylamine-*N*-oxide and trimethylamine, metabolites normally excreted by the kidney. Accumulation of these metabolites and their breakdown products in patients with CKD may be associated with the development of neurotoxicity and "uremic breath."[481,487,492]

COMPARISON TO OTHER GUIDELINES

- The European Pediatric Peritoneal Dialysis Working Group stated that there is no precise place for carnitine supplementation in the treatment of anemia in pediatric PD patients.[493]

RESEARCH RECOMMENDATIONS

- Prospective studies should be conducted to evaluate the impact of carnitine therapy on the cardiac structure/function of patients with CKD stage 5D.
- Additional studies should evaluate the influence of long-term (> 6 months) treatment of anemia hyporesponsive to erythropoiesis-stimulating agents with L-carnitine supplementation.
- Further definition of the L-carnitine response should be studied by taking an outcomes approach to patients treated with L-carnitine. Can patient groups be identified who are likely to respond to L-carnitine for 1 or more of its proposed indications? Are certain individuals uniform responders across indications or do certain patient characteristics predict specific responses?

RECOMMENDATION 10: NUTRITIONAL MANAGEMENT OF TRANSPLANT PATIENTS

INTRODUCTION

Transplantation is not a cure. It is a state of CKD regardless of GFR or other markers of kidney damage.[494] Management of children with a kidney transplant includes care of the graft, but also care of the complications of CKD.[495,496] Children continue to require dietary modifications after transplantation to address nutrition-related issues. Early in the transplantation period, dietary management of hypertension, hyperkalemia, hypophosphatemia, hypomagnesemia, and hyperglycemia are required to aid in the management of side effects of immunosuppressive drugs. Long-term interventions are needed to prevent or aid management of excessive weight gain/obesity, dyslipidemia, and steroid-induced osteoporosis. Children with CKD stages 2 to 5T require dietary management of protein and phosphorus in the same way as children with similar GFRs before transplantation. Continued assessment of nutrient intake, activity level, growth, laboratory values, and medications is suggested to ensure the best short- and long-term outcomes for children after transplantation.

10.1 Dietary assessment, diet modifications, and counseling are suggested for children with CKD stages 1 to 5T to meet nutritional requirements while minimizing the side effects of immunosuppressive medications. ***(C)***

10.2 To manage posttransplantation weight gain, it is suggested that energy requirements of children with CKD stages 1 to 5T be considered equal to 100% of the EER for chronological age, adjusted for PAL and body size (ie, BMI). ***(C)*** **Further adjustment to energy intake is suggested based upon the response in rate of weight gain or loss.** ***(C)***

10.3 A balance of calories from carbohydrate, protein, and unsaturated fats within the physiological ranges recommended by the AMDR of the DRI is suggested for children with CKD stages 1 to 5T to prevent or manage obesity, dyslipidemia, and corticosteroid-induced diabetes. ***(C)***

10.4 For children with CKD stages 1 to 5T and hypertension or abnormal serum mineral or electrolyte concentrations associated with immunosuppressive drug therapy or impaired kidney function, dietary modification is suggested. ***(C)***

10.5 Calcium and vitamin D intakes of at least 100% of the DRI are suggested for children with CKD stages 1 to 5T. ***(C)*** **In children with CKD stages 1 to 5T, it is suggested that the total oral and/or enteral calcium intake from nutritional sources and phosphate binders not exceed 200% of the DRI (see Recommendation 7.1).** ***(C)***

10.6 Water and drinks low in simple sugars are the suggested beverages for children with CKD stages 1 to 5T with high minimum total daily fluid intakes (except those who are underweight, ie, BMI-for-height-age < 5th percentile) to avoid excessive weight gain, promote dental health, and avoid exacerbating hyperglycemia. ***(C)***

10.7 Attention to food hygiene/safety and avoidance of foods that carry a high risk of food poisoning or food-borne infection are suggested for immunosuppressed children with CKD stages 1 to 5T. ***(C)***

RATIONALE

10.1: Dietary assessment, diet modifications, and counseling are suggested for children with CKD stages 1 to 5T to meet nutritional requirements while minimizing the side effects of immunosuppressive medications. (C)

The short- and long-term effects of immunosuppressive medications present new and familiar nutritional challenges to children and their caregivers that change during the course of the posttransplantation period. Goals of nutrition in the immediate and short-term posttransplantation period are to encourage intake, promote

anabolism and wound healing, maintain blood pressure control, and maintain glucose, mineral, and electrolyte balance. In the long-term stage of transplantation, nutritional goals are targeted to preventing chronic complications of immunosuppressive therapy, such as excessive weight gain/obesity, hyperlipidemia, hypertension, and corticosteroid-induced hyperglycemia and/or osteoporosis. Diet counseling should begin early to review the dietary prescription, nutrition-related medication side effects, and the nutrition care plan.

The first 3 to 6 months after transplantation can be very challenging for children and their caretakers, with many new routines and medications to learn. Because diets are advanced immediately after transplantation, it is recommended that patients be evaluated for appropriate energy, protein, carbohydrate, and fat intakes. If there is delayed normalization of kidney function, it is prudent to follow restrictions similar to those described for those with CKD stages 2 to 5 until kidney function normalizes. Over time, as immunosuppressant dosages decrease and their associated side effects recede, dietary modifications can be liberalized. Although many patients resist needing to follow a special posttransplantation diet, this is an appropriate time to instruct a healthy diet for age with a strong emphasis on regular exercise.

Table 29 lists nutrition-related side effects of currently used immunosuppressive agents in transplant patients.

Several of the side effects listed are transient and may last for only several weeks or months. Just as in the pretransplantation period, adaptation to some side effects often is possible, enabling a child to return to normal activities of living despite them. However, others present potentially life-long issues that will need to be considered for at least the duration of the transplant.

The frequency of nutritional assessment may be highest in the early posttransplantation period and decreases as the dosage and side effects of immunosuppressive medications are reduced. At a minimum, the frequency of nutritional assessment should be compatible with age- and stage-of-CKD–matched recommendations for children with CKD stages 2 to 5 and 5D (Recommendation 1, Table 1).

10.2: To manage posttransplantation weight gain, it is suggested that energy requirements of children with CKD stages 1 to 5T be considered equal to 100% of the EER for chronological age, adjusted for PAL and body size (ie, BMI). (C) Further adjustment to energy intake is suggested based upon the response in rate of weight gain or loss. (C)

There is no evidence that children who are transplanted have increased or decreased energy requirements compared with healthy children; however, excessive weight gain in children who

Table 29. Nutrition-Related Side-Effects of Immunosuppressive Medications

Maintenance Agents	Nutrition Side-Effects
Azathioprine	Nausea, vomiting, sore throat, altered taste acuity
Corticosteroids (prednisone, methylprednisolone)	Hyperglycemia, hyperlipidemia, sodium retention, hypertension, increased appetite and weight gain, osteoporosis, calciuria, muscle wasting, peptic ulcer disease, impaired wound healing, electrolyte disturbances
Calcineurin inhibitors (cyclosporine, tacrolimus)	Hyperlipidemia, hyperglycemia, hypomagnesemia, hyperkalemia, hypertension Avoid grapefruit
Sirolimus	Hyperlipidemia, gastrointestinal symptoms
Mycophenolate or Mycophenolic acid	Diarrhea, nausea
Induction Agents	**Nutrition Side-Effects**
Daclizumab	Minimal side-effects
OKT-3	Nausea, vomiting, diarrhea, loss of appetite
Rabbit antithymocyte globulin (ATG, thymoglobulin)	Decreased appetite

Adapted with permission.[497]

underwent transplantation can occur due to improved appetite associated with feeling well, as well as appetite stimulation from corticosteroid immunosuppressive medications. Recent data from the NAPRTCS show a rapid increase in weight for all age groups in the first 6 months after transplantation, with children increasing an average of 0.89 SD in weight in the first year after transplantation, with relative stability in average standardized weight scores during the next 5 years.[21] Whether a child is under- or overweight going into transplantation, calorie goals should be established after transplantation to achieve appropriate weight gain, maintenance, or loss.

Although most children with CKD are not overweight, recent data for growth and transplantation show that height and weight at the time of transplantation have increased and that more children are obese going into transplantation. The difference between mean pretransplantation height and weight SDS in 1987 was around 1 SDS, but had increased to 1.5 SDS in 2006 (web.emmes.com/study/ped; last accessed March 30, 2008), suggesting that children are now heavier for their height (overweight) at the time of transplantation. This is reflected in the increased prevalence of obesity in the pretransplantation setting from 8% before 1995 to 12.4% after 1995.[21] Obesity may develop after transplantation, and weight gain may be more significant in those who were obese before transplantation.[176] Mitsnefes et al[176] found that the frequency of obesity doubled during the first year after transplantation.

Obese children going on to kidney transplantation have shown increased risk of mortality and decreased long-term kidney allograft survival.[176,498] Additionally, in a retrospective review of pediatric kidney allograft recipients, children who were obese (BMI $\geq$ 95th percentile) at the time of transplantation had significantly worse 1-year allograft function compared with children who were not obese at the time of transplantation, but who became obese after 1 year and children who were not obese before transplantation or 1 year later.[176] The difference remained significant after adjusting GFR to height. A greater incidence of posttransplantation hypertension in obese children may explain the observed association between pretransplantation obesity and decreased GFR.

In the general population, obese children are at risk of high total cholesterol levels (15.7% versus 7.2%), high LDL (11.4% versus 7.7%) or borderline LDL cholesterol levels (20.2% versus 12.5%), low HDL cholesterol levels (15.5% versus 3%), high TG levels (6.7% versus 2.1%), high fasting glucose levels (2.9% versus 0%), high glycohemoglobin levels (3.7% versus 0.5%), and high systolic blood pressure (9.0% versus 1.6%) compared with healthy-weight children.[242] Given that the major cause of mortality in the CKD stage 5 population is cardiac related, the pediatric population, who are relatively young in the CKD process, stand to benefit from interventions to reduce obesity early in life.

For these reasons, it is important that patients and families be counseled on the potential risks of excessive weight gain and educated about appropriate dietary and exercise modification for weight control both before and after kidney transplantation.[21] Interventional strategies for treatment of child and adolescent overweight and obesity in the non-CKD population[45] may be helpful.

Data from studies in the general population and the lack of adverse effects make compelling reasons for recommending that exercise, in combination with diet, be encouraged in transplant recipients to prevent and/or aid in the management of overweight, hypertension, and dyslipidemia. Recommendations for children include encouraging time spent in active play (goal $\geq$ 1 h/d) and limiting screen time (television + computer + video games) to 2 h/d or less.[173] For adolescents and adults, recommendations include moderate physical activity 3 to 4 times weekly (20- to 30-minute periods of walking, swimming, and supervised activity within ability), as well as resistance exercise training.[499]

10.3: A balance of calories from carbohydrate, protein, and unsaturated fats within the physiological ranges recommended by the AMDR of the DRI is suggested for children with CKD stages 1 to 5T to prevent or manage obesity, dyslipidemia, and corticosteroid-induced diabetes. (C)

Dyslipidemia occurs frequently after kidney transplantation and promotes atherosclerosis; it may be associated with proteinuria in chronic

allograft nephropathy, recurrent disease, obesity, and/or immunosuppressive medications. The reported prevalence of increased LDL cholesterol levels (>100 mg/dL) in pediatric kidney transplant recipients studied in the 1990s ranged from 72% to 84%.[223,500-503] The risk and rates of posttransplantation dyslipidemia may differ based on the type of immunosuppression used, with lower prevalences reported with more recent protocols, including those that are steroid free.[504-506] It is estimated that there are 20 cardiovascular events/1,000 patients per year after transplantation.[507] Immunosuppressive agents, especially calcineurin inhibitors, directly contribute to side effects of hypertension, hyperlipidemia, and nephrotoxicity.[508,509] It is generally accepted that dietary protein and carbohydrate intake do not influence CVD risk as much as fat intake. A study performed primarily to follow the effect of diet on plasma fatty acid levels in 29 children and adolescents concluded that diets containing protein intakes appropriate for age (RDA), a generous carbohydrate intake featuring a low glycemic load, and fat intakes less than 30% of total caloric intake were reasonable goals of diet therapy after transplantation.[510] Another study of 45 patients did not find diet to conclusively explain the higher prevalence of dyslipidemia in their transplant patients compared with healthy controls.[284] However, they recommended that all patients with CKD be counseled in a diet high in polyunsaturated fats and low in saturated fats. Children adhering to the Step II AHA diet (≤30% total calories from fat, <7% calories from saturated fat, 10% polyunsaturated fat, <200 mg/d cholesterol)[511] had an 11% reduction in TG levels and a 14% reduction in LDL cholesterol concentration. In a study of the role of dietary intervention on metabolic abnormalities and nutritional status after transplantation, adults who followed a prescribed diet (AHA Step I Diet) and exercise regimen for the first year after transplantation showed significant improvements in weight, body fat, fasting glucose, and cholesterol levels; nonadherent patients experienced small, but insignificant, increases in the first 3 parameters and a significant increase in serum cholesterol levels.[512] Therefore, a first-line treatment should include a trial of diet modification limiting saturated fat, cholesterol, and simple sugars. More current dietary recommendations aimed at the early prevention of CVD are available from the AHA.[239] In children who resist overt dietary modification, healthy food preparation methods should at least be emphasized, including the use of such heart-friendly fats as canola or olive oils and margarines.

Glucose intolerance and hyperglycemia occur early after transplantation in association with surgical stress and corticosteroid and calcineurin inhibitor therapy, with serum glucose levels decreasing as immunosuppressant dosages decrease. Patients should be counseled to avoid simple sugars in the early posttransplantation period (the first 3 to 6 months) when steroid doses are highest and weight gain is most rapid. When blood sugar levels stabilize, it may still be necessary to restrict simple sugars to manage weight gain and hypertriglyceridemia. Posttransplantation diabetes mellitus occurs occasionally in pediatric kidney patients (2.6%) and is seen most frequently within the first year of transplantation.[513] Children with a family history of diabetes are at higher risk of posttransplantation diabetes.

Previous recommendations for increased DPI in the early posttransplantation period are no longer warranted. Given the quick postoperative recovery of most children and the current steroid-free or rapid-steroid-taper protocols used, compensation for increased nitrogen losses, protein catabolism, and decreased protein anabolism associated with surgical stress and high-dose corticosteroid therapy is no longer justified.

10.4: For children with CKD stages 1 to 5T and hypertension or abnormal serum mineral or electrolyte concentrations associated with immunosuppressive drug therapy or impaired kidney function, dietary modification is suggested. (C)

The majority of children who underwent transplantation are hypertensive and receive antihypertensive medications throughout the immediate and follow-up posttransplantation period. Approximately 80% of children are hypertensive in the early posttransplantation period. This rate decreases to 65% to 73% at 2 years and 59% to 69% at 5 years after transplantation (web.emmes.com/study/ped; last accessed March 30, 2008). Dietary sodium restriction is indicated to aid in blood pressure management (see Recommendation 8).

Table 30. Recommended Frequency of Measurement of Calcium, Phosphorus, PTH and Total CO_2 After Transplant

Parameter	Week 1	First 2 Months	2-6 Months	>6 Months
Calcium	Daily	Weekly	Monthly	As per guidelines for stage of CKD
Phosphorus	Daily	Weekly	Monthly	
PTH	Optional	At 1 month, then optional	If normal initially, optional	
Total CO_2	Daily	Weekly	Monthly	

Adapted with permission.[121]

Hyperkalemia in the immediate posttransplantation period occurs frequently in association with the medications cyclosporin and tacrolimus, especially when blood levels achieve or exceed therapeutic targets. Serum potassium levels should be monitored and a low-potassium diet should be implemented as indicated (see Recommendation 8).

Hypophosphatemia is a common complication seen in the early stage of kidney transplantation, occurring in up to 93% of adults during the first few months posttransplantation.[514] Low serum levels occur in association with an increase in urinary phosphate excretion, decreased intestinal phosphate absorption, and hyperparathyroidism that persists beyond the pretransplantation period.[514] Children with hypophosphatemia can be encouraged to consume a diet high in phosphorus (see Recommendation 5, Table 13); however, phosphorus supplements usually are required.[121]

Hypomagnesemia, a common side effect of calcineurin inhibitors, occurs early in the posttransplantation period. Increased dietary magnesium intake may be attempted; however, as in the case of hypophosphatemia, the amount of magnesium required to correct serum levels typically requires a magnesium supplement.

10.5: Calcium and vitamin D intakes of at least 100% of the DRI are suggested for children with CKD stages 1 to 5T. (C) In children with CKD stages 1 to 5T, it is suggested that the total oral and/or enteral calcium intake from nutritional sources and phosphate binders not exceed 200% of the DRI (see Recommendation 7.1). (C)

After transplantation, children are predisposed to progressive bone disease and osteoporosis for several reasons. They are likely to have preestablished metabolic bone disease associated with CKD. After transplantation, corticosteroids, calcineurin inhibitors, and residual hyperparathyroidism may increase the risk of bone demineralization,[121] with bone loss most rapid during the first year after transplantation.[515] Osteopenia has been confirmed by using bone biopsy data and/or bone densitometry.[516] Interpretation of DXA measurement of bone mineral density is complicated in children with delayed growth and maturation,[121,517] and estimates of the perceived prevalence of moderate plus severe osteopenia vary according to analysis based on chronological age (42%), height-age (15%), or sex-matched (23%) reference data.[516] Whether deficits in bone mineral density are reversible upon discontinuation of glucocorticoids is unclear. Pediatric kidney transplant recipients also are at increased risk of developing disabling bone disease, such as avascular necrosis and bone fractures. In addition, transplantation is part of the continuum of CKD, and progressive damage to the graft will result in bone mineral disorders similar to the effects of CKD in the native kidney.[121]

Because of these issues, it is recommended that serum levels of calcium, phosphorus, total CO_2, and PTH continue to be monitored after transplantation (Table 30).[121]

To minimize bone mineral loss, daily supplementation at the level of the DRI for calcium and 800 to 1,000 IU of vitamin D has been suggested; however, there are no data for efficacy in children. Children with CKD stages 3 to 5T with bone mineral disorders should be managed according to established recommendations for nontransplantation children with similar GFRs (see Recommendation 7).

10.6: Water and drinks low in simple sugars are the suggested beverages for children with CKD stages 1 to 5T with high minimum total daily fluid intakes (except those who are

Table 31. General Food Safety Recommendations for Immunosuppressed Children

- Clean: To avoid spreading bacteria throughout the kitchen, wash hands and food preparation surfaces often.
- Separate: Avoid spreading bacteria from one food to another by keeping high-risk foods such as raw meat, poultry, seafood, and eggs away from ready-to-eat foods.
- Cook to proper temperatures: Foods are safely cooked when they are heated to the USDA-recommended safe minimum internal temperature.
- Chill: Refrigerate foods promptly to slow the growth of harmful bacteria.
- Read labels to avoid purchasing food that is past its "sell by" or "use by" date.
- Buy only pasteurized milk, cheese, and other dairy products from the refrigerated section. Read labels to be sure that fruit juice selected from the refrigerated section of the store is pasteurized.
- Purchase canned goods that are free of dents, cracks, or bulging lids.
- When eating out, avoid foods containing uncooked ingredients such as eggs, meat, poultry, or fish. Avoid buffets, which may contain undercooked foods or foods that have been at room temperature too long.

Source: US Department of Agriculture (USDA).[519]

underweight, ie, BMI-for-height-age < 5th percentile) to avoid excessive weight gain, promote dental health, and avoid exacerbating hyperglycemia. (C)

Good graft function after transplantation affects fluid and electrolyte balance. A high volume of fluid intake generally is prescribed to stimulate kidney function, replace high urine output, and regulate intravascular volume. Consumption of large volumes of fluids with high calorie, fat, or simple sugar content can contribute to obesity and exacerbate increased serum levels of glucose and TG. With the exception of children needing to gain weight, the majority of fluid intake should come from water, fat-free or low-fat milk, and sugar-free drinks. Increasing fluid intake frequently is challenging for children who followed a strict fluid restriction or were tube fed before transplantation. In some children, including infants and toddlers receiving an adult kidney, enteral hydration continues to be needed after transplantation.

10.7: Attention to food hygiene/safety and avoidance of foods that carry a high risk of food poisoning or food-borne infection are suggested for immunosuppressed children with CKD stages 1 to 5T. (C)

Immunosuppressed patients are more prone to develop infections, potentially including those brought on by disease-causing bacteria and other pathogens that cause food-borne illness (eg, *Escherichia coli, Salmonella,* and *Listeria monocytogenes*). Many patients are given gastric acidity inhibitors after transplantation; these medications have been associated with increased risk of intestinal and respiratory infections in nontransplanted children.[518] Of concern are the common symptoms of food-borne illness that include diarrhea and vomiting, both of which may lead to dehydration and/or interfere with absorption of immunosuppressive medications. Foods that are most likely to contain pathogens fall into 2 categories: uncooked fresh fruits and vegetables, and such animal products as unpasteurized milk, soft cheeses, raw eggs, raw meat, raw poultry, raw fish, raw seafood, and their juices. Although the risk of infection from food sources in immunosuppressed kidney transplant patients is unknown, it seems prudent that transplant patients be educated about safe practices when handling, preparing, and consuming foods (Table 31).[519] Theoretically, food safety would be most important during periods when immunosuppression dosing is at its highest and liberalization or discontinuation could occur as immunosuppressant doses decrease.

COMPARISON TO OTHER GUIDELINES

The KDIGO Transplant Guideline is in development.

LIMITATIONS

The majority of research in posttransplantation nutrition has been conducted in adults. There are no controlled studies of the effect of calcium and vitamin D supplementation on bone mineral density after transplantation.

RESEARCH RECOMMENDATIONS

- Determine energy and protein requirements of children on corticosteroid therapy after transplantation;
- Determine whether dietary intervention is effective in minimizing posttransplantation weight gain, and if so, methods to motivate children to embrace a heart-healthy diet and regular exercise after transplantation;
- Determine whether posttransplantation calcium and vitamin D supplementation in children on corticosteroid therapy positively impact on bone mineral density and decrease the risk of osteopenia, osteoporosis, avascular necrosis, and fractures.

APPENDIX 1: PROCEDURES FOR MEASURING GROWTH PARAMETERS

GROWTH PARAMETERS TO BE MEASURED

Standard measurement techniques should be used for all growth parameters.[298] Ideally, length/height and head circumference measures should be performed by the same person each time.

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 1 side; pen and paper for recording. Two persons are necessary: 1 to hold the head and another to measure.

Procedure

(i) The infant may be measured in light clothing, without foot coverings. (ii) Place the infant on the table, lying on his back. (iii) 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. (iv) While the head remains in contact with the headboard, a second measurer grasps 1 or both feet at the ankle. (v) 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. (vi) 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

(i) 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. (ii) Place the head projection at the crown of the head. (iii) Hold the block steady and have the child step away from the wall. (iv) Note the measurement and record it to the nearest 0.1 cm. (v) Perform 3 measurements that are within 0.2 cm of each other and use the average of the 3 for the final value.

WEIGHT USING AN INFANT SCALE

Equipment

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

Procedure

(i) Undress the infant completely. (ii) Place a clean paper liner in the tray of the scale. (iii) Calibrate the scale to zero. (iv) Lay or seat the infant in the tray. (v) Read the weight according to the type of scale. Make sure the infant is unable to touch the wall or surrounding furniture. (vi) Record the weight to the nearest 0.1 kg.

STANDING WEIGHT

Equipment

Scale; pen and paper for recording.

Procedure

(i) The child should be weighed in light clothing without footwear. (ii) Calibrate the scale to zero. (iii) Assist the child onto the platform of the scale. (iv) Instruct the child to stand in the center of the platform with feet flat and heels touching, as erect as possible. (v) 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. (vi) Read the measurement from the scale, looking squarely at the increments rather than from an angle. (vii) 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

(i) Have the person assisting hold the infant so that the head is upright. (ii) Locate the occipital bone at the back of the head, also the supraorbital ridges. (iii) Apply the tape firmly around the head just above the supraorbital 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. (iv) Record the measurement to the nearest 0.1 cm.

EVALUATION OF MEASUREMENTS

Anthropomorphic measures should be plotted on the appropriate growth chart: standing height or recumbent length, weight, BMI, and head circumference. Low height for chronological age or a low head circumference in proportion to height may reflect long-term nutritional deficits, particularly in infants. Parental heights should be considered when interpreting growth charts. One-time measurements reflect size, whereas serial measurements are necessary for the assessment of growth. Low BMI-for height-age may reflect a nutritional deficit. In some situations, BMI may be better assessed relative to chronological age; for example, in a fully mature (Tanner stage 5) adolescent.

Individual measurements are evaluated by determining SDS (or *z* scores) or percentiles. Growth SDS represent the difference, in SD units, of an individual child's value (eg, height or weight) and the mean value of a sample population (eg, mean height or weight of healthy children of the same age and sex). Percentiles and SDS are interchangeable; they are 2 ways of expressing the same information. For example, a child on the 50th percentile of height for age would have an SDS of 0. About 95% of healthy children will have an SDS between −2.0 (~3rd percentile) and +2.0 (~97th percentile).

Measures may be plotted on the standardized growth charts enclosed in these guidelines (Appendix 5).[33,34,52] These growth charts were generated by using a statistical method called LMS.[520] Calculation of exact SDS can be done by using data from tables of L, M, and S values for each measure and entering them into the following equation:

$$\text{SDS} = [(\text{observed measure} \div \text{M})^{\text{L}} - 1] \div (\text{L} \times \text{S})$$

The US National Center for Health Statistics 2000 Growth Charts LMS tables are available on-line at: www.cdc.gov/nchs/about/major/nhanes/growthcharts/datafiles.htm.

The WHO Growth Standards LMS tables are available in downloadable documents[34,52] on-line at: www.who.int/childgrowth/standards/technical_report/en/index.html.

EXAMPLE: To calculate the height-for-age SDS for an 8.5-year-old girl, one would look up the L, M, and S values from the appropriate table and enter them into the equation, along with her observed height (eg, 120.6 cm):

$$\text{SDS} = [(120.6 \div \text{M})^{\text{L}} - 1] \div (\text{L} \times \text{S})$$

$$\text{SDS} = [(120.6 \div 130.6)^{0.0027} - 1] \div (0.0027 \times 0.0463)$$

$$\text{SDS} = -1.72$$

Alternatively, several on-line calculators or downloadable software packages are available to perform these calculations. On-line resources, the data sources for each, and the measures included in each are provided in Appendix 2.

APPENDIX 2: RESOURCES FOR CALCULATING ANTHROPOMETRIC SDS/PERCENTILES, ENERGY REQUIREMENTS, AND MIDPARENTAL HEIGHT

Table 32. Resources for Calculating Anthropometric SDS and Percentiles

Source	Program	Link	Weight-for-Age z-Score	Height-for-Age z-Score	Head Circumference-for-Age z-Score	BMI-for-Age z-Score	Height Velocity z-Score
U.S. Centers for Disease Control & Prevention (CDC)	Epi Info NutStat-based on 2000 CDC growth charts	http://www.cdc.gov/epiinfo/	✓	✓	✓	✓	
World Health Organization (WHO)	WHO Anthro—based on 2006 WHO Growth Standards (birth-5 years)	http://www.who.int/childgrowth/software/en/	✓	✓	✓	✓	
North American Pediatric Renal Transplant Cooperative Study (NAPRTCS)	Growth Chart Calculator-based on 2000 CDC growth charts	http://spitfire.emmes.com/study/ped/resources/htwtcalc.htm	✓	✓			
Genentech	GenenCALC-based on 2000 CDC growth charts	Diskette obtained from Genentech representative	✓	✓		✓	✓
StatCoder	STAT Growth-BP for hand-helds	http://www.statcoder.com/growthcharts.htm	✓	✓		✓	✓
Baylor College of Medicine	Kids BMI Calculator	http://www.kidsnutrition.org/bodycomp/bmiz2.html				✓	

Table 33. Resources for Calculating Midparental Height

Source	Program	Link
UpToDate	Calculator: Midparental Target Height Prediction	http://www.uptodate.com/patients/content/topic.do?topicKey=pediendo/2375

Table 34. Resources for Calculating Estimated Energy Requirements

Source	Program	Link
Baylor College of Medicine	Kids Energy Calculator	http://www.kidsnutrition.org/energy_calculator.htm

APPENDIX 3: NUTRIENT CONTENT INFORMATION

Table 35. Actual and Adjusted Amounts and Ratios of Phosphorus to Protein in Specific Foods

Food	Amount	Actual Content of Phosphorus (mg)	Actual Content of Protein (g)	Ratio of mg Phosphorus to g Protein	Phosphorus Content (mg) Adjusted for Bioavailability	Protein Content (g) Adjusted for Digestibility	Ratio of mg Phosphorus to g Protein Adjusted for Digestion and Absorption
Meat/Poultry/Egg							
Pork loin	3 oz	146	22	6.6	102	20.9	4.9
Chicken thigh	3 oz	148	22	6.7	104	20.9	4.9
Turkey	3 oz	210	28	7.5	147	26.6	5.5
Chicken breast	3 oz	196	27	7.3	137	25.7	5.4
Beef sirloin	3 oz	203	25	8.1	142	23.8	6.0
Veal loin	3 oz	189	22	8.6	132	20.9	6.3
Lamb chop	3 oz	190	22	8.6	133	20.9	6.3
Ham	3 oz	239	19	12.6	167	18.1	9.3
Egg, large	1	86	6	14.3	60	5.7	10.5
Fish/Seafood							
Shrimp	3 oz	116	18	6.4	81	17.1	4.7
Crab, dungeness	3 oz	149	19	7.8	104	18.1	5.7
Lobster	3 oz	157	17	9.0	110	16.5	6.6
Halibut	3 oz	214	23	9.3	150	21.9	6.9
Crab, blue	3 oz	175	17	10.3	123	16.2	7.6
Salmon	3 oz	282	21	13.4	197	20.0	9.9
Fish sticks	3 oz	153	9	17	107	8.6	11.3
Beans/Legumes/ Tofu/Seeds							
Soybeans, roasted	1 cup	624	61	10.2	312	51.9	6.0
Tofu, firm	100 g	76	6	12.7	38	5.1	7.5
Tofu, soft	100 g	52	4	13.0	26	3.4	7.6
Beans, lima	1 cup	209	15	13.9	105	12.8	8.2
Soybeans, boiled	1 cup	421	29	14.5	211	24.7	8.5
Beans, refried	1 cup	217	14	15.5	109	11.9	9.1
Beans, black	1 cup	241	15	16.1	121	12.8	9.5
Beans, kidney	1 cup	251	15	16.7	126	12.8	9.8
Peas, pigeon	1 cup	200	12	16.7	100	10.2	9.8
Beans, navy	1 cup	286	16	17.9	143	13.6	10.5
Chickpeas	1 cup	216	12	18.2	108	10.2	10.7
Sunflower seeds	1 oz	322	6	53.7	161	5.1	31.6
Nuts/Nut Butter							
Peanut butter, chunky	2 Tbsp	101	8	12.6	51	6.8	7.4
Peanut butter, smooth	2 Tbsp	118	8	14.8	59	6.8	8.7
Peanuts, roasted	1 oz	147	8	18.4	74	6.8	10.8
Pistachios	1 oz	137	6	22.8	69	5.1	13.4
Almonds	1 oz	139	6	23.2	70	5.1	13.6
Walnuts	1 oz	98	4	24.5	49	3.4	14.4
Macadamia	1 oz	56	2	28.0	28	1.7	16.5
Sunflower seeds	1 oz	327	5	65.4	164	4.3	38.4
Fast Foods							
Hamburger	1	207	27	7.7	124	24.3	5.1
Taco	Large	313	31	10.1	188	27.9	6.7
Hot dog	1	99	9	11	59	8.1	7.3
Cheeseburger	1	310	28	11.0	186	25.4	7.3
Sausage patty	1	106	10	10.7	74	9.4	7.9
Bean/cheese burrito	2 small	180	15	12.0	108	13.5	8
Sub sandwich, cold cuts	1	287	22	13.2	172	19.6	8.8
Chicken sandwich	1	405	29	13.8	243	26.5	9.2
Pepperonl pizza	1 slice	222	16	13.9	133	14.4	9.3
Peanut butter sandwich	1	168	12	14	101	10.8	9.3
Cheese sandwich, grilled	1	194	10	19	116	9.0	12.7
Beans with pork, tomato sauce	1 cup	285	13	21.9	171	11.7	14.6
Macaroni & cheese, boxed	1 cup	265	11	24.1	159	9.9	16.1
Breakfast sandwich, fast food	1 egg/ cheese/ bacon	459	16	28.2	275	14.7	18.8

(Continued)

Table 35 (Cont'd). Actual and Adjusted Amounts and Ratios of Phosphorus to Protein in Specific Foods

Food	Amount	Actual Content of Phosphorus (mg)	Actual Content of Protein (g)	Ratio of mg Phosphorus to g Protein	Phosphorus Content (mg) Adjusted for Bioavailability	Protein Content (g) Adjusted for Digestibility	Ratio of mg Phosphorus to g Protein Adjusted for Digestion and Absorption
Milk/Dairy							
Cottage cheese, nonfat	1 cup	151	25	6.0	106	23.8	4.4
Cottage cheese, regular	1 cup	297	28	10.6	208	26.6	7.8
Cottage cheese, 2%	1 cup	340	31	11.0	238	29.5	8.1
Milk, soy, unfortified	1 cup	126	8	15.8	88	7.6	9.3
Cream cheese	2 Tbsp	30	2	15.0	21	1.9	11.0
Cheese, mozzarella	1 oz	100	6	16.6	70	5.7	12.2
Cheese, cheddar	1 oz	145	7	20.7	102	6.7	15.3
Cheese, swiss	1 oz	171	8	21.4	120	7.6	15.8
Sour cream	1 Tbsp	32	1	26.7	22	1.1	19.7
Yogurt, regular	4 oz	107	4	26.8	75	3.8	19.7
Yogurt, lowfat	4 oz	162	6	27.0	113	5.7	19.9
Light cream	1 cup	192	7	27.4	134	6.7	20.2
Ice cream, vanilla	1 cup	138	5	27.6	97	4.8	20.3
Milk, whole	1 cup	227	8	28.4	159	7.6	20.9
Milk, 2%	1 cup	232	8	29.0	162	7.6	21.4
Milk, 1%	1 cup	235	8	29.4	165	7.6	21.7
Yogurt, nonfat	4 oz	177	6	29.5	124	5.7	21.7
Heavy cream	1 cup	149	5	29.8	104	4.8	22.0
Milk, nonfat	1 cup	247	8	30.9	173	7.6	22.8
Milk, chocolate	1 cup	255	7	36.4	179	6.7	26.8
Hot fudge sundae	1 small	227	6	37.8	159	5.7	27.9
Other Sources of Phosphorus							
Iced tea, bottled	12 oz	95	0		90		
Candy, milk chocolate	1 oz	62	2	27	59		
Cola or pepper-type	12 oz	44	0		42		
Beer	12 oz	43	1		41		

Table 36. Nutrient Content* of Feeds and Supplements Used in Children with CKD

			Per 100 mL									
	Product	Manufacturer	kcal	Protein (g)	CHO (g)	Fat (g)	Na (mmol)	K (mmol)	Ca (mg)	PO4 (mg)	Osmolality mOsm/kg/H_2O	Water Content (%)
Infant Feedings												
	Breast Milk		69	1.3	7.2	4.1	0.7	1.5	60	15	290	
	Enfamil Lipid	Mead Johnson	67	1.4	7.3	3.5	0.8	1.9	76	29	300	89
	Cow & Gate 1*	Cow & Gate	67	1.4	7.5	3.5	0.8	1.6	64	25		
	Similac/Similac Advance	Abbott	68	1.4	7.3	3.7	0.7	1.8	72	28	300	90
	SMA Gold*	SMA	67	1.4	7.3	3.6	0.7	1.7	68	24	291	
Infant Feedings Favorable for CKD												
	Good Start	Nestle	67	1.4	7.5	3.4	0.8	1.8	72	25	265	90
	Similac PM 60/40	Abbott	68	1.5	6.9	3.8	0.7	1.4	56	19	280	90
Infant Feedings Favorable for Hypercalcemia												
	Calcilo XD	Abbott	67	1.5	6.8	3.8	0.7	1.4	<6.7	17	190	91
	Locasol*	Scientific Hospital Supplies	66	1.9	7	3.4	1.2	2	<7.2	46	310	
Other												
	Cows milk (full fat)		66	3.2	4.8	3.9	2.4	3.6	144	95	315	
Pediatric Feedings												
	Kindercal	Mead Johnson	106	3	13.5	4.4	1.6	3.4	101	85	440	85
	Nutren Junior	Novartis/Nestle	100	3	12.7	4.2	2	3.4	136	80	350	85
	Nutrini*	Nutricia	100	4.8	12.3	4.4	2.6	2.8	112	50	260	86
	Nutrini Energy*	Nutricia	150	4.1	18.5	6.7	3.9	4.2	168	75	410	78
	Pediasure	Abbott	100	3	13.1	3.8	1.7	3.4	136	85	335	84
	Resource Just for Kids	Novartis/Nestle	100	3	11	5	2.6	2.9	116	80	390	85

(Continued)

Table 36 (Cont'd). Nutrient Content* of Feeds and Supplements Used in Children with CKD

			Per 100 mL									
	Product	Manufacturer	kcal	Protein (g)	CHO (g)	Fat (g)	Na (mmol)	K (mmol)	Ca (mg)	PO4 (mg)	Osmolality mOsm/ kg/H_2O	Water Content (%)
	Resource Just for Kids 1.5	Novartis/Nestle	150	4.2	16.5	7.5	3	3.3	132	99	390–405†	72
Adolescent/Adult Feedings												
	Boost	Novartis/Nestle	101	4.2	17.3	1.7	2.4	4.3	127	127	630	85
	Boost Plus	Novartis/Nestle	152	5.9	19	5.8	3.1	4.1	148	127	670	78
	Ensure	Abbott	106	3.8	17	2.5	3.7	4	128	106	590	85
	Ensure Plus	Abbott	150	5.5	21	4.7	4.4	4.6	127	128	680	77
	Fortisip*	Nutricia	150	6	18.4	5.8	3.9	4.1	78	2.3	420-590†	78
	Nutren 1.0	Nestle	100	4	12.7	3.8	3.8	3.2	67	67	315-370†	85
	Nutren 1.5	Nestle	150	6	16.9	6.8	5.1	4.8	100	100	430-510†	78
Renal Feedings												
	Kindergen*	Scientific Hospital Supplies	101	1.5	11.8	5.3	2	0.6	22.4	18.6	215	80
	Magnacal Renal	Mead Johnson	200	7.5	20	10.1	3.5	3.2	101	80	570	71
	Nepro with Carb Steady	Abbott	180	8.1	16.7	9.6	4.6	2.7	108	70	585	73
	Novasource Renal	Nestle	200	7.4	20	10	3.9	2.1	84	65	700	71
	Nutren Renal	Nestle	200	7	20.5	10.4	3.2	3.2	128	70	650	70
	RenalCal	Nestle	200	3.4	29	8.2	0	0	0	0	600	70
	Renilon 7.5*	Nutricia	200	7.5	20	10	2.6	0.3	12	6	575	71
	Suplena with Carb Steady	Abbott	180	4.5	20.5	9.6	3.4	2.9	116	70	600	74
Carbohydrate Modules					**per 100 g**							
Glucose Polymers	Maxijul powder*	Scientific Hospital Supplies	380	0	95	0	<0.3	<0.05	<1.7	<1.7		
	Maxijul liquid* (per 100 ml)	Scientific Hospital Supplies	200	0	50	0	<1	<0.1	0	<5		
	Polycal	Nutricia	384	0	96	0.1	0	0	0	0		
	Polycose	Abbott	380	0	94	0	5.7	0.3	12	15		
Fat Modules					**per 100 mL**							
	Calogen	Nutricia	450	0	0	50	0	0	0	0		
	Microlipid	Nestle	450	0	0	50	0	0	0	0		
	MCT oil	Nestle	770	0	0	86	0	0	0	0		
	Canola or corn oil		825	0	0	93	0	0	0	0		
Combined CHO/ Fat Modules					**per 100 g**							
	Duocal	Scientific Hospital Supplies	492	0	72.7	22.3	≤0.9	≤0.13	≤5.2	≤5		
Protein Modules					**per 100 g**							
	Vitapro*	Vitaflo	360	75	9	6	<13	<18	<400	<320		
	Beneprotein	Nestle	357	86	0	0	9.3	12.8	512	215		
	Protifar	Scientific Hospital Supplies	373	88.5	<1.5	1.6	1.3	1.3	52	700		

*For most current nutrient content check product label or manufacturer's product monograph. Values listed here are American content, unless otherwise indicated with an asterisk (*) for products available in UK only.

†Dependent on flavor.

Table 37. Nutrient Content of Selected Foods High in Fiber

Product	Serving Size	Fiber (g)	Potassium (mg)	Phosphorus (mg)
Fiber One	1/2 cup	13	230	150
All Bran	1/2 cup	10	310	300
Kellogg's Raisin Bran	1 cup	8.2	350	200
Post Raisin Bran	1 cup	8	380	250
Post Bran Flakes	2/3 cup	6	180	150
Quaker Crunchy Bran	3/4 cup	5	56	36
Ralston Oatmeal	3/4 cup cooked	4.6	116	110
Green peas, frozen, boiled	1/2 cup	4.4	134	72
Raspberries, raw	1/2 cup	4.2	94	8
Bulgur, cooked	1/2 cup	4.1	62	36
Mixed vegetables, frozen	1/2 cup	4.0	15	46
Common Sense Oat Bran	1/2 cup	4.0	120	150
Pear, canned, water pack	1 cup	4.0	129	17
Blackberries, raw	1/2 cup	3.8	141	15
Quaker Old Fashioned Oatmeal	1/2 cup dry	3.7	143	183
Apple, raw, skin	1 Medium	3.7	159	10
Oat Bran, raw	2 Tbsp	3.6	133	172
Brown rice, cooked	1 cup	3.5	84	162
Peaches, canned, water pack	1 cup	3.2	242	24
Wheat bran, raw	2 Tbsp	3.1	86	73
Orange, navel, raw	1 medium	3.1	233	25
Unifiber®	1 Tbsp	3.0	0	0
Barley, cooked	1/2 cup	3.0	73	42
Cheerios	1 cup	3.0	90	100
General Mills Wheaties	1 cup	3.0	110	100
General Mills Raisin Bran	3/4 cup	3.0	220	150
Carrots, sliced, boiled	1/2 cup	2.6	177	23
Quaker Oat Bran cereal	1/2 cup	2.3	100	118
Corn, boiled	1/2 cup	2.3	204	84
Broccoli, boiled	1/2 cup	2.3	228	4.6
Spinach, boiled	1/2 cup	2.2	419	150
Pumpernickel bread	1 slice	2.1	67	57
Brussels sprouts, boiled	1/2 cup	2.0	247	44
Celery, raw	2 large stalks	2.0	332	30
American rye bread	1 slice	1.9	53	40
Whole-wheat bread	1 slice	1.9	71	64

Adapted with permission.[223]

APPENDIX 4: INITIATING AND ADVANCING TUBE FEEDINGS

Table 38. Suggested Rates for Initiating and Advancing Tube Feedings

Age	Initial Hourly Infusion	Daily Increases	Goal*
Continuous Feedings			
0-1 y	10-20 mL/h or 1-2 mL/kg/h	5-10 mL/8h or 1mL/kg/h	21-54 mL/h or 6 mL/kg/h
1-6 yrs	20-30 mL/h or 2-3 mL/kg/h	10-15 mL/8h or 1 mL/kg/h	71-92 mL/h or 4-5 mL/kg/h
6-14 yrs	30-40 mL/h or 1 mL/kg/h	15-20 mL/8h or 0.5 mL/kg/h	108-130 mL/h or 3-4 mL/kg/h
>14 yrs	50 mL/h or 0.5-1 mL/kg/h	25 mL/8h or 0.4-0.5 mL/kg/h	125 mL/h
Bolus Feedings			
0-1 y	60-80 mL q 4h or 10-15 mL/kg/feed	20-40 mL q 4h	80-240 mL q 4h or 20-30 mL/kg/feed
1-6 yrs	80-120 mL q 4h or 5-10 mL/kg/feed	40-60 mL q 4h	280-375 mL q 4h or 15-20 mL/kg/feed
6-14 yrs	120-160 mL q 4h or 3-5 mL/kg/feed	60-80 mL q 4h	430-520 mL q 4h or 10-20 mL/kg/feed
>14 yrs	200 mL q 4h or 3 mL/kg/feed	100 mL q 4h	500 mL q 4h or 10 mL/kg/feed

Note: Calculating rates based on age and per kilogram body weight is useful for small-for-age patients.

Adapted with permission.[521]

*Goal is expected maximum that child will tolerate; individual children may tolerate higher rates or volumes. Proceed cautiously for jejunal feedings. Goals for individual children should be based on energy requirements and energy density of feeding and therefore may be lower than expected maximum tolerance.

APPENDIX 5: CLINICAL GROWTH CHARTS

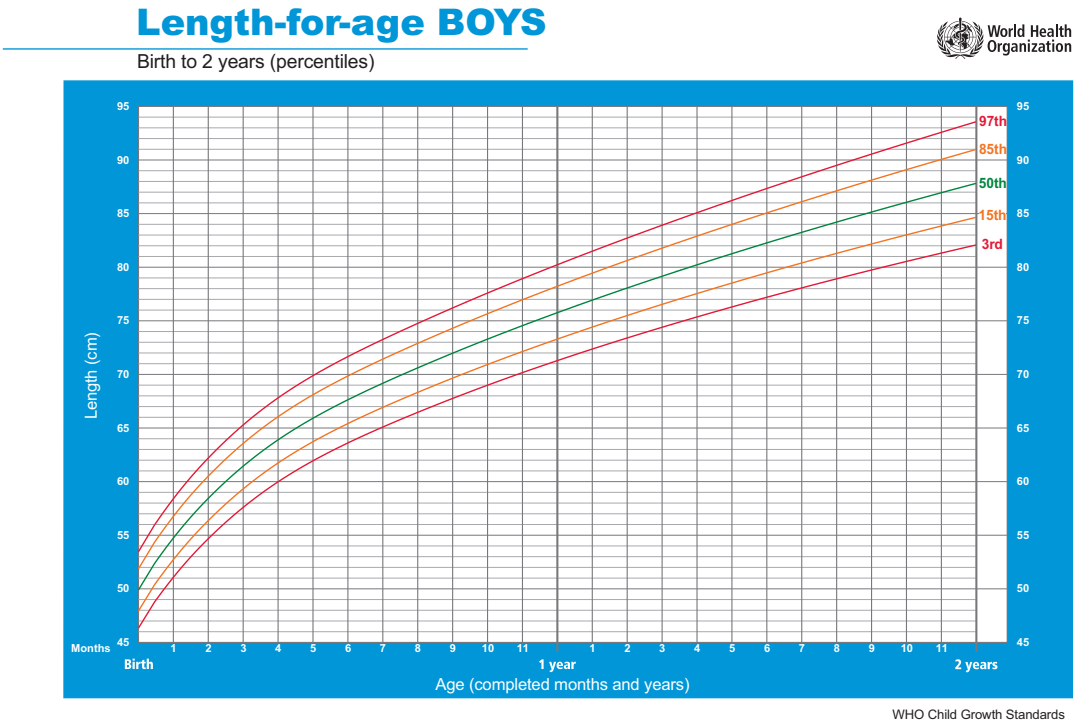


Figure 1. WHO Child Growth Standards: Boys length-for-age, birth to 2 years. Reprinted with permission.[34]

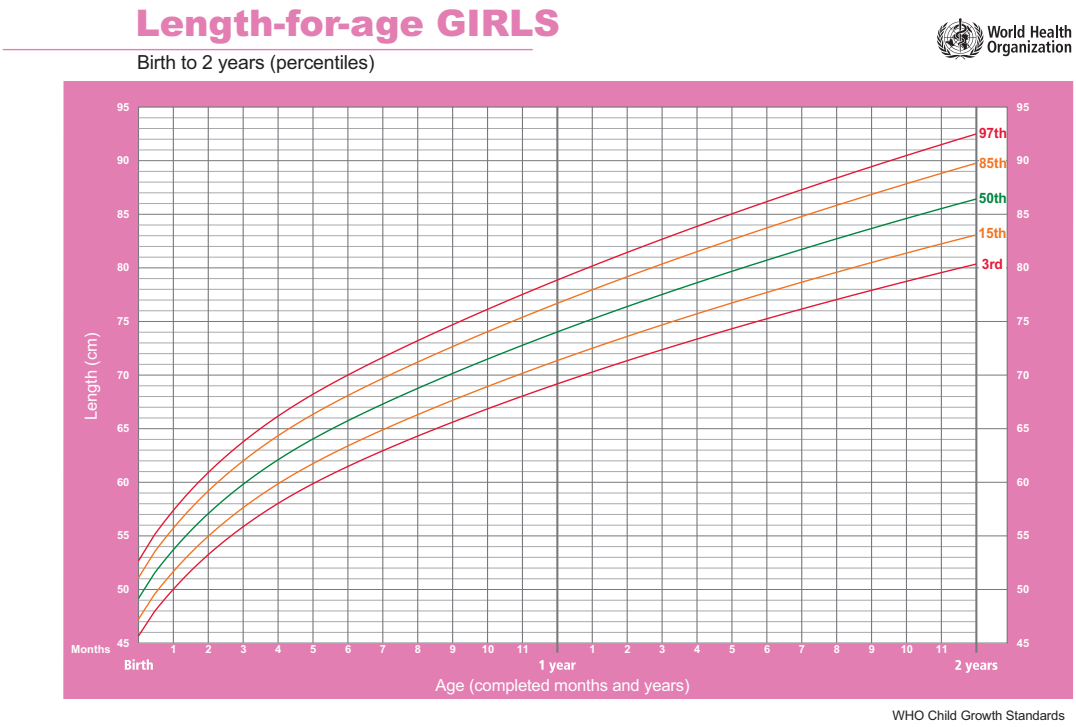


Figure 2. WHO Child Growth Standards: Girls length-for-age, birth to 2 years. Reprinted with permission.[34]

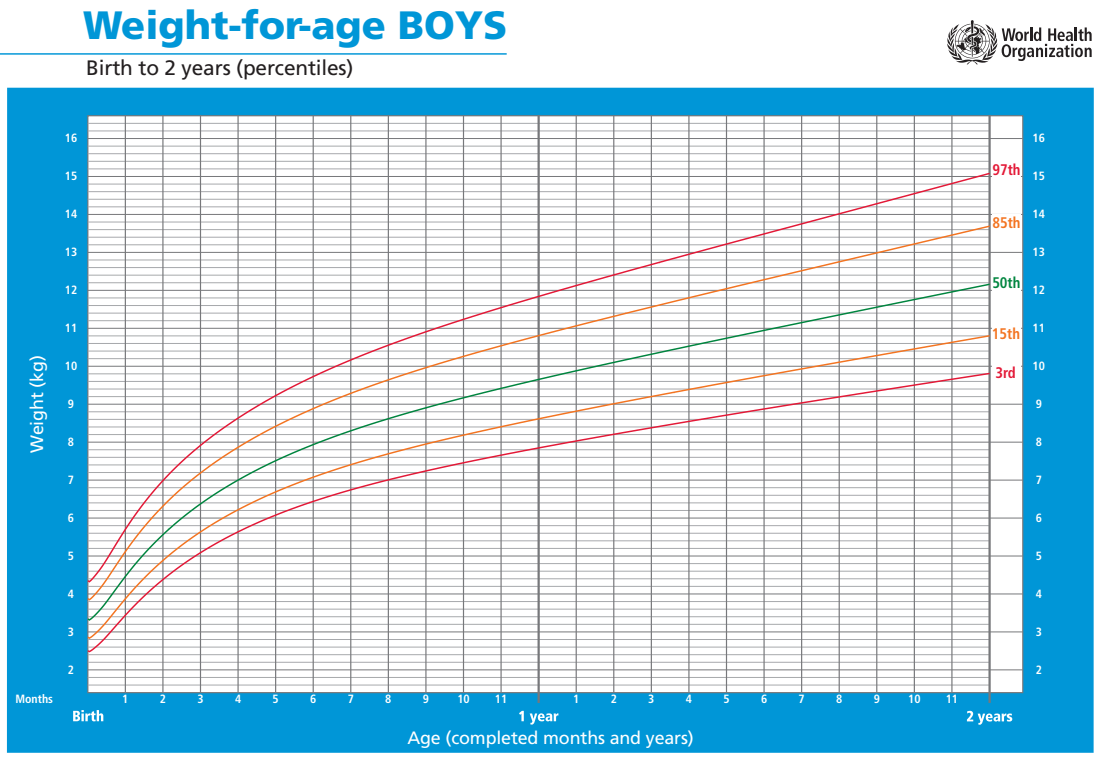


Figure 3. WHO Child Growth Standards: Boys weight-for-age, birth to 2 years. Reprinted with permission.[34]

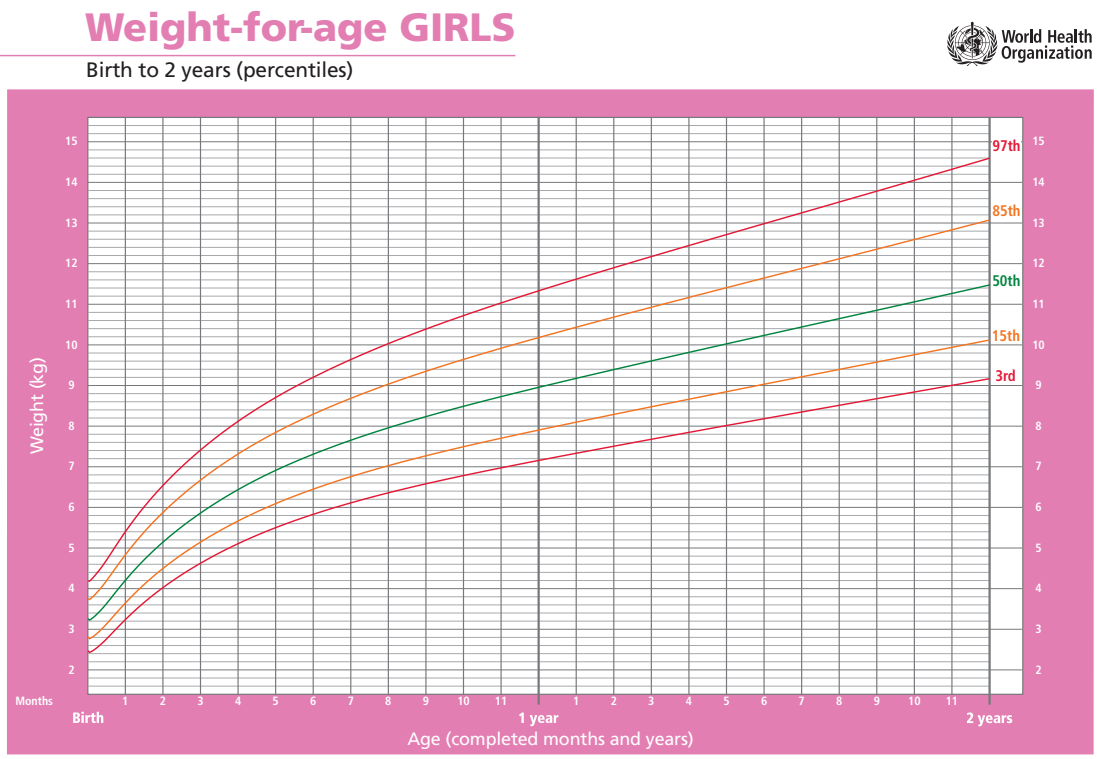


Figure 4. WHO Child Growth Standards: Girls weight-for-age, birth to 2 years. Reprinted with permission.[34]

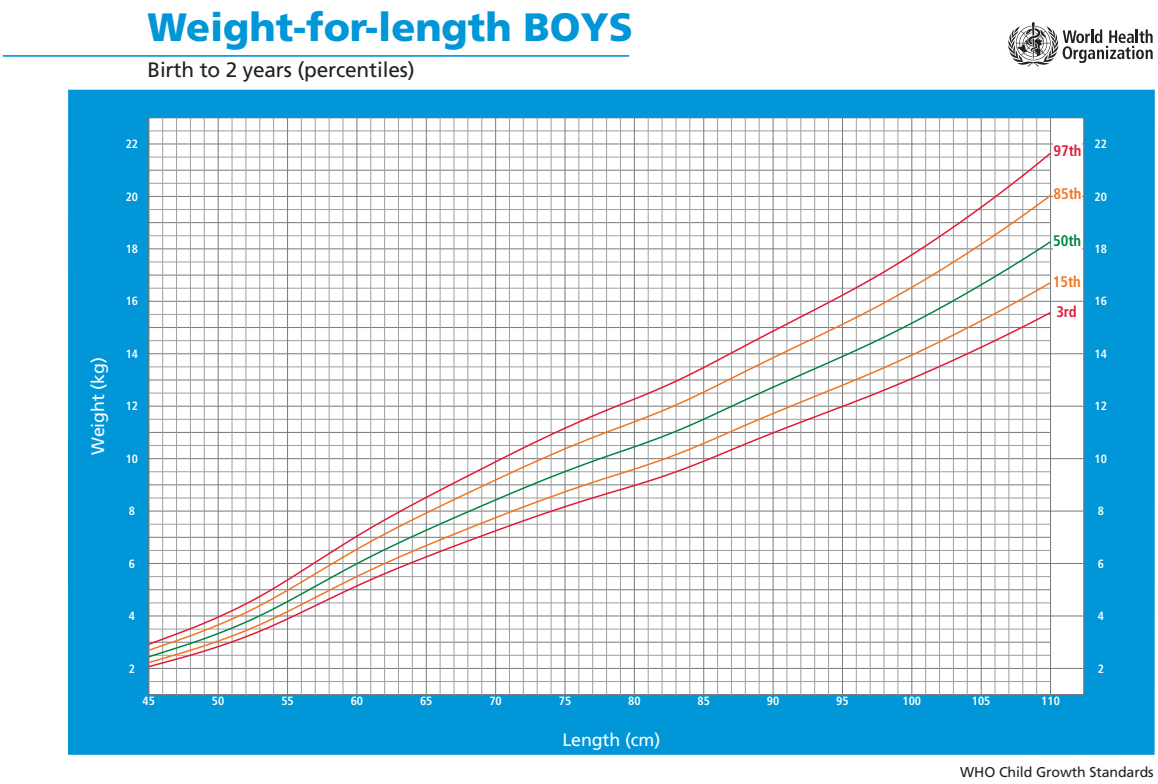


Figure 5. WHO Child Growth Standards: Boys weight-for-length, birth to 2 years. Reprinted with permission.[34]

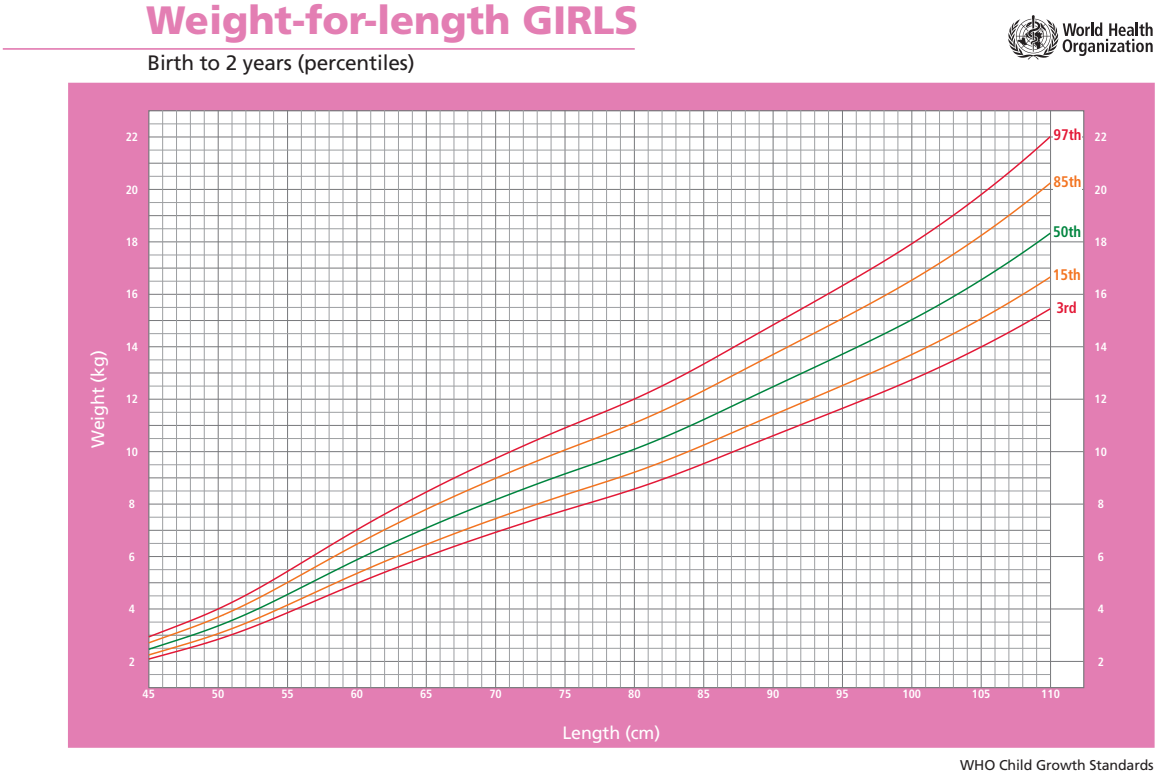


Figure 6. WHO Child Growth Standards: Girls weight-for-length, birth to 2 years. Reprinted with permission.[34]

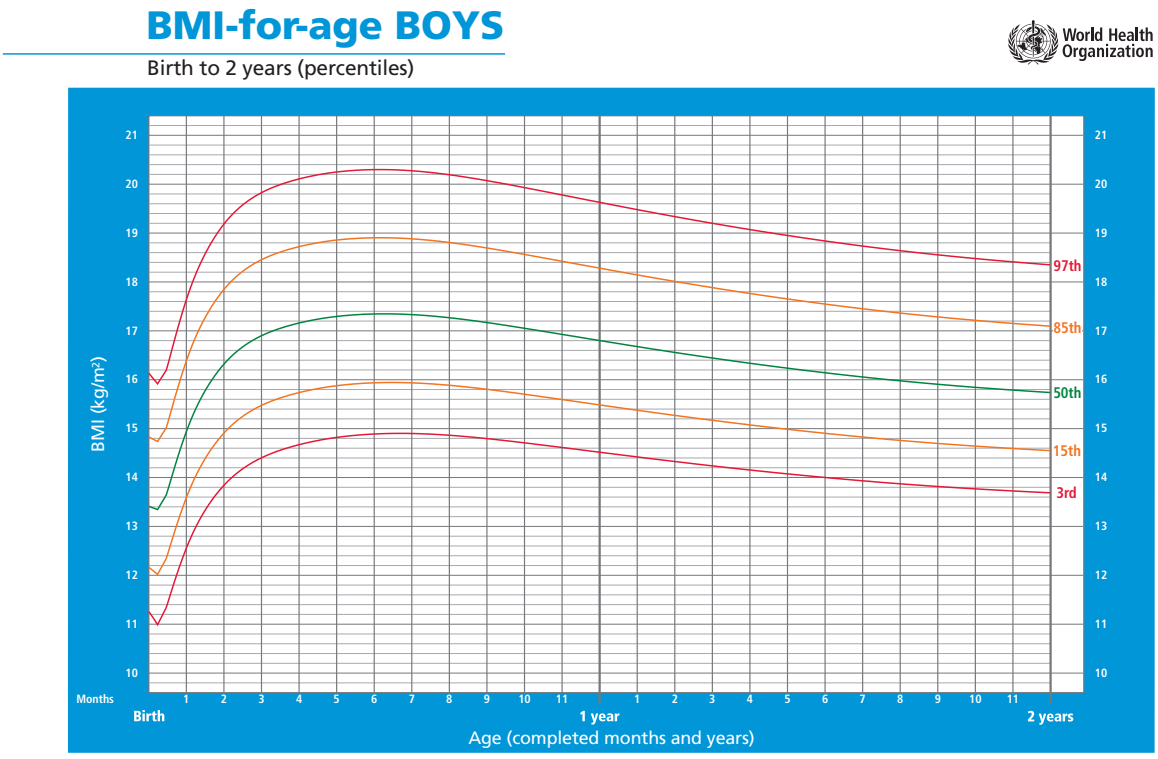


Figure 7. WHO Child Growth Standards: Boys BMI-for-age, birth to 2 years. Reprinted with permission.[34]

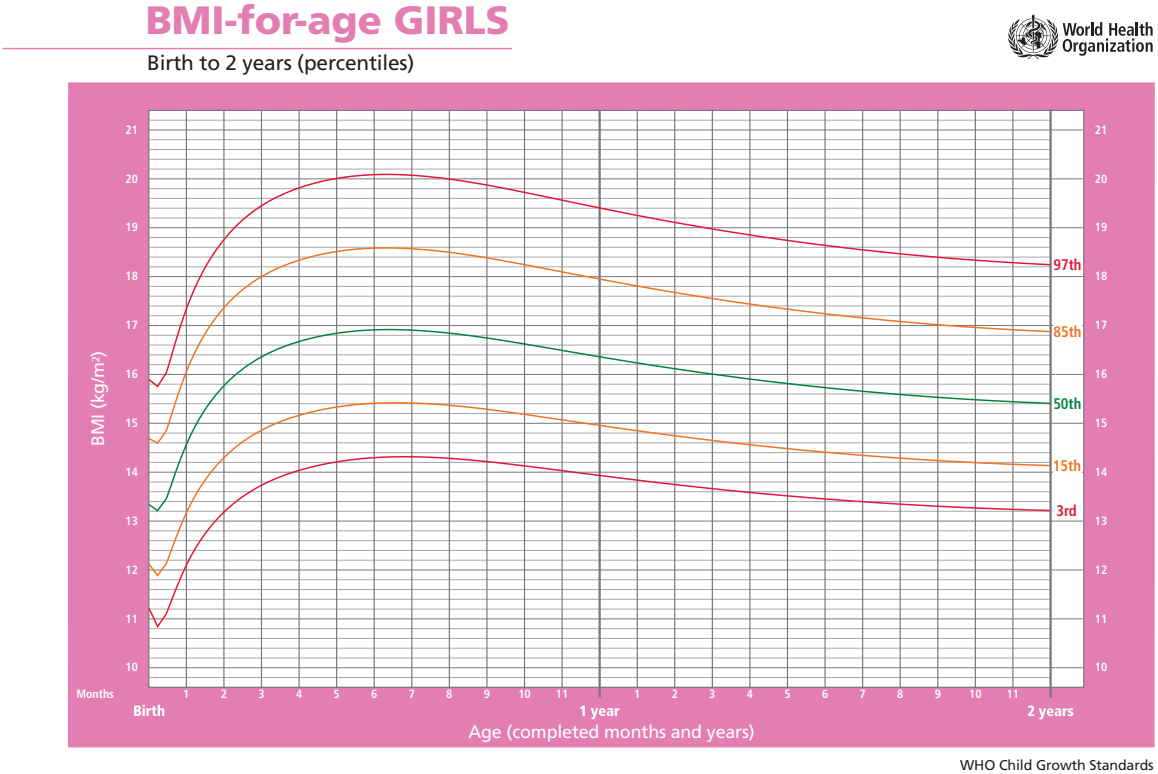


Figure 8. WHO Child Growth Standards: Girls BMI-for-age, birth to 2 years. Reprinted with permission.[34]

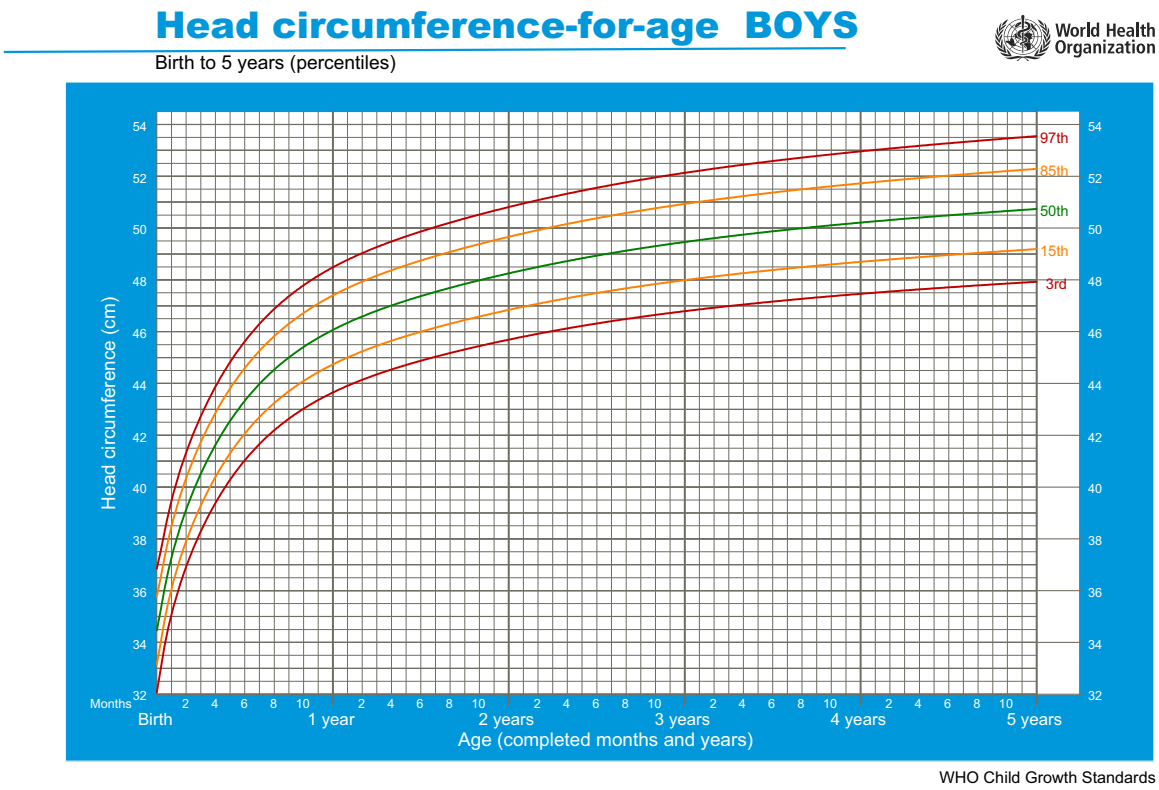


Figure 9. WHO Child Growth Standards: Boys head circumference-for-age, birth to 5 years. Reprinted with permission.[52]

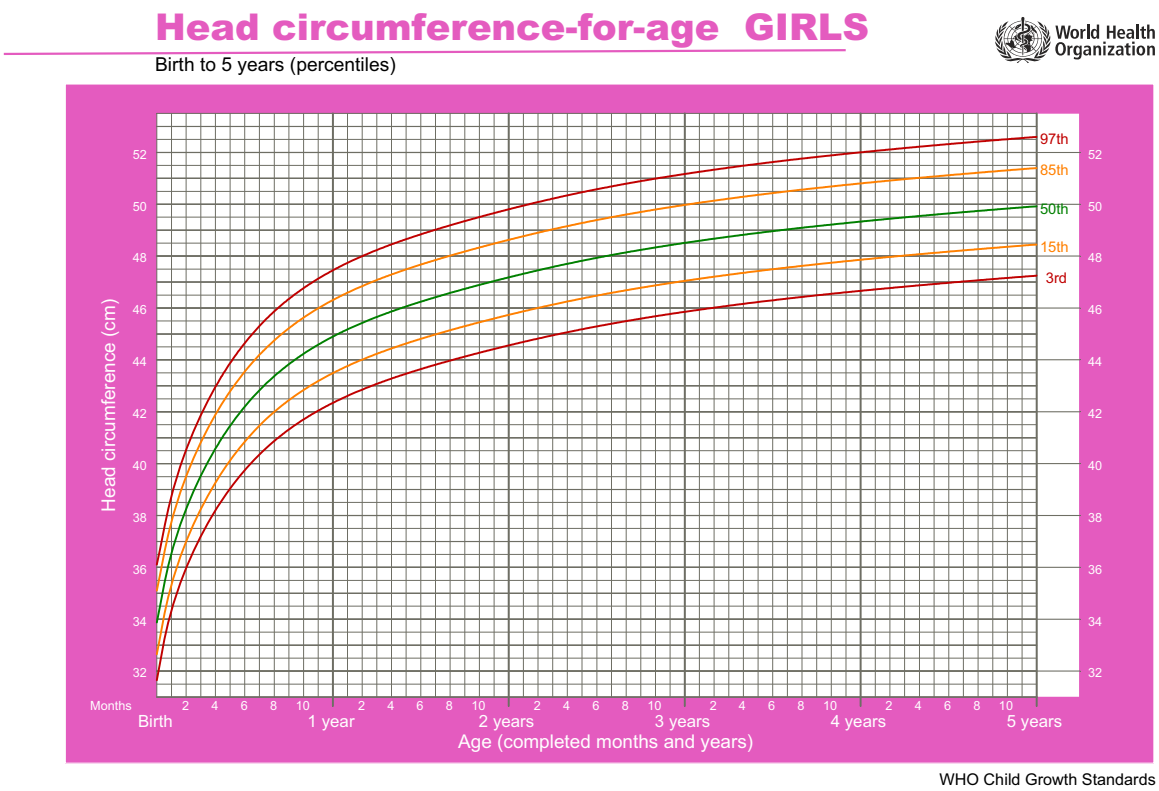


Figure 10. WHO Child Growth Standards: Girls head circumference-for-age, birth to 5 years. Reprinted with permission.[52]

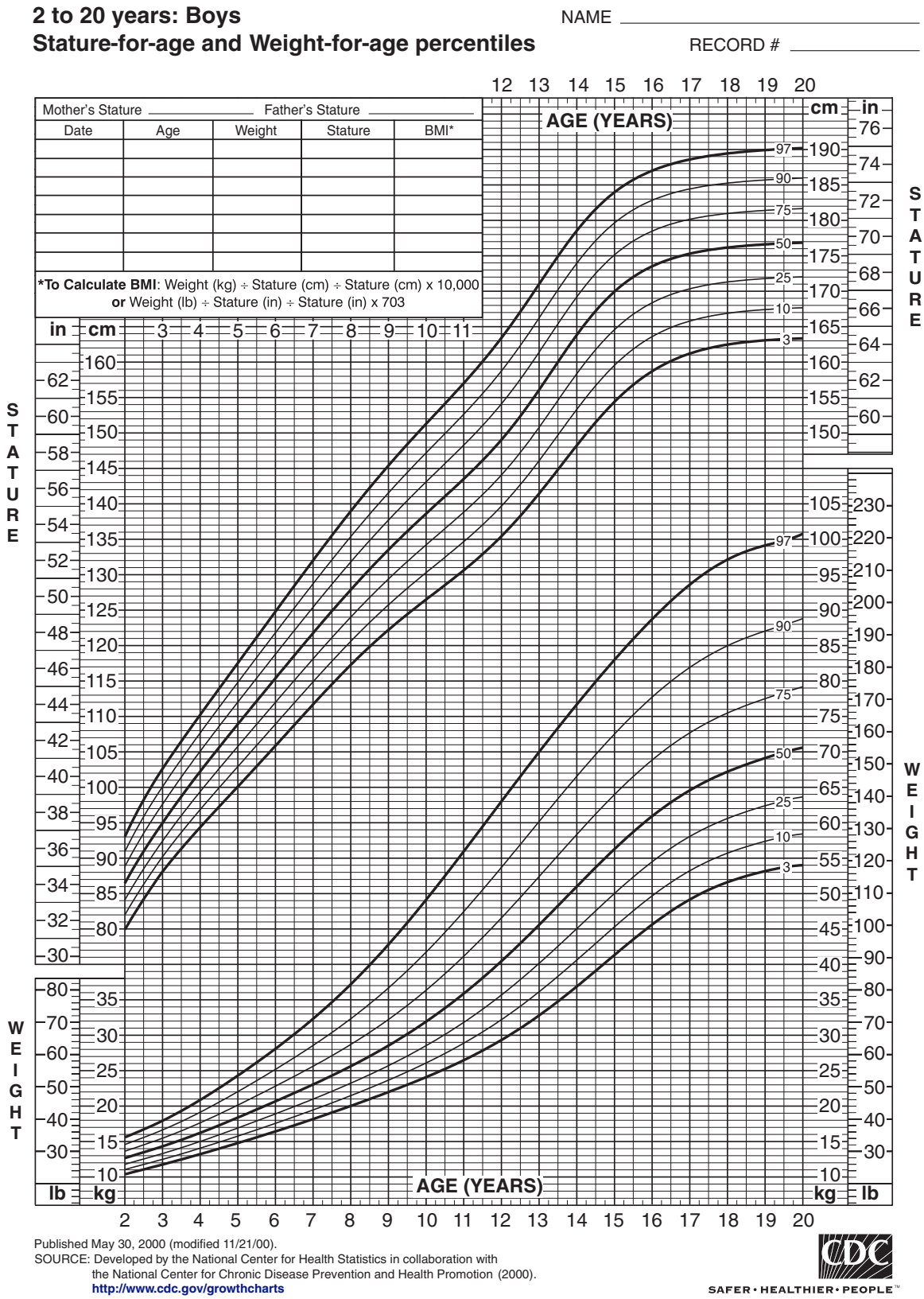


Figure 11. CDC Clinical Growth Charts: Children 2 to 20 years, Boys stature-for-age and weight-for-age.

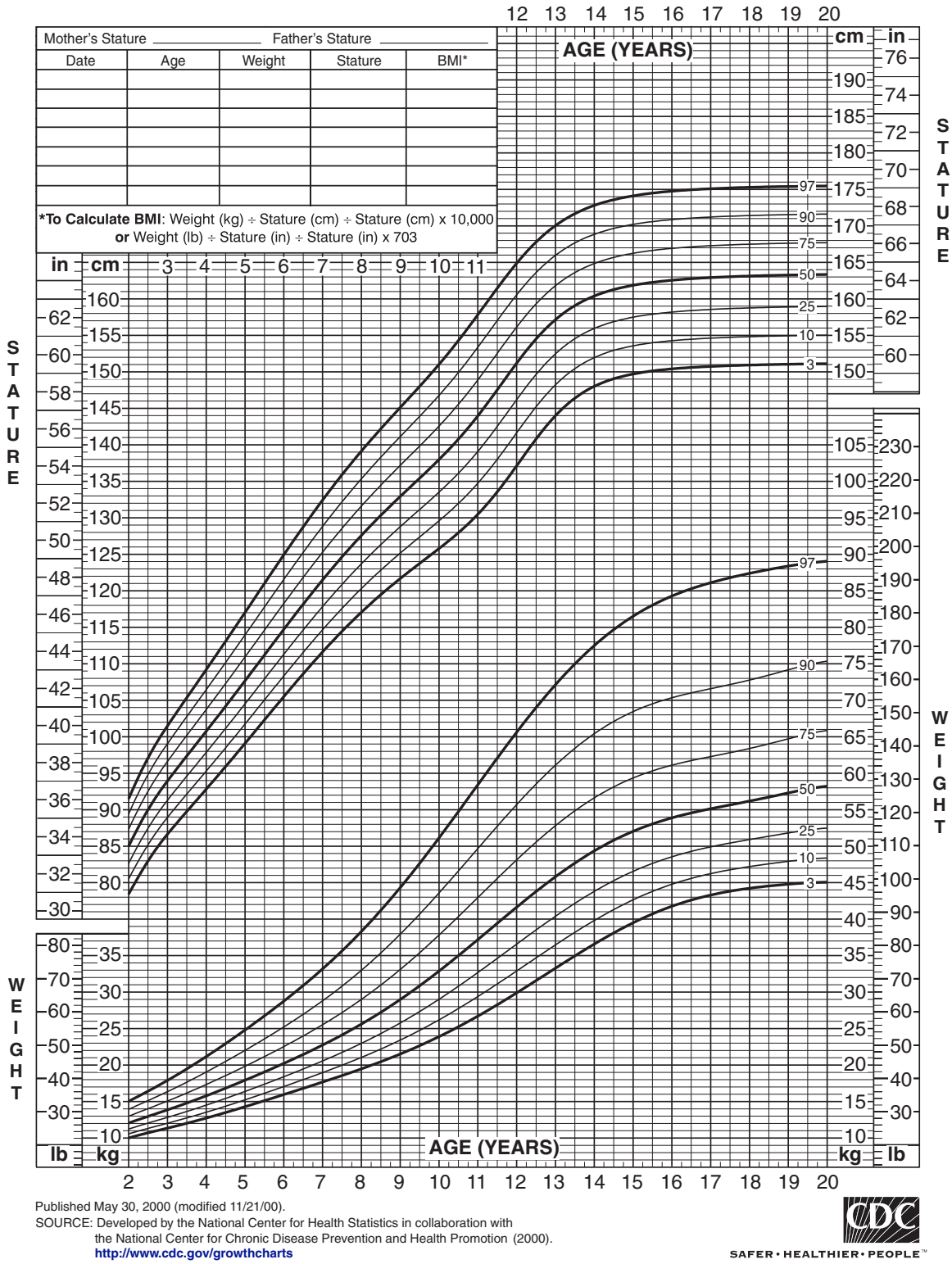


Figure 12. CDC Clinical Growth Charts: Children 2 to 20 years, Girls stature-for-age and weight-for-age.

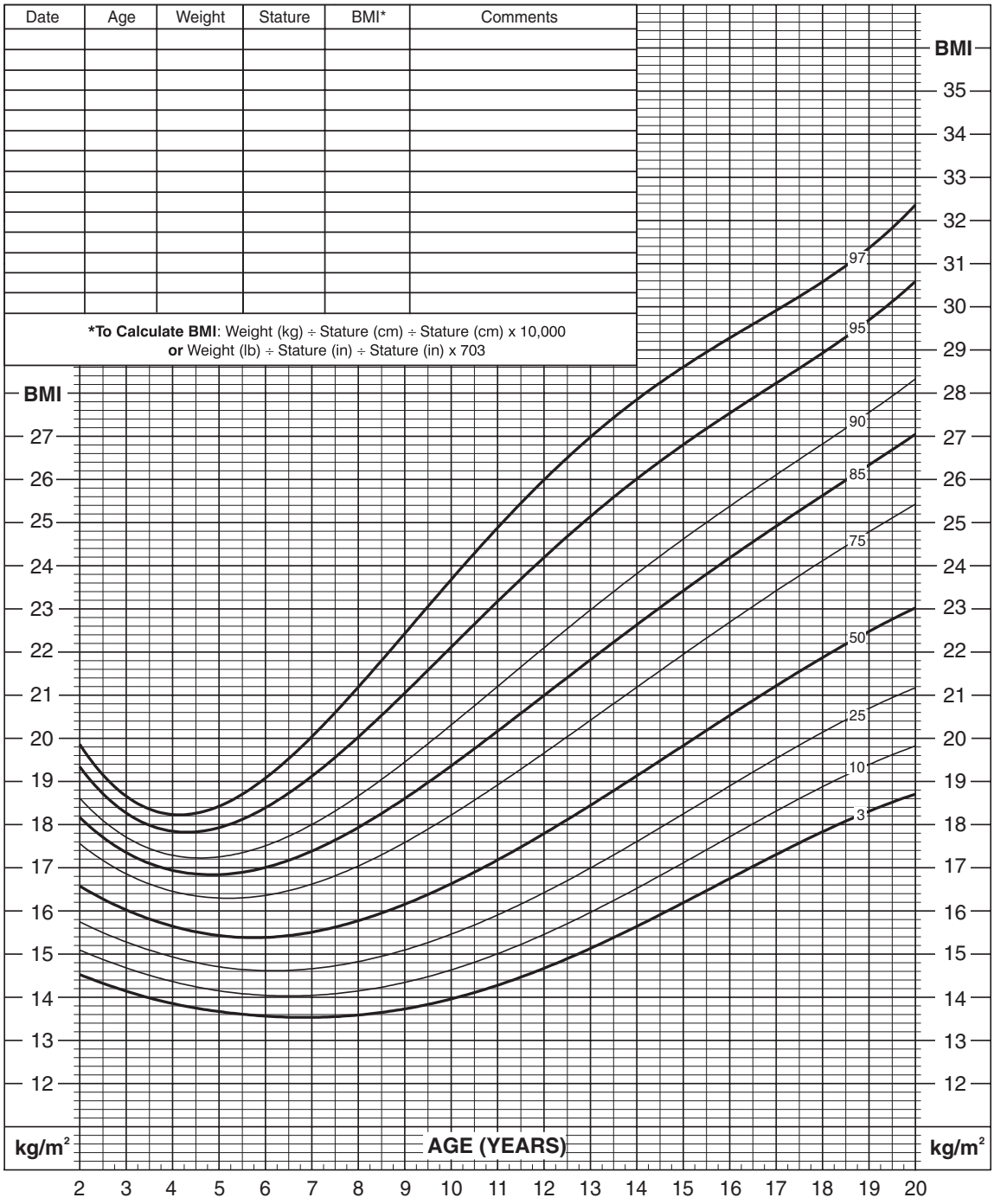
2 to 20 years: Boys
Body mass index-for-age percentiles

NAME _____

RECORD # _____

Date	Age	Weight	Stature	BMI*	Comments

***To Calculate BMI**: Weight (kg) ÷ Stature (cm) ÷ Stature (cm) x 10,000
or Weight (lb) ÷ Stature (in) ÷ Stature (in) x 703



Published May 30, 2000 (modified 10/16/00).
SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).
http://www.cdc.gov/growthcharts

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Figure 13. CDC Clinical Growth Charts: Children 2 to 20 years, Boys BMI-for-age.

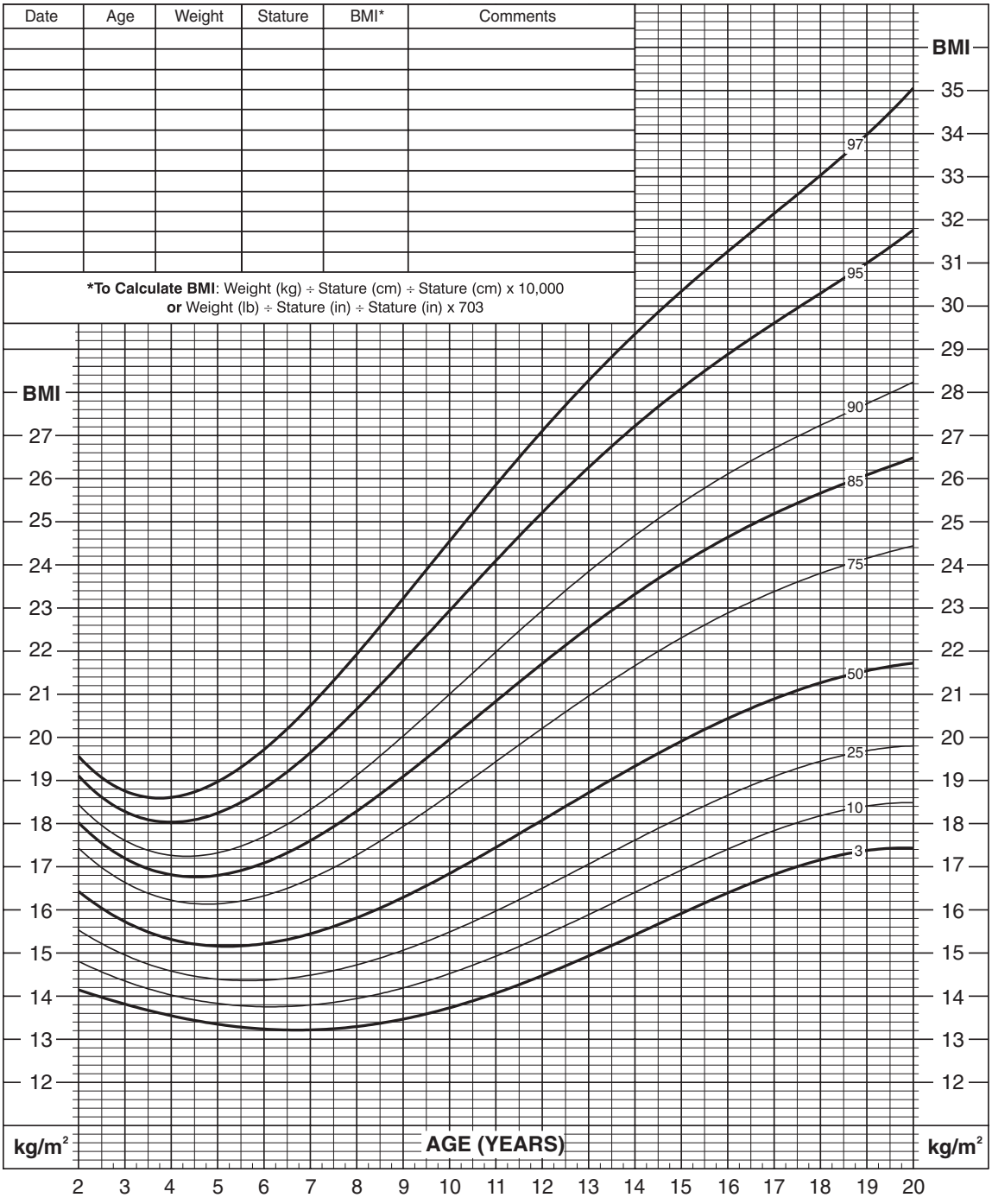
2 to 20 years: Girls
Body mass index-for-age percentiles

NAME _____

RECORD # _____

Date	Age	Weight	Stature	BMI*	Comments

***To Calculate BMI**: Weight (kg) ÷ Stature (cm) ÷ Stature (cm) x 10,000
or Weight (lb) ÷ Stature (in) ÷ Stature (in) x 703



Published May 30, 2000 (modified 10/16/00).
SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).
http://www.cdc.gov/growthcharts

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Figure 14. CDC Clinical Growth Charts: Children 2 to 20 years, Girls BMI-for-age.

APPENDIX 6: DESCRIPTION OF GUIDELINE DEVELOPMENT PROCESS

The KDOQI Clinical Practice Guideline on Nutrition and Children with CKD: Update 2008 was developed to incorporate new evidence and reference data that have emerged since the 2000 guidelines were published and to harmonize the recommendations with those of other guidelines that have since been issued. A scope of work was drafted by the Work Group Chairs and vetted by the NKF-KDOQI Board.

In the spring of 2007, Bradley A. Warady, MD, and Donna Secker, PhD, RD, were appointed Co-Chairs of the Work Group. Work Group members were selected by the Co-Chairs for their clinical and research expertise in related areas of nutritional assessment and therapy in children with CKD. The multidisciplinary group of pediatric nephrologists and dietitians included representatives from North America, the United Kingdom, and Europe. Method guidance was provided by Katrin Uhlig, MD, MS from Tufts Center for Kidney Disease Guideline Development and Implementation, with additional methods input provided by Ethan Balk, MD, MPH, also at the Center.

The Work Group drafted narrative reviews based on their expertise and knowledge of the relevant literature. References were used to support the write-ups. Systematic literature review was not undertaken for any topic given the low-quality evidence known to exist in this field. This paucity of evidence made it unlikely that an inclusive systematic search, to supplement what the experts already knew, would substantially improve the quality of the evidence base and the confidence that could be derived from it.

The Work Group convened regularly by telephone and/or e-mail to refine the topics, recommendations, and supporting rationale. The methods consultant provided ongoing guidance and support throughout the guideline development process by participating in the Work Group's teleconferences and e-mail communications and reviewing guideline drafts.

The KDOQI approach regarding grading of the strength of the guideline recommendations followed the approach adopted by KDIGO (see Tables 39 and 40). The strength of most guideline recommendations was graded as C to signify that they were based predominantly on the expert judgment of the Work Group. Overall, given the heterogeneity and often unique circumstances of the disease conditions in children with CKD and the great human cost of the disease in this age group, the Work Group adopted a perspective of erring in favor of issuing recommendations of potential use with lesser importance attached to potential monetary costs.

The public review process was initiated in September 2008. Participants were given 4 weeks to provide comments. Those who took part in the public review included members of the KDOQI Advisory Board and the NKF Council on Renal Nutrition; experts identified by the Work Group; representatives from nephrology, dietetic, or other allied health–related professional associations; organizations involved in the care of pediatric patients with kidney diseases; and professional individuals who requested to take part in the review process. Overall, all comments received were carefully considered by the Work Group Chairs and, with input from the Work Group, incorporated into the final guideline as appropriate.

Table 39. KDIGO Nomenclature and Description for Rating Guideline Recommendations

Strength of the Recommendation	Wording of the Recommendation	Prerequisite	Assumption	Expectation
A	An intervention "should" be done	The quality of the evidence is "high" or additional considerations support a "strong" recommendation	Most well-informed individuals will make the same choice	The expectation is that the recommendation will be followed unless there are compelling reasons to deviate from it in an individual. A strong recommendation may form the basis for a clinical performance measure
B	An intervention "should be considered"	The quality of the evidence is "high" or "moderate," or additional considerations support a "moderate" recommendation	A majority of well informed individuals will make this choice, but a substantial minority may not	The expectation is that the recommendation will be followed in the majority of cases
C	An intervention is "suggested"	The quality of the evidence is "moderate," "low," or "very low," or additional considerations support a weak recommendation based predominantly on expert judgment	A majority of well-informed individuals will consider this choice	The expectation is that consideration will be given to following the recommendation

Table 40. Checklist for Guideline Reporting for the Update of the KDOQI Pediatric Nutrition Guideline*

Topic	Description	Discussed in KDOQI Pediatric Nutrition Guideline
1. Overview material	Provide a structured abstract that includes the guideline's release date, status (original, revised, updated), and print and electronic sources.	See Executive Summary
2. Focus	Describe the primary disease/condition and intervention/service/technology that the guideline addresses. Indicate any alternative preventative, diagnostic, or therapeutic interventions that were considered during development.	This guideline addresses the population of infants, children, and adolescents with CKD of congenital, hereditary, acquired, or metabolic etiology. The guideline considers evaluation of nutritional status and therapeutic interventions, including enteral feeding, intradialytic parenteral nutrition, growth hormone therapy, and restriction or supplementation of various macro- and micronutrients.
3. Goal	Describe the goal that following the guideline is expected to achieve, including the rationale for development of a guideline on this topic.	This guideline is intended to assist the practitioner caring for infants, children, and adolescents with CKD in the evaluation of their nutritional status, and in counseling and selecting nutrition therapies that are age- and CKD stage-appropriate to improve their survival, health, and quality of life.
4. User/setting	Describe the intended users of the guideline (eg, provider types, patients) and the settings in which the guideline is intended to be used.	The intended audience for the guideline is: 1) Practitioners: nephrologists, nephrology fellows, dietitians, nurse practitioners, nurses. 2) Patients: infants, children and adolescents with CKD Stages 2–5, 5D, and 1–5T and their relatives and friends. 3) Policy makers and those in related health fields. The settings for guideline implementation are in-patient or outpatient clinics, and satellite dialysis centers.

(Continued)

Table 40 (Cont'd). Checklist for Guideline Reporting for the Update of the KDOQI Pediatric Nutrition Guideline*

Topic	Description	Discussed in KDOQI Pediatric Nutrition Guideline
5. Target population	Describe the patient population eligible for guideline recommendations and list any exclusion criteria.	Pediatric patients with CKD Stages 2–5, 5D, and 1–5T Excluded were those with minimal-change nephrotic syndrome, or acute renal failure.
6. Developer	Identify the organization(s) responsible for guideline development and the names/credentials/potential conflicts of interest of individuals involved in the guideline's development.	NKF-KDOQI nominated the Work Group chairs and the methods consultant. It provided administrative support and organizational oversight. Names/credentials/potential conflicts of interest of individuals involved in the guideline's development are presented in the Work Group Biographical and Disclosure Information
7. Funding source/sponsor	Identify the funding source/sponsor and describe its role in developing and/or reporting the guideline. Disclose potential conflict of interest.	NKF-KDOQI did not receive corporate support for the development of this guideline.
8. Evidence collection	Describe the methods used to search the scientific literature, including the range of dates and databases searched, and criteria applied to filter the retrieved evidence.	The scope of work was to update the prior pediatric nutrition guidelines, published in 2000 as part of the larger Clinical Practice Guidelines for Nutrition in Chronic Renal Failure. The Work Group drafted narrative reviews based on its expertise and knowledge of the literature in the field and used references to support its write-up. Systematic literature review was not undertaken for any topic given the low-quality evidence known to exist in this field, which made it unlikely that an inclusive systematic search to supplement what the experts already knew would substantially improve the quality of the evidence base. The Work Group convened regularly by phone and/or e-mail to refine the topics, recommendations, and write-ups. Methodological guidance was provided by a staff member of the Tufts Center for Kidney Disease Guideline Development and Implementation at Tufts Medical Center with expertise in guideline development and critical literature appraisal.
9. Recommendation grading criteria	Describe the criteria used to rate the quality of evidence that supports the recommendations and the system for describing the strength of the recommendations. Recommendation strength communicates the importance of adherence to a recommendation, and is based on both the quality of the evidence and the magnitude of anticipated benefits and harm.	Formal grading of quality of studies or bodies of evidence was not undertaken. The strength of the recommendations was graded in a 3-tiered grading system, which was adopted for grading of guidelines by KDOQI leadership.
10. Method for synthesizing evidence	Describe how evidence was used to create recommendations, eg, evidence tables, meta-analysis, decision analysis.	Narrative reviews by experts who could conduct their own literature searches.
11. Prerelease review	Describe how the guideline developer reviewed and/or tested the guidelines prior to release.	Guideline underwent internal and external review, with 68 reviews received. Feedback was discussed initially in a conference call with the Co-Chairs, KDOQI Chair, Methods Consultants, and NKF-KDOQI Guideline Development Staff, followed by phone calls with individual Work Group members. Feedback was incorporated into the revised recommendations as the Work Group saw fit.
12. Update plan	State whether or not there is a plan to update the guideline and, if applicable, expiration dates for this version of the guideline.	The need to update this guideline will be periodically determined by the KDOQI Board. The needs assessment will include the review of new evidence that would change the content of the recommendations or their strength.

(Continued)

Table 40 (Cont'd). Checklist for Guideline Reporting for the Update of the KDOQI Pediatric Nutrition Guideline*

Topic	Description	Discussed in KDOQI Pediatric Nutrition Guideline
13. Definitions	Define unfamiliar terms and those critical to correct application of the guideline that might be subject to misinterpretation.	See Glossary of Definitions and List of Abbreviations and Acronyms.
14. Recommendations and rationale	State the recommended action precisely and the specific circumstances under which to perform it. Justify each recommendation by describing the linkage between the recommendation and its supporting evidence. Indicate the quality of evidence and the recommendation strength, based on the criteria described in #9 above.	Recommendations are highlighted in each section and the supporting rationale is provided in the narrative that follows. The strength of the recommendation is provided in parenthesis after each recommendation.
15. Potential benefits and harm	Describe anticipated benefits and potential risks associated with implementation of guideline recommendations.	The balance between estimated medical benefits and harm, and the certainty from the supporting evidence , were considered in the formulation of the guideline recommendations. Implementation of the guideline requires skilled personnel and resources.
16. Patient preferences	Describe the role of patient preferences when a recommendation involves a substantial element of personal choice or values.	Less than "strong" recommendations inherently indicate a greater need for the practitioner to help each patient (or proxy) to arrive at a management decision consistent with her or his values and preferences on behalf of the patient.
17. Algorithm	Provide (when appropriate) a graphical description of the stages and decisions in clinical care described by the guideline.	Tables, procedures for anthropometric measurements, copies of growth charts, and a list of resources for calculating anthropometric z-scores are provided to help with implementation.
18. Implementation considerations	Describe anticipated barriers to application of the recommendations. Provide reference to any auxilliary documents for providers or patients that are intended to facilitate implementation. Suggest review criteria for measuring changes in care when the guideline is implemented.	Limitations to the recommendations were discussed and recommendations were provided for future research. Comparison was made with other pediatric clinical guidelines to highlight consensus or identify controversy. No review criteria were developed.

*This checklist was developed by the Conference on Guideline Standardization for Reporting Clinical Practice Guidelines.[522]

BIOGRAPHICAL AND DISCLOSURE INFORMATION

Bradley A. Warady, MD (Work Group Co-Chair), is Associate Chairman, Department of Pediatrics, Chief of Nephrology and Director of Dialysis and Transplantation at The Children's Mercy Hospital, and Professor of Pediatrics at the University of Missouri–Kansas City School of Medicine. He is a member of the Board of Directors of the NAPRTCS. Dr Warady helped establish the International Pediatric Peritonitis Registry (IPPR) and he currently serves as Co-Principal Investigator of the International Pediatric Peritoneal Dialysis Network (IPPN) and the National Institutes of Health (NIH)-funded Chronic Kidney Disease in Children (CKiD) study. He coedited the books *CAPD/CCPD in Children* and *Pediatric Dialysis* and he has published more than 250 articles and book chapters. He is Chairman of the Pediatric Liaison Committee of the International Society of Peritoneal Dialysis and he has been a member of the KDOQI PD Adequacy, Pediatric Nutrition and Pediatric Bone Work Groups for the NKF. Dr Warady also serves as an Associate Editor for *Peritoneal Dialysis International* and sits on the Editorial Boards of *Pediatric Nephrology* and the *Clinical Journal of the American Society of Nephrology*.

Advisor/Consultant: AMAG Pharmaceuticals, Amgen, Watson

Speaker: Amgen, Genentech, Watson

Grant/Research Support: NIH, Amgen, Baxter

Donna Secker, PhD, RD (Work Group Co-Chair), is an Academic and Clinical Specialist, Department of Clinical Dietetics, Division of Nephrology and The Transplant Centre at The Hospital for Sick Children, Toronto, Canada, and Project Investigator, Clinical Research Centre Research Institute, The Hospital for Sick Children. Dr Secker completed her PhD in Medical Sciences and Masters in Nutritional Sciences at University of Toronto and maintains a research interest in pediatric nutritional assessment and malnutrition in children with CKD. She is a recipient of a CIHR Clinician Scientist Training Program scholarship and is a Fellow of Dietitians of Canada. Dr Secker is a current editorial board member for *Journal of Renal Nutrition* and has served as a reviewer for numerous journals, including *Advances in Chronic Kidney Disease, Journal of Dietetic Practice and Research, Peritoneal Dialysis International,* and *Journal of Pediatric Research.* Dr Secker has also recently contributed book chapters in *Nutrition and Kidney Disease* and *Clinical Pediatric Nephrology*.

Dr Secker reported no relevant financial relationships.

Bethany J. Foster, MD, is an Assistant Professor of Pediatrics at McGill University in Montreal, Canada, where she is also an Associate Member of the Department of Epidemiology, Biostatistics and Occupational Health. She holds a Masters degree in Clinical Epidemiology from the University of Pennsylvania. She has studied body composition and nutrition in children with CKD, using a variety of methods. She is a member of the American Society of Nephrology, the Canadian Society of Nephrology, the Canadian Association of Pediatric Nephrologists, the International Society of Nephrology, the American Heart Association, and the American Society for Transplantation.

Dr Foster reported no relevant financial relationships.

Stuart Goldstein, MD, is an Associate Professor of Pediatrics at the Baylor College of Medicine in Houston, TX. He is the Medical Director of the Dialysis Unit and Pheresis Service at the Texas Children's Hospital, also in Houston. Dr Goldstein is a member of the American Academy of Pediatrics, the American Society of Nephrology, the International Pediatric Nephrology Association, the American Society of Pediatric Nephrology, the International Society of Nephrology, and the Society for Pediatric Research. In addition, he is Chairman of the Medical Advisory Committee to the FORUM of ESRD Networks and a member of the Medical Review Board for the End-Stage Renal Disease Network of Texas, is the Pediatric Nephrologist Representative for the International Society of Nephrology Commission of Acute Renal Failure, and is on the Clinical Affairs Committee for the American Society of Pediatric Nephrology. Dr Goldstein has investigated the use of IDPN to treat malnourished pediatric patients receiving HD and has assessed the use of nPCR as a marker of nutrition status in pediatric patients receiving HD.

Advisor/Consultant: Dialysis Solutions, Inc; Gambro Renal Products

Grant/Research Support: Baxter; Dialysis Solutions, Inc; Gambro Renal Products

Frederick Kaskel, MD, PhD, is Professor of Pediatrics, Vice Chairman for Affiliate & Network Affairs and Chief, Section on Nephrology, at Children's Hospital at Montefiore. Dr Kaskel is a Distinguished Alumnus of Monmoth College, Monmouth, IL and University of Cincinnati College of Medicine and has completed a nephrology fellowship at Albert Einstein College of Medicine, NY. He is Past President of the American Society of Pediatric Nephrology; Past Chairman of the NKF Council of Pediatric Nephrology and Urology; and also has served as an Advisor to the Food and Drug Administration on the Cardiovascular Renal Advisory Committee. He received numerous honors, including the National Medical Award in Pediatric Nephrology from the Kidney and Urology Foundation of America and a citation in *The Best Doctors in America*. Dr Kaskel is a principal investigator on the NIH grant Focal Segmental Glomerulosclerosis in Children and Young Adults and President of the Fifteenth Congress of the International Pediatric Nephrology Association to be held in NYC, Aug 29 to Sept 2, 2010. He has also published extensively with more than 100 publications in peer-reviewed journals and various book chapters and monographs.

Grant/Research Support: NIH

Sarah Ledermann, MB, MRCPCH, is an Associate Specialist in Pediatric Nephrology and Honorary Lecturer at Great Ormond Street Hospital (GOSH) for Children NHS Trust in London. Her primary remit for the past 20 years has been to care for infants and children with chronic kidney disease. She established a specialized clinic for this group of patients and has implemented an intensive feeding program resulting in improved growth and outcome, the results of which are internationally recognized. She developed specific protocols in CKD, including management of bone disease, prevention of anemia, immunizations schedules, safe placement of gastrostomies, and treatment of peritonitis and exit-site infections. Some of these now form the basis for recommendations in the Renal Association's Paediatric Standards Document. Dr Ledermann had a major role in the establishment of the infant PD programme at GOSH and during the last 3 years helped to develop a combined low clearance/dialysis clinic for all age groups to facilitate successful renal transplantation. Attention to detail and close collaboration with urologists, radiologists, transplant surgeons, dieticians, social workers, and clinical nurse specialists, as well as clear communication with families and local teams, is vital for high-quality patient care and has been a particular feature of her work.

She has authored several research articles relating to improvements in the management of the child with CKD published in *Pediatric Nephrology*, *The Journal of Pediatrics*, and *Pediatric Transplantation*.

Dr Ledermann reported no relevant financial relationships.

Franz S. Schaefer, MD, is Professor of Pediatrics and Chief of the Pediatric Nephrology division at Heidelberg University Medical Center. Dr Schaefer received his MD at Würzburg University Medical School. He established several important clinical research consortia in pediatric nephrology, such as the Mid European Pediatric Peritoneal Dialysis Study Group (MEPPS), the European Study Group on Progressive Chronic Kidney Disease in Children (ESCAPE), the International Pediatric Peritonitis Registry (IPPR), and the International Pediatric Peritoneal Dialysis Network (IPPN). Dr Schaefer is also a member of the KDIGO Work Group for Acute Kidney Injury and a current council member of the International Pediatric Nephrology Association (IPNA) and the International Society of Peritoneal Dialysis (ISPD). He has published more than 250 articles and book chapters and coedited the books *Comprehensive Pediatric Nephrology* and *Pediatric Dialysis.* Dr Schaefer serves as an Assistant Editor for *Pediatric Nephrology*, Pediatric Section Editor for *Nephrology Dialysis Transplantation,* and sits on the Editorial Boards of *Peritoneal Dialysis International*, *BioMed Central Nephrology,* and *Current Pediatric Reviews*.

Advisor/Consultant: Amgen, AstraZeneca

Nancy S. Spinozzi, RD, LDN, has been a Renal Dietitian Specialist at Children's Hospital, Boston, MA, since 1974. She completed her undergraduate degree in nutrition at Cornell University and Dietetic Internship at Massachusetts General Hospital. Ms Spinozzi is a current mem-

ber of the American Dietetic Association and the Council on Renal Nutrition. She has served on several NKF committees, including Patient Services Committee, Early Intervention and Prevention Task Force, and the Family Focus Advisory Group. As a member of the Council on Renal Nutrition, she has served on editorial boards of *CRN Quarterly* and *Journal of Renal Nutrition* and as Chairman of Communications Committee, Annual Scientific Program and Nominating Committee. Ms Spinozzi is also a recipient of the NKF of New England Gift of Life Outstanding Nephrology Nutrition Award and NKF Trustees Award and has contributed chapters to numerous texts, including most recently *Nutrition in Pediatrics* and *Manual of Pediatric Nutrition*.

Ms Spinozzi reported no relevant financial relationships.

KDOQI Chair

Michael V. Rocco, MD, MSCE, is Professor of Medicine at Wake Forest University in Winston-Salem, NC. He received his MD degree from Vanderbilt University in Nashville, TN, and also served his Internal Medicine residency at Vanderbilt. He completed a nephrology fellowship at the University of Pennsylvania in Philadelphia, PA, and received a master's degree in epidemiology at Wake Forest University. He has been on the faculty of the Wake Forest University School of Medicine since 1991 and currently holds the Vardaman M. Buckalew Jr Chair in Nephrology. He has more than 100 manuscripts and book chapters in the areas of HD, PD, nutrition, chronic renal failure, and epidemiology. He has served as the clinical center Principal Investigator at Wake Forest for several NIH trials, including the HEMO Study, the Acute Renal Failure Trial Network, the Dialysis Access Consortium, and the Frequent Hemodialysis Network. Dr Rocco served as the Vice-Chair for KDOQI from 2003 to 2008 and was Vice-Chair for the NKF-KDOQI Hypertension Work Group. He was also a work group member of the Centers for Medicare & Medicaid Services (CMS) ESRD Clinical Performance Measures Quality Improvement Committee and served as the chair of the PD subcommittee.

Advisor/Consultant: Amgen; DaVita; Mitsubishi-Tanabe; Renaissance Health Care

Methods Consultants

Katrin Uhlig, MD, MS, is the Director, Guideline Development at the Tufts Center for Kidney Disease Guideline Development and Implementation, in Boston, MA; Assistant Professor of Medicine at Tufts University School of Medicine; and a nephrologist at Tufts Medical Center. Dr Uhlig completed training in internal medicine, nephrology, and rheumatology in Germany (Aachen University Hospital and Munich University Hospital) and the United States (Georgetown University Medical Center and Tufts Medical Center). Since 2001, she participates in or directs the evidence review for KDOQI and KDIGO guidelines. In 2005, she co-chaired the KDIGO Evidence Rating Group to develop a consensus on grading of KDIGO guidelines. From 2006 to 2007, she served as Co-Editor of the *American Journal of Kidney Diseases*. Her focus in teaching and research is in evidence-based medicine, systematic review, CPG development, and critical literature appraisal.

Dr Uhlig reported no relevant financial relationships.

Ethan Balk, MD, MPH, is Director, Evidence-based Medicine at the Tufts Center for Kidney Disease Guideline Development and Implementation, in Boston, MA, and Assistant Professor of Medicine at Tufts University School of Medicine. Dr Balk completed a fellowship in Clinical Care Research. His primary research interests are evidence-based medicine, systematic review, CPG development, and critical literature appraisal.

Dr Balk reported no relevant financial relationships.

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