

NKF K/DOQI Clinical Practice Guidelines

The NKF K/DOQI clinical practice guidelines have been widely adopted in the United States. The scope of these guidelines has evolved to encompass the spectrum of Chronic Kidney Disease (CKD) before the need for dialysis arises, and to improve the outcomes of patients who develop end-stage kidney disease (ESKD). These guidelines have become the focus of many quality improvement initiatives and have served as the basis for the ESKD Clinical Performance Measures Project.

Unfortunately, due to a lack of evidence-based outcomes in pediatric CKD patients, the original K/DOQI guidelines did not specifically define clinical practice guidelines for many areas in pediatrics. In the original K/DOQI documents, pediatric guidelines were either not discussed or incorporated into the adult guidelines. These original K/DOQI guidelines include: Hemodialysis Adequacy, Peritoneal Dialysis Adequacy, Vascular Access, and Anemia Management. Since that time, there has been a concerted effort to approach the pediatric patients independently, and to separate out the guidelines, which apply to pediatric patients with CKD. More recently, the Nutrition guidelines included an entirely separate pediatric section, while the guidelines on CKD (Evaluation, Classification, and Stratification; Management of Dyslipidemias in Kidney Failure; Clinical Practice Guidelines for Blood Pressure Management and use of Antihypertensive Agents in CKD) defined specific pediatric recommendations within their guidelines. The new workgroups who developed the more recent K/DOQI recommendations have all included separate pediatric workgroups.

The purpose of this document is to make available in one separate listing, all the existing K/DOQI clinical practice guidelines (opinion- or evidence-based) which apply to pediatric patients. The goal of this separate document is to improve the care for pediatric patients with CKD under the care of a Pediatric or an Internal Medicine Nephrologist. Guidelines listed will be numbered, corresponding with the original K/DOQI guidelines. If noted in the original K/DOQI guidelines, we documented in this paper whether the guidelines were evidence- or opinion-based for pediatrics. When felt to be helpful, the appropriate workgroup's rationale for the guideline were included.

We have updated this compilation with the 2006 updates and as of publication of this page, we believe that this represents an up-to-date compilation. However, frequent updates and development of new guidelines frequently occur, so we urge members to consult the [K/DOQI](#) website regularly. Furthermore, to simplify this compilation, some of the tables, figures and literature references have been removed. These are available on the K/DOQI website.

1) Hemodialysis Adequacy (2006 Update)

GUIDELINE 8. PEDIATRIC HEMODIALYSIS PRESCRIPTION AND ADEQUACY

8.1 Initiation of HD:

- **8.1.1 Dialysis initiation considerations for the pediatric patient should follow the adult patient guideline of a GFR less than 15 mL/min/1.73 m². (A)**
- **8.1.2 For pediatric patients, GFR can be estimated by using either a timed urine collection or the Schwartz formula. (A)**
- **8.1.3 Dialysis therapy initiation should be considered at higher estimated GFRs when the patient's clinical course is complicated by the presence of the signs and symptoms listed in [Table 11](#), CPR 1 for adult patients, as well as malnutrition or growth failure for pediatric patients. Before dialysis is undertaken, these conditions should be shown to be refractory to medication and/or dietary management. (A)**

8.2 Measurement of HD adequacy:

- **8.2.1 spKt/V, calculated by either formal urea kinetic modeling or the second-generation natural logarithm formula, should be used for month-to-month assessment of delivered HD dose. (B)**
- **8.2.2 Assessment of nutrition status is an essential component of HD adequacy measurement. nPCR should be measured monthly by using either formal urea kinetic modeling or algebraic approximation. (B)**
- **8.2.3 Principles and statements regarding slow-flow methods for postdialysis sampling and inclusion of RKF (or lack thereof) outlined in the adult guidelines also pertain to pediatric patients. (B)**

8.3 Prescription of adequate HD:

- **8.3.1 Children should receive at least the delivered dialysis dose as recommended for the adult population. (A)**
- **8.3.2 For younger pediatric patients, prescription of higher dialysis doses and higher protein intakes at 150% of the recommended nutrient intake for age may be important. (B)**

8.4 Non-dose-related components of adequacy:

Accurate assessment of patient intravascular volume during the HD treatment should be provided to optimize ultrafiltration. (B)

BACKGROUND

Provision of evidence-based pediatric HD adequacy guidelines is hampered by a number of epidemiological issues. Stage 5 CKD remains a relatively uncommon disease, and renal transplantation is still the predominant and preferred KRT modality for children. In addition, PD is a viable modality option for many pediatric patients. Finally, children with CKD stage 5 show significantly better survival rates compared with adult patients. As a result of these factors, no long-term pediatric outcome study comparable to the HEMO Study or the National Cooperative Dialysis Study (NCDS) would be adequately powered to detect an effect of delivered HD dose on pediatric patient outcome. Nevertheless, some recent pediatric data exist to describe the most accurate methods for quantifying urea removal, correlate delivered dose of dialysis with inflammation, and examine other components of the dialysis prescription, including ultrafiltration and nutrition provision. These data can serve as the basis for CPRs in caring for children receiving HD. For areas in which no pediatric

data exist, CPGs and CPRs for adult patients should serve as a minimum standard for pediatric patients.

RATIONALE

Although the Schwartz formula overestimates GFR, especially at lower GFR levels, recent pediatric data show that GFR estimated by using the Schwartz formula of $15 \text{ mL/min/1.73 m}^2$ or less had excellent negative predictive value for a measured GFR of $20 \text{ mL/min/1.73 m}^2$ by iothalamate clearance. Because 24-hour urine collections often are not possible for smaller non-toilet-trained children, reliance on serum creatinine-based formulas is essential in this subset. As with the MDRD equation, use of the Schwartz formula is simple and does not depend upon collection of urine samples. The Schwartz formula contains a cofactor that accounts for patient sex and age to incorporate estimates of lean muscle mass.

Modality choice is governed by a number of factors, including patient size, availability of a caregiver to competently perform home dialysis, and the expected length of waiting time for a renal allograft. Children weighing less than 10 kg are better suited for PD because HD in very small children requires extensive nursing expertise. Also, because infants require greater nutritional needs to promote growth on a per-kilogram basis, thrice-weekly HD often is insufficient to maintain acceptable fluid, potassium, and electrolyte balances. HD should be strongly considered for patients who do not have one, and preferably two, caregivers who are competent and motivated to provide home PD. For patients who have a consenting living renal allograft donor available and who have substantial urine output and electrolyte control, initiation of maintenance dialysis therapy may be avoided if a preemptive transplantation can be scheduled expeditiously.

Monthly solute clearance and nutrition status measurement using urea as the surrogate small molecule are essential to assess the dose of dialysis in pediatric patients because patients receiving optimal dialysis should grow and gain weight through adolescence. Thus, assessment of Kt/V will guide the practitioner to increase dialyzer size, blood flow rates, or dialysis treatment time as patients grow. Single-center pediatric data exist that show the Daugirdas formula reliably estimates spKt/V derived by using formal urea kinetic modeling. An essential component of adequacy measurement is nutrition status assessment because recent pediatric data show that increased delivered dialysis dose does not in and of itself lead to improved nutritional intake. Pediatric data show that nPCR is more sensitive than serum albumin concentration as a marker of protein-energy malnutrition in a small group of malnourished children receiving HD.

No large-scale studies exist to validate a target spKt/V or eKt/V as adequate for the pediatric HD population, although methods for accurate measurement of each have been validated in children. Certainly, because infants and young children have greater nutritional requirements to support growth, pediatric patients should receive at least the minimum dialysis dose as prescribed for adults. A study showed that pediatric patients who receive a thrice-weekly Kt/V of 2.0 and 150% of the recommended daily allowance of protein were able to show catch-up linear growth without the use of recombinant growth hormone. Chronic inflammatory mediator levels seem to be inversely proportional to eKt/V in pediatric HD patients, although an optimal eKt/V level has not been established to mitigate chronic inflammation, which is related in large part to dialysis vintage. Thus, a case can be made for providing pediatric patients with a Kt/V greater than the adult-based guideline of 1.2, but a larger scale study is warranted to determine an optimal Kt/V target. Such a strategy will ensure that smaller growing pediatric patients receive enough nutrition and adequate waste product clearance. Observational pediatric data exist showing that older, larger, and African-American children are less likely to receive an spKt/V greater than 1.2 consistently; therefore, practitioners should be informed to make specific efforts to ensure the provision of adequate dialysis in these vulnerable populations.

Management of pediatric HD patient fluid status is especially difficult because children are expected to grow and gain weight from infancy through adolescence. Thus, distinguishing between real weight accretion versus fluid overload is critical to prevent a chronic fluid-overloaded state that can lead to chronic hypertension and resultant CVD. Given the relative high ultrafiltration rate to dialysis treatment time ratio and the relative inability of younger patients to accurately verbalize symptoms from overly rapid ultrafiltration, the means to accurately assess patient intravascular volume can help

optimize ultrafiltration to attain patient true target dry weight while minimizing intradialytic symptoms. Noninvasive monitoring (NIVM) of hematocrit during the dialysis treatment uses an in-line sensor to reflect the change in patient blood volume as an inverse change in patient hematocrit during fluid removal. Ultrafiltration guided by NIVM algorithms that adjust UFRs and targets based on hourly NIVM blood volume changes have been shown to decrease patient symptoms, hospitalization, extra treatments for fluid overload and hypertension, antihypertensive medication requirements, and fourth weekly HD treatments for pediatric patients receiving HD.

LIMITATIONS

Any pediatric study to determine either an adequate or optimal delivered dialysis dose requires practical end points to be valid. Whereas death and hospitalization rates are easily measurable end points, their relative infrequency in the pediatric HD population and the low prevalence of pediatric CKD stage 5 make an adequately powered study using these end points a virtual impossibility.

CLINICAL PRACTICE GUIDELINES FOR PERITONEAL DIALYSIS ADEQUACY

GUIDELINE 6. PEDIATRIC PERITONEAL DIALYSIS

INTRODUCTION

The provision of evidence-based pediatric PD adequacy guidelines is hampered by a number of epidemiological issues. CKD stage 5 remains a relatively uncommon disease in children, while kidney transplantation is still the predominant mode of KRT. In addition, HD is a viable modality option for many pediatric patients, especially adolescents. Finally, children with CKD stage 5 show significantly better survival rates compared with adult patients. As a result of these factors, no long-term pediatric outcome study similar to the ADEMEX Study is adequately powered to detect an effect of the delivered PD dose on pediatric patient outcome.³⁸ Nevertheless, pediatric data exist, for example, to describe the most accurate methods for assessing peritoneal membrane transport capacity and quantifying urea removal.¹⁴⁶⁻¹⁴⁸ These data and others can serve as a basis for CPGs in children receiving PD. For areas in which no pediatric-specific data exist, the CPGs and CPRs for adult patients should serve as a minimum standard for pediatric patients, but the overall clinical “wellness” of the individual pediatric patient should be the primary factor that influences the quantity and quality of the care provided.

6.1 Recommended laboratory measurements for peritoneal membrane function:

- 6.1.1 The PET is the preferred approach to the clinical assessment of peritoneal membrane transport capacity in pediatric patients and should be performed to aid in the prescription process. (A)

6.2 Maintenance of euvolemia and normotension:

- 6.2.1 The frequent presence of hypertension and associated cardiac abnormalities in children receiving PD requires strict management of blood pressure, including attention to fluid status. (A)

6.3 Quality improvement programs:

- 6.3.1 The CQI process has been shown to improve outcomes in many disciplines, including CKD stage 5. (A)
 - 6.3.1.1 Each home training unit should establish quality improvement programs with the goal of monitoring clinical outcomes and implementing programs that result in improvements in patient care. In children, growth and school attendance/performance are clinical activities to be monitored in addition to those recommended for adult patients.

- 6.3.1.2 Quality improvement programs should include representatives of all disciplines involved in the care of the pediatric PD patient, including physicians, nurses, social workers, dietitians, play therapists, psychologists, and teachers.
- 6.3.1.3 Single-center trends in pediatric clinical outcomes should be compared with national and international data.

RATIONALE

Recommended Laboratory Measurements for Peritoneal Membrane Function

The PET is the most common technique used clinically in children to assess peritoneal membrane transport capacity and guide the prescription process, although other means of membrane assessment have been reported. Addition of a volume marker during the PET also can provide valuable information regarding fluid handling. Institution of a standardized PET procedure for children has resulted from recognition of the age-independent relationship between BSA and peritoneal membrane surface area and the resultant recommendation for use of a test exchange volume scaled to BSA when one conducts studies of peritoneal transport kinetics in children. Based on 2 large-scale studies and resultant normative data, the PET in children should be performed with an exchange volume of 1,000 to 1,100 mL/m² BSA. Provision of a smaller volume characteristically results in more rapid equilibration of solute between blood and dialysate and the artifactual appearance of an inherently increased (more rapid) membrane transport capacity. Repeated PET testing is recommended when knowledge of the patient's current membrane transport capacity is necessary for determination of the patient's PD prescription (eg, in the setting of suboptimal clearance), especially when clinical events have occurred (eg, repeated peritonitis) that may have altered membrane transport characteristics. Kinetic modeling programs have been developed that use peritoneal membrane transport test data from the standard PET and PD capacity (PDC) tests to help in prescription management. These have been validated for clinical use in pediatrics.

Maintenance of Euvolemia and Normotension

Hypertension is a common complication of children receiving dialysis. As delineated in the KDOQI CVD Guidelines, determination and management of blood pressure in children should follow recommendations by the Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents. In that report, it is recommended that the optimal (normal) SBP and DBP should be <90th percentile for age, sex, and height.

A recent analysis of data from the North American Pediatric Renal Transplant Cooperative Study (NAPRTCS) found that 56.9% of nearly 4,000 dialysis patients had uncontrolled hypertension (blood pressure > than the age-, sex-, and height-specific 95th percentile) and an additional 19.7% of patients had controlled hypertension (blood pressure < the 95th percentile with antihypertensive medication). In addition, marked echocardiographic changes have been documented in pediatric patients at both the initiation of dialysis therapy and during maintenance dialysis therapy. A retrospective study of 64 long-term dialysis patients found that 48 children (75%) had LVH, including 26 of 38 children (68%) on PD therapy. Similarly, another report showed increased left ventricular mass (LVM) and LVMI in children receiving dialysis compared with a healthy population. Whereas the cause of the elevated blood pressure is multifactorial, others found that high blood pressure and cardiac impairment were most frequent in the younger and nephrectomized dialysis patients for whom volume overload appeared to be the most important etiologic factor.

Proper fluid management requires knowledge and repeated monitoring of the patient's daily residual kidney volume and daily ultrafiltration volume. Efforts to modify the dialysis prescription with the goal of enhancing ultrafiltration with the lowest possible dialysate dextrose concentration are conducted best with knowledge of the patient's peritoneal membrane transport capacity as derived from the PET. If patients are characterized as high/rapid transporters and are unable to achieve the ultrafiltration necessary for blood pressure control with standard dialysis solutions, consideration should be given to the use of an icodextrin-based dialysis solution. Whereas its use has been associated with enhanced ultrafiltration in pediatric patients, a recent report suggests that icodextrin-associated fluid removal correlated significantly with age and

that icodextrin may behave differently in young children in whom ultrafiltration may not be as successful. This experience has not been duplicated in other centers and requires confirmation.

Recommendations for antihypertensive therapy in children are provided in the Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents, as well as in the KDOQI Clinical Practice Guidelines on Hypertension and Antihypertensive Agents in CKD.

Finally, in some patients who are polyuric, negative net daily ultrafiltration may be desirable because of its potential to replenish decreased intravascular volume and improve RKF. When negative net daily ultrafiltration is not possible, provision of additional fluids is recommended.

Quality Improvement Programs

A CQI program should be instituted in all dialysis facilities that care for children receiving PD, based on evidence that improvements in patient care are best achieved in this manner. In addition to monitoring outcomes related to, for example, complications related to infection, achievement of solute clearance targets, adequacy of nutrition, osteodystrophy, anemia management, and QOL, school attendance/performance and growth are key issues to be monitored in any program caring for children receiving long-term dialysis. Not surprisingly, data collected by the NAPRTCS showed that children receiving PD regularly show better school attendance than those on HD therapy. However, differences exist in the PD population when attendance is stratified by race, an issue that requires attention and often intervention. The recommendation for regular growth assessment, as previously delineated in the pediatric component of the KDOQI Nutrition Guidelines, results from the negative impact that CKD can have on height velocity and the association between poor growth and poor outcome in children receiving dialysis. The use and influence of medical interventions (eg, correction of acid-base abnormalities, control of secondary hyperparathyroidism and renal osteodystrophy, provision of adequate nutrition, and institution and effect of recombinant human growth hormone therapy) also should be monitored.

Although programs with varying levels of pediatric expertise coordinate the care of children receiving long-term dialysis, ideally, a treatment facility should be able to provide the necessary multidisciplinary services required by children and families through a team of specialists with pediatric experience. All these disciplines should be involved in the CQI process.

In view of the relatively small number of children who receive PD in any one center, it is imperative that single-center data be compared with results contained in large pediatric databases to determine whether modification of a center's program is deemed necessary. Organizations such as the NAPRTCS and USRDS provide such data.

LIMITATIONS

Although attention to fluid management likely will benefit blood pressure control and help prevent the development of CVD in children receiving PD, no large-scale study of the pediatric CKD stage 5 population has proved this to be true.

Although CQI programs generally are considered to be beneficial, there are no studies of pediatric PD facilities that document the efficacy of such programs in terms of their ability to improve patient outcomes.

While it is intuitively beneficial for the CQI program to be multidisciplinary in nature, quality standards for some disciplines in terms of their application to the pediatric PD population have not yet been established.

II. CLINICAL PRACTICE RECOMMENDATIONS FOR PERITONEAL DIALYSIS ADEQUACY

CLINICAL PRACTICE RECOMMENDATIONS FOR GUIDELINE 6: PEDIATRIC PERITONEAL DIALYSIS

6.1 Dialysis initiation:

- 6.1.1 Dialysis initiation should be considered for the pediatric patient when GFR is 9 to 14 mL/min/1.73 m² BSA and should be *recommended* when GFR is 8 mL/min/1.73 m² or less. GFR can be estimated by either averaging the measured creatinine and urea clearances by using a timed urine collection, using the Schwartz formula, or using a timed urine collection to determine CCr after a dose of cimetidine. Dialysis therapy initiation should be considered at the greater estimated GFR levels when the patient's clinical course is complicated by the presence of malnutrition, fluid overload, hypertension, hyperkalemia, hyperphosphatemia, acidosis, growth failure/decreasing height velocity, or neurological consequences of uremia. Before dialysis is undertaken, these conditions should be shown to be persistent and refractory to medication and/or dietary management.

6.2 Modality selection:

- 6.2.1 The decision regarding the selection of PD as a dialysis modality for the pediatric patient should take a variety of factors into account, including patient/family choice, patient size, medical comorbidities, and family support.

6.3 Solute clearance targets and measurements:

- 6.3.1 In the absence of definitive data correlating solute removal and clinical outcome in children, current recommendations for solute clearance in pediatric patients receiving PD are as follows:
 - 6.3.1.1 The pediatric patient's clinical status should be reviewed at least monthly, and delivery of the prescribed solute clearance should render the patient free of signs and symptoms of uremia.
 - 6.3.1.2 All measurements of peritoneal solute clearance should be obtained when the patient is clinically stable and at least 1 month after resolution of an episode of peritonitis.
 - 6.3.1.3 More frequent measurements of peritoneal solute clearance and RKF should be considered when clinical events are likely to have resulted in decreased clearance or when new/worsening signs or symptoms of uremia develop.
 - 6.3.1.4 Regardless of the delivered dose of dialysis, if a patient is not doing well and has no other identifiable cause other than kidney failure, a trial of increased dialysis is indicate.
- 6.3.2 For patients with RKF (defined as urine $Kt/V_{\text{urea}} > 0.1/\text{wk}$):
 - 6.3.2.1 The minimal “delivered” dose of total (peritoneal and kidney) small-solute clearance should be a Kt/V_{urea} of at least 1.8/wk.
 - 6.3.2.2 Total solute clearance should be measured within the first month after initiating dialysis and *at least* once every 6 months thereafter.
 - 6.3.2.3 If the patient has RKF and residual kidney clearance is being considered as part of the patient's total weekly solute clearance goal, a 24-hour urine collection for urine volume and solute clearance determinations should be obtained at a minimum of every 3 months.
- 6.3.3 For patients without RKF (defined as urine $Kt/V_{\text{urea}} < 0.1/\text{wk}$) or for those in whom RKF is unable to be measured accurately:
 - 6.3.3.1 The minimal “delivered” dose of small-solute clearance should be a peritoneal Kt/V_{urea} of at least 1.8/wk.
 - 6.3.3.2 The peritoneal solute clearance should be measured within the first month after starting dialysis and *at least* once every 6 months thereafter.
- 6.3.4 When calculating Kt/V_{urea} , one should estimate V or TBW by using the sex-specific nomograms based upon

the following equations:

Males: $TBW=0.010 \times (\text{height} \times \text{weight})^{0.68} - 0.37 \times \text{weight}$

Females: $TBW=0.14 \times (\text{height} \times \text{weight})^{0.64} - 0.35 \times \text{weight}$

6.4 Preservation of RKF:

- 6.4.1 Techniques that may contribute to the preservation of RKF in pediatric patients receiving PD should be incorporated as a component of dialysis care whenever possible.
 - 6.4.1.1 Nephrotoxic insults in those with normal or impaired kidney function should be assumed, in the absence of direct evidence, to also be nephrotoxic in patients on PD therapy who have RKF and therefore should be avoided.
 - 6.4.1.2 Aminoglycoside antibiotics should be avoided whenever possible to minimize the risk for nephrotoxicity, as well as ototoxicity and vestibular toxicity.
 - 6.4.1.3 “Prekidney” and “postkidney” causes of a decrease in RKF should be considered in the appropriate clinical setting.
 - 6.4.1.4 Infections of the urinary tract should be treated promptly.
 - 6.4.1.5 Diuretics should be used to maximize urinary salt and water excretion.
 - 6.4.1.6 An ACE inhibitor or ARB should be considered in a PD patient who requires antihypertensive medication and has RKF.

6.5 Writing the PD prescription:

- 6.5.1 In addition to solute clearance, QOL, ultrafiltration/volume control, and possibly the clearance of middle molecules should be considered when writing the PD prescription.
 - 6.5.1.1 The patient's dialysis schedule and QOL as it relates to such issues as school and work attendance/performance should be taken into account when designing the dialysis prescription.
 - 6.5.1.2 To optimize small-solute clearance, minimize cost, and possibly decrease the frequency of exchanges, one should first increase the instilled volume per exchange (target range, 1,000 to 1,200 mL/m² BSA; maximum, 1,400 mL/m² BSA), as tolerated by the patient, before increasing the number of exchanges per day. The volume of the supine exchange(s) should be increased first because this position has the lowest intra-abdominal pressure. Objective evidence of patient tolerance may require assessment of IPP.
 - 6.5.1.3 The patient's record of PD effluent volume should be reviewed monthly, with particular attention to the drain volume from the overnight dwell of CAPD and daytime dwell of CCPD.
 - 6.5.1.4 Factors to be considered when attempting to optimize total body volume include:
 - a. Dietary sodium and fluid restriction may be implemented in patients unable to maintain euvolemia/normotension with dialysis alone.
 - b. In patients with RKF, diuretics may be preferred over increasing the dialysate dextrose concentration to achieve euvolemia.
 - c. Drain volume should be optimized after the overnight dwell of CAPD and the daytime dwell(s) of CCPD to maximize solute clearance and ultrafiltration volume.
 - d. In patients who are hypertensive or in whom there is evidence of volume overload, ultrafiltration generally should be positive for all daytime or nighttime exchanges.
 - e. An effort should be made to determine the lowest possible dialysate dextrose concentration required to achieve the desired ultrafiltration volume.
 - 6.5.1.5 To optimize middle-molecule clearance in patients who have minimal RKF, the PD prescription

should preferentially include the use of CCPD with dwells 24 h/d or CAPD. This is recommended even if small-molecule clearance is above target without the longer dwell.

- 6.5.1.6 The use of NIPD (eg, no daytime dwell) can be considered in pediatric patients who are clinically well, whose combined dialysis prescription and RKF achieves or exceeds the target solute clearance, and who are without evidence of hyperphosphatemia, hyperkalemia, hypervolemia, or acidosis.

6.6 Other aspects of the care of the pediatric PD patient:

- **6.6.1 All children on PD therapy with anemia should follow the KDOQI Guidelines for Management of Anemia that pertain to pediatrics.**
- **6.6.2 Management of dyslipidemias for prepubertal children on PD therapy should follow recommendations by the National Cholesterol Expert Panel in Children and Adolescents Postpubertal children or adolescents on PD therapy should follow the pediatric recommendations provided in the KDOQI Clinical Practice Guidelines for Managing Dyslipidemia in CKD.**
- **6.6.3 All children on PD therapy should follow the pediatric-specific recommendations provided in the KDOQI Clinical Practice Guidelines for CVD in Dialysis Patients and the KDOQI Clinical Practice Guidelines on Hypertension and Antihypertensive Agents in CKD.**
- **6.6.4 All children on PD therapy should follow the recommendations provided in the KDOQI Clinical Practice Guidelines for Nutrition in Chronic Renal Failure.**

RATIONALE

Dialysis Initiation

The gold standard for measurement of GFR is inulin clearance, but this technique is impractical to perform clinically. Whereas the use of such radioisotopic measures as chromium-51, iothalamate sodium, and technetium 99m-DTPA are alternative measures to inulin, these techniques are expensive, require multiple blood samples, and are not ideal for frequent monitoring.

A measured CCr requires a timed urine collection, most often 12 to 24 hours in duration. The accuracy of the assessment as a means of estimating GFR is complicated by the need for a complete urine collection and that creatinine secretion results in overestimation of GFR, especially at lower levels of kidney function. At lower levels of GFR, accuracy is improved by measuring both creatinine and urea clearances on the same timed urine collection and averaging the values to obtain the estimated GFR.

The accuracy of the GFR estimate by CCr can be increased by the provision of cimetidine to the patient before the timed urine collection. A study of children showed that as a result of cimetidine's capacity to block the kidney's tubular secretion of creatinine, its use in a formal outpatient protocol is associated with GFR results that approximate those obtained with inulin.

The Schwartz formula also overestimates GFR, especially at lower GFR levels, and provides a less accurate means of estimating the target clearance for dialysis consideration than what can be determined with a complete timed urine collection. However, recent pediatric data show that a GFR of 15 mL/min/1.73 m² or less estimated by using the Schwartz formula had an excellent negative predictive value for a measured GFR of 20 mL/min/1.73 m² by using iothalamate clearance.

Because a timed urine collection often is not possible for smaller non-toilet-trained children, reliance on a serum creatinine-based formula, such as the Schwartz formula, is essential in this subset of patients.

Finally, a variety of signs and symptoms may be present in the pediatric patient with CKD stage 4 (GFR, 15 to 29 mL/min/1.73 m²) that are not routinely associated with the presence of uremia, but that remain unresponsive to medical and/or dietary therapy. A trial of dialysis may on occasion result in marked clinical improvement.

Modality Selection

PD is the preferred initial long-term dialysis modality worldwide for the pediatric patient with CKD stage 5. Its use is particularly advantageous in the very small patient for whom maintenance of a functional and complication-free vascular access can be problematic. The provision of PD, often in association with the use of an automated cycling device, also facilitates regular school attendance for most age-appropriate children. The use of PD is preferred over HD when there are contraindications to the use of anticoagulation, in children who have cardiovascular instability, and in children who live far from a pediatric HD center.

However, there are absolute and relative contraindications to the use of PD in children that include the following:

Absolute contraindications:

- Omphalocele
- Gastroschisis
- Bladder extrophy
- Diaphragmatic hernia
- Obliterated peritoneal cavity
- Peritoneal membrane failure

Relative contraindications:

- Inadequate living situation for home dialysis
- Lack of appropriate caregiver
- Impending/recent major abdominal surgery
- Imminent living-related donor transplantation (within 6 months of dialysis initiation)

Recognition of the burden of care for families that coexists with the provision of this home therapy is paramount so that appropriate support systems may be put in place. Assessment of the patient's and caregiver's perception of QOL may aid in this process .

PD Solute Clearance Targets and Measurements

The clinical status of the pediatric patient should be monitored closely as an important qualitative means of determining whether the patient is receiving an adequate quantity of dialysis. Irrespective of the delivered dose of dialysis, adequate dialysis likely is provided if the patient's clinical status is characterized by adequate growth, blood pressure control, and nutritional status; avoidance of hypovolemia and sodium depletion; and adequate psychomotor development.

Clinical manifestations of inadequate dialysis may include the following:

- CHF
- Hyperphosphatemia/excessive serum calcium × phosphorus product
- Uncontrolled hypertension/hypervolemia
- Overt uremia (uremic pericarditis, pleuritis)
- Repeated hyperkalemic episodes
- Clinical or biochemical signs of malnutrition or wasting

- Poor school performance

Factors contributing to inadequate dialysis include:

- Loss of RKF
- Prescription inadequate for peritoneal membrane transport characteristics
- Reduced peritoneal surface area caused by extensive intra-abdominal adhesions
- Loss of membrane solute transport/ultrafiltration capacity because of peritonitis
- Noncompliance with PD prescription
- Poorly functioning PD catheter

Current clinical opinion supports the recommendation that the target “delivered” solute clearance in pediatric patients should meet or exceed adult standards. The term “delivered” refers to the actual dose the patient is receiving based on measurement, in contrast to an estimated value using a kinetic modeling program. Data from pediatric and adult patients found serum albumin level to be a predictor of patient survival, and a Kt/V_{urea} of 1.8 or greater in adult PD patients has been associated with better serum albumin values. The ADEMEX Study did not show a clinical benefit associated with Kt/V_{urea} greater than 1.7/wk in adult CAPD patients, whereas other studies provided evidence for a recommended minimal Kt/V_{urea} greater than 1.7/wk and an optimal Kt/V_{urea} of 1.8/wk based on survival data in anuric adult CAPD patients. No similar large-scale studies have been performed in children. Pediatric studies have presented data suggestive of a correlation between patient outcome (especially growth) and total solute clearance; however, the number of patients in these and other pediatric studies is small and the potential role of RKF can be confounding, and thus data correlating solute clearance to outcome cannot be considered definitive. Nevertheless, it is recommended that solute clearance assessments take place at least every 6 months in all cases and that more frequent assessments be conducted when dialysis clearance may have been compromised (eg, after peritonitis), there is a progressive loss of RKF, or there is clinical evidence of inadequate dialysis.

Historically, both Kt/V_{urea} and CCr have served as measures of dialysis clearance. In addition, the averaged urea and CCr from a timed urine collection has been recommended as the most accurate means to estimate RKF and remains a preferred approach to estimate GFR when considering dialysis therapy initiation. Nevertheless, determination of dialysis and urine Kt/V_{urea} alone currently is recommended for follow-up based upon the simplicity of the calculation and because studies of adult patients on PD therapy have not provided evidence of a benefit in terms of patient outcome when expressing clearance in any manner other than Kt/V_{urea} . The age-related differences in the residual urine volume of children with CKD stage 5 precludes duplication of the adult preference to universally characterize the presence of RKF as urine volume greater than 100 mL/d.

Accurate estimation of TBW or V is a critical component of the dialysis prescription in PD. Because gold-standard isotope dilution techniques are laborious, cost-ineffective, and not widely available, anthropometric prediction equations based on height and weight commonly are used to determine TBW. During childhood, complex changes in body composition occur that necessitate the use of appropriate allometric formulae. Whereas such equations have been established in healthy populations, recent studies showed that the use of these equations routinely overestimates TBW in pediatric patients receiving PD. Conversely, the recent determination of TBW by heavy water (H_2O^{18} or D_2O) dilution in 64 pediatric patients receiving PD has allowed for the development of TBW prediction equations that perform equally well in male and female, North American and European, obese and nonobese, and growth-retarded and normally sized children. The sex-specific nomograms designed to estimate TBW, which are based upon the prediction equations, are shown in Table 17 and Table 18. (AVAILABLE ON THE K/DOQI WEBSITE).

Because the height • weight parameter also predicts BSA, use of the Gehan and George equation for BSA allows for

TBW-estimating equations that can be simplified, but with slightly less precision, compared with the best fitting equations to:

$$\text{Male: TBW} = 20.88 \times \text{BSA} - 4.29$$

$$\text{Female: TBW} = 16.92 \times \text{BSA} - 1.81$$

Whereas several approaches to the calculation of BSA are used in pediatrics, the Gehan and George equation for BSA was derived from the greatest number of study subjects. The Gehan and George equation is as follows:

$$\text{BSA (m}^2\text{)} = 0.0235 \times (\text{height[cm]})^{0.42246} \times (\text{weight[kg]})^{0.51456}$$

Based on this equation, BSA can be determined by height and weight by referring to Table 19 (AVAILABLE ON K/DOQI WEBSITE).

Preservation of RKF

There are no large-scale studies in pediatrics that provide evidence of a correlation between RKF and patient outcome in children receiving PD. However, in a single-center observation of a pediatric PD population, it was shown that superior growth velocity occurred in a group of children with RKF versus a group of children without RKF despite the achievement of similar mean total solute clearance in the 2 groups of patients. Thus, it is possible that growth, as well as achievement of solute clearance goals, benefits from RKF and emphasizes the need to prevent nephrotoxic insults whenever possible. In addition, there is evidence that pediatric patients on PD therapy lose RKF at a slower rate than patients on HD therapy.

While there is no experience regarding the use of ACE inhibitors or ARBs in children with CKD stage 5 similar to that in adults, use of an ACE inhibitor in children with CKD has been associated with marked slowing of kidney deterioration. In the setting of CKD stage 5, close monitoring for the presence of hyperkalemia is mandatory when an ACE inhibitor or ARB is used.

Writing the PD prescription

Both CAPD and APD are used by children, and the prescription designed for either modality is best tailored to the needs of the individual patient. APD is the preferred PD modality in children, in large part because its use is characterized by freedom from procedures during the daytime hours. The pediatric PD patient's QOL and the influence that the dialysis prescription has on it is an issue that should be reassessed regularly because of the impact that CKD can have on the child's overall development. Although there are not yet any validated measures of QOL designed for the pediatric CKD stage 5 population, the PedsQL™ 4.0 Generic Core Scales and the Child Health Questionnaire have both been used successfully in the pediatric dialysis population.

Pediatric data have provided evidence that the prescription of an exchange volume that results in an exceedingly high IPP may result in patient intolerance and poor ultrafiltration. Whereas the target range for the exchange volume of patients older than 2 years is 1,000 to 1,200 mL/m² BSA, the initial prescribed volume should be somewhat lower for smaller infants (~600 to 800 mL/m² BSA). A stepwise increase in volume as tolerated by the patient usually is possible. While the limitation of dietary sodium in children may have a positive influence on total body volume, this recommendation should be instituted with caution in patients with high RKF and/or dialysis-related sodium losses. Salt depletion may result in hypotension and impaired growth.

The removal of “middle molecules” and low-molecular-weight proteins ideally also should be taken into account in the prescription process because of the influence it may have on clinical outcome, especially in patients without RKF.

However, few data exist on the topic in pediatrics, prompting it to currently have a minor role in prescription considerations for children.

Although the PD prescription is characterized most often by 24-hour dwells, in some circumstances, NIPD without the use of a daytime dwell can be used effectively. Its use requires that the patient's clinical status be monitored closely and consideration be given to a 24-hour dwell prescription if NIPD is not fully effective. This recommendation has been made previously by the European Pediatric PD Working Group.

LIMITATIONS

No large-scale prospective study has been conducted in children on PD therapy that correlates solute removal (PD and RKF) with patient outcome. This precludes the ability to make an evidence-based recommendation regarding the target solute clearance.

Few data are available for children that compare the impact of RKF versus peritoneal solute removal on patient outcome. Although data are available from the adult CKD stage 5 population showing the benefit of ACE-inhibitor and ARB therapy as a means of preserving RKF, no similar pediatric data are available.

The ability to assess the QOL of the pediatric PD patient and his or her family is limited by the absence of a QOL tool that has been validated in the pediatric CKD stage 5 population.

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3) Vascular Access Guidelines (2006 Update)

CLINICAL PRACTICE RECOMMENDATION 8: VASCULAR ACCESS IN PEDIATRIC PATIENTS

8.1 Choice of access type:

* 8.1.1 Permanent access in the form of a fistula or graft is the preferred form of vascular access for most pediatric patients on maintenance HD therapy.

* 8.1.2 Circumstances in which a CVC may be acceptable for pediatric long-term access include lack of local surgical expertise to place permanent vascular access in small children, patient size too small to support a permanent vascular access, bridging HD for PD training or PD catheter removal for peritonitis, and expectation of expeditious kidney transplantation.

* 8.1.3 If surgical expertise to place permanent access does not exist in the patient's pediatric setting, efforts should be made to consult vascular access expertise among local adult-oriented surgeons to either supervise or place permanent vascular access in children.

* 8.1.4 Programs should evaluate their patients' expected waiting times on their local deceased-donor kidney transplant waiting lists. Serious consideration should be given to placing permanent vascular access in children greater than 20 kg in size who are expected to wait more than 1 year for a kidney transplant.

8.2 Stenosis surveillance:

An AVG stenosis surveillance protocol should be established to detect venous anastomosis stenosis and direct patients for surgical revision or PTA.

8.3 Catheter sizes, anatomic sites, and configurations:

* 8.3.1 Catheter sizes should be matched to patient sizes with the goal of minimizing intraluminal trauma and obstruction to blood flow while allowing sufficient blood flow for adequate HD.

* 8.3.2 External cuffed access should be placed in the internal jugular with the distal tip placed in the right atrium.

* 8.3.3 The BFR of an external access should be minimally 3 to 5 mL/kg/min and should be adequate to deliver the prescribed HD dose.

INTRODUCTION

Applicability of Previous KDOQI Vascular Access Guidelines to Pediatric Patients

Provision of validated evidence-based pediatric vascular guidelines is hampered by a number of pediatric CKD stage 5–related epidemiological issues. Most of the recommendations outlined in the first edition of the KDOQI Vascular Access Guidelines are pertinent to pediatric patients, although few published data exist to support more than opinion-based recommendations. Some pediatric HD vascular access descriptive and comparative clinical research has been conducted since the first edition of the KDOQI Vascular Access Guidelines, which provide data to formulate a first set of both evidence- and opinion-based recommendations for children receiving maintenance HD. Rather than restating the previous CPGs in their entirety with annotation of the few areas in which the emphasis may be different for pediatric patients, we

have opted to present separate pediatric Vascular Access Guidelines based on the available pediatric literature. For specific vascular access areas not addressed in these pediatric guidelines, the practitioner should refer to the relevant adult KDOQI Guidelines.

RATIONALE

Choice of Access Type (CPR 8.1)

Kidney transplantation remains the preferred and predominant therapy for pediatric patients with CKD stage 5; therefore, many pediatric patients receive maintenance HD through an indwelling catheter in light of short deceased-donor waiting list times or a readily available living-related donor. Because fewer than 800 pediatric patients receive maintenance HD therapy in the United States, surgical expertise for placing fistulae or grafts in small patients may be limited by the infrequent need and sporadic caseload. Smaller patients, especially those less than 10 kg, present technical challenges in terms of both surgical and nursing skill; therefore, the majority of smaller patients receive PD for their maintenance dialysis modality.

Recent data show that AVFs and AVGs typically function longer than catheters in pediatric patients receiving maintenance HD therapy. Functional survival rates of AVFs and AVGs are similar to adult patient standards and those recommended by KDOQI Vascular Access Guidelines, with centers recently reporting 4-year functional survival rates of 40% to 60%. Despite this, the most recent CMS CPM and North American Pediatric Renal Transplant Cooperative Study data show that 62% to 78% of pediatric maintenance HD patients have catheters as their vascular access. While reports of successful permanent vascular access in children less than 10 kg in size exist, maturation can take up to 4 to 6 months, making routine permanent access placement impractical in many pediatric situations. Since the late 1970s, both AVFs and AVGs have been placed in children requiring maintenance HD. The major complications of pediatric fistulae include a primary nonfunction rate of 20% to 33%, usually because of lack of maturation or clotting. Pediatric fistulae can develop stenosis anywhere along the fistula, most of which is amenable to either surgical correction or PTA. Given the relatively long life expectancy for pediatric patients with CKD stage 5 (79% at 10 years and 66% at 20 years), all efforts should be made to use distal sites for initial fistula creation, ie, the radiocephalic fistula configuration. For patients less than 10 kg in size with a creatinine clearance between 20 and 25 mL/min/1.73 m² in whom imminent dialysis is not required, microsurgical techniques should be used for fistula creation. Fistulae in smaller children may require 4 to 6 months for adequate maturation.

Stenosis Surveillance (CPR 8.2)

AVGs offer the advantage of more flexible surgical configurations, which include the use of thigh vessels. Recent data show that AVGs can function well in pediatric patients receiving maintenance HD, with functional survival rates similar to adult patient standards and KDOQI Vascular Access Guidelines. As with AVFs, the more distal anatomic sites should be used for first access to preserve more proximal sites for access in later life. AVG venous outflow stenosis predisposes pediatric patients to AVG thrombosis. Recent pediatric data show that UDTs are very sensitive to predict venous stenosis. A proactive ultrasound dilution venous stenosis assessment protocol directing patients to angioplasty with a corrected access flow less than 650 mL/min can lead to a significant decrease in AVG thrombosis rates. One pediatric study found that static venous pressure monitoring did not help in the diagnosis of venous stenosis. No data exist about the long-term effect of decreased thrombosis rates on AVG survival in children.

Catheter Sizes, Anatomic Sites, and Configurations (CPR 8.3)

The choice of catheter size and configuration depends on the size of the patient. Studies to date suggested that children as

small as 4 to 5 kg can tolerate dual-lumen 8 Fr catheters, and as the child becomes larger in size, a larger volume access can be placed. Choices often are limited based on availability, but considerations should include flow characteristic, recirculation risk, and ease of placement. Data suggest that for the appropriately sized patient, twin single-lumen catheters (the Tesio System) may provide better performance than standard dual-lumen catheters. Longer and more narrow catheters result in greater resistance to flow.

Catheter placement considerations in pediatrics are similar to those in adults, with a preference for internal jugular veins over subclavian veins. Right atrial placement may prevent inlet or outlet hole occlusion by blood vessels and thus allow for the high flow rates needed to provide adequate dialysis. Data have suggested that subclavian stenosis occurs in excess of 80% of patients in pediatrics who have subclavian catheters. Femoral access can be used when upper-anatomy venous access is no longer available.

Flow rates for vascular access should be sufficient to result in a $Kt/V > 1.2$. Kt/V is influenced further by the recirculation rate. Because flow rates in pediatrics vary by the size of catheter, which varies by the size of the patient, a recommended flow rate of 3 to 5 mL/kg/min is acceptable in most patients.

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4) Anemia Guidelines

Guideline 1: When to Initiate the Work-Up of Anemia (Pediatric Evidence-Based)

An anemia work-up should be initiated in patients with chronic kidney disease (CKD) when the:

- Hgb < 11 g/dL (Hct is < 33%) in pre-menopausal females and pre-pubertal patients (Evidence)
- Hgb < 12g/dL (Hct is < 37%) in adult males and post-menopausal females (Evidence)

RATIONALE

The Anemia Work Group notes that:

Anemia is defined in terms of the Hgb or Hct concentrations. In this guideline, they recommend that a work-up of anemia be initiated when the Hgb/Hct level declines to approximately 80% of the mean level for defined healthy, normal subgroups. Differences in average Hgb/Hct levels between adult men and women are likely due to differences in estrogen and testosterone production that emerge at puberty, but subside after menopause. Anemia is likely to be present in individuals when Hgb/Hct concentrations are below these levels. However, the mean Hgb/Hct in the general population is only a statistical benchmark and may not be the best indication of anemia in every individual. For example, there is a 75% likelihood of anemia in an adult female with a Hct of 34% or a Hgb of 11 g/dL, or in a male with a Hct of 39% or a Hgb of 12.5 g/dL. Moreover, many individuals have Hgb/Hct concentrations which are physiologically normal for them, but which would be defined as anemia in terms of the general population data. Others have a Hgb/Hct level that may be physiologically inadequate for them (e.g., patients with chronic obstructive pulmonary disease), even though it falls within the range considered normal for the general population.

Table IV-I. Mean Normal Values of Hemoglobin and Hematocrit for the Healthy, Normal Population*

Age/Gender	Hemoglobin (g/dL)	Hematocrit (%)
Birth	16.5 ± 3.0	51 ± 9
1 month	14.0 ± 4.0	43 ± 6
2 to 6 months	11.5 ± 2.5	35 ± 7

6 months to 2 years	12.0 ± 1.5	36 ± 3
2 to 6 years	12.5 ± 1.0	37 ± 3
6 to 12 years	13.5 ± 2.0	40 ± 5
12 to 18 years (male)	14.5 ± 1.5	43 ± 6
Menstruating female	14.0 ± 2.0	41 ± 5
Adult male/post-menopausal female	15.5 ± 2.0	47 ± 6

*Mean±Standard Deviation

Guideline 3: Erythropoietin (EPO) Deficiency (Pediatric Opinion-Based)

If no cause for anemia other than CKD is detected, and the serum creatinine is >2: 2 mg/dL, anemia is most likely due to EPO deficiency. Measurement of serum EPO levels usually is not indicated.

RATIONALE

The Anemia Work Group notes that:

As kidney function declines, the likelihood of anemia associated with EPO deficiency increases because the diseased kidneys are unable to produce sufficient quantities of EPO. Anemia can develop relatively early in the course of CKD, however, and has been associated with serum creatinine as low as 2.0 mg/dL, and occasionally even lower, particularly in individuals with a reduced muscle mass. On the other hand, there is a wide range of Hgb/Hct levels for any degree of kidney dysfunction. Two studies have found a linear relationship between Hct and creatinine clearance in pediatric patients. A linear relationship between GFR and Hct was observed in 48 pediatric patients in one study, and in 31 CKD pediatric patients in another study when the GFR was estimated from the serum creatinine. In these two studies, significant anemia was noted when the GFR was less than 20 and 35 mL/min/1.73 m², respectively.

Guideline 4: Target Hemoglobin/Hematocrit for Epoetin Therapy

The Clinical Practice Guideline for target hemoglobin/hematocrit has been updated due to the recent controversy over ESA therapy. Please [click here](#) for the most recent pediatric recommendations, published in the September 2007 issue of the American Journal of Kidney Diseases.

Guideline 8: Administration of Supplemental Iron

A. Supplemental iron should be administered to prevent iron deficiency and to maintain adequate iron stores so that CKD patients can achieve and maintain an Hgb 11 to 12 g/dL (Hct 33% to 36%) in conjunction with the use of an erythropoiesis-stimulating agent (ESA) therapy (Adult Evidence-Based)

B. If oral iron is given, it should be administered at a daily dose of at least 200 mg of elemental iron for adults and 2 to 3 mg/kg for pediatric patients. (Pediatric Evidence-Based)

C. The adult CKD, home hemodialysis, and peritoneal dialysis (PD) patient may not be able to maintain adequate iron status with oral iron. (Adult Evidence-Based) Therefore, 500 to 1,000 mg of iron dextran may be administered IV in a single infusion, and repeated as needed, after an initial one-time test dose of 25 mg. As of January 2000, it is not recommended to give these large doses of iron gluconate as a single infusion. (Adult Opinion-Based)

D. A trial of oral iron is acceptable in the hemodialysis patient (Adult Opinion-Based), but is unlikely to maintain the TSAT > 20%, serum ferritin > 100 ng/mL, and Hgb/Hct at 11 to 12 g/dL/33% to 36%. (Adult Evidence-Based)

E. To achieve and maintain an Hgb 11 to 12 g/dL (Hct of 33% to 36%), most hemodialysis patients will require intravenous iron on a regular basis. (Adult Evidence-Based)

F. Intravenous iron can be given on a variety of dosage schedules, if the TSAT is < 20% and/or the serum ferritin is < 100 ng/mL, the Anemia Work Group recommends that, in adults, 100 to 125 mg of iron be administered IV at every hemodialysis for 10 to 8 doses, respectively. If the TSAT remains < 20% and/or the serum ferritin < 100ng/mL, another course of IV iron (100 to 125 mg per week for 10 to 8 weeks) is recommended (Adult Opinion-Based). Once the patient's TSAT is < 20% and the serum ferritin is < 100 ng/mL, the Anemia Work Group recommends that 25 to 125 mg of iron be given IV once per week. (Adult Opinion-Based) Schedules for IV iron administration ranging from three times per week to once every 2 week are also reasonable in order to provide 250 to 1,000 mg of iron within 12 weeks. (Adult Opinion-Based)

G. Most patients will achieve an Hgb 11 to 12g/dL (Hct of 33% to 36%) with TSAT and serum ferritin levels < 50% and < 800 ng/mL, respectively. In patients in whom TSAT is > 50% and/or serum ferritin is > 800 ng/mL, IV iron should be withheld for up to 3 months, at which time the iron parameters should be re-measured before iron is resumed (Adult Evidence-Based). When the TSAT and serum ferritin have fallen to < 50 % and < 800 ng/mL, IV iron can be resumed weekly at a dose reduced by one third to one-half (Adult Opinion-Based).

H. It is anticipated that once optimal Hgb/Hct and iron stores are achieved, the required maintenance dose of IV iron may vary from 25 to 125 mg/week for hemodialysis patients. The goal is to provide a weekly dose of IV iron in hemodialysis patients that will allow the patient to maintain the target Hgb/Hct at a safe and stable iron level. The maintenance iron status should be monitored by measuring the TSAT and serum ferritin no less than every 3 months. (Adult Opinion-Based)

I. Oral iron is not indicated for the CKD patient who requires maintenance doses of IV iron. (Adult Opinion-Based)

RATIONALE

The Anemia Work Group notes that:

Normal body iron stores are 800 to 1,200 mg. If the initial Hct is 25% and the target Hct is 35%, the magnitude of supplemental iron required by patients during the first 3 months of ESA therapy is approximately 1,000 mg. Of this, approximately 400 mg of iron are needed simply to replace iron losses during 3 months of hemodialysis. The other 600 mg of iron are needed to support production of sufficient numbers of red blood cells to achieve the target Hgb/Hct. Once the target Hgb/Hct is achieved, approximately 400 to 500 mg of supplemental iron will be needed every 3 months to replace iron losses and maintain adequate iron stores.

In children, mean daily intestinal blood losses (pre-dialysis) are 6 mL/m² BSA, and dialysis-associated blood losses are 8 mL/m² per treatment. Cumulative annual iron losses therefore approximate 1.6 g/1.73 m² in pediatric hemodialysis patients, and 0.9 g/1.73 m² in predialysis pediatric patients and probably in those on PD. Although there are no data on the calculated iron needs in pediatric patients on dialysis, the rationale for iron supplementation is similar to that described for adults.

Guideline 9: Administration of a Test Dose of IV Iron (Pediatric Opinion-Based)

Prior to initiating IV iron dextran therapy, a one-time test dose of 25 mg (in adults) should be given IV. For pediatric patients weighing <10 kg, the test dose should be 10 mg; for pediatric patients weighing 10-20 kg, the test does should be 15 mg. If no immediate allergic reaction occurs, subsequent routine doses can be given without a test dose. According to the package insert, iron dextran should be administered by slow IV push at a rate not to exceed 1.0 mL (50 mg, if undiluted) per minute (Adult Opinion-Based).

Prior to initiating IV iron gluconate therapy in adults, a one-time test dose of 25 mg should be given IV. If no immediate allergic reaction occurs, subsequent routine doses can be given without a test dose. According to the package insert, the test dose should be diluted in 50 mL of 0.9% sodium chloride for injection and administered over 60 minutes. Also,

according to the package insert, iron gluconate has not been established to be safe and effective in pediatric patients.

Guideline 12: Initial ESA Administration

A. Subcutaneous (SC) Administration (Evidence-Based)

1. When an ESA is given SC to adult patients, the dose should be 80 to 120 units/kg/wk (typically 6,000 units/wk) in two to three doses per week.
2. Pediatric patients < 5 years old frequently require higher dose (300 units/kg/wk) than older pediatric patients and adults.

B. IV Administrations (Adult Evidence-Based)

If the initial administration of an ESA is IV for Hemodialysis patients, the dose should be 120 to 180 units/kg/wk (typically 9,000 units/wk), given in three divided doses.

RATIONALE

The Anemia Work Group notes that:

In pediatric PD patients, the median weekly ESA dose required to maintain a target Hct of 28% to 30% was 136 units/kg/wk in those older than 15 years.

A higher dose requirement for pediatric patients < 5 years has been noted in two multicenter trials. The basis for this difference has not been established. On the other hand, 19 of 22 children (peritoneal dialysis [10], hemodialysis [2], and chronic kidney impairment [10]) between the ages of 4 months to 16 years (mean, 9 years) achieved target Hgb (9 to 11 g/dL) after 4 months of 50 U/kg of ESA given SC, twice weekly.

Guideline 18: Intraperitoneal ESA Administration (Adult Evidence-Based)

For peritoneal dialysis patients in whom SC or IV administration of ESA is not feasible, intraperitoneal (IP) administration may be considered. IP administration must be done into a dry abdomen or one with a minimal amount of dialysate. IP dose requirements may be higher than those associated with IV or SC administration.

RATIONALE

The Anemia Work Group notes that:

An ESA administered into the abdominal cavity will be diluted if mixed with dialysate, thus slowing its absorption. Perhaps for this reason, ESA doses are higher with IP administration, if mixed with dialysate, than with either N or SC administration. A "dry" abdomen results in better absorption. For example, in pediatric patients, if an ESA is administered intraperitoneally into a full dialysate dwell volume, absorption of ESA is less than 50% of that attained with SC administration, but absorption is enhanced if instilled with a small amount (50mL) of dialysate. Therefore, in pediatric patients, if IP administration of an ESA is used, it is best to infuse it into a "dry" abdomen or one with a minimal amount of dialysate.

Guideline 20: Causes for Inadequate Response to ESA (Pediatric Opinion-Based)

The most common cause of an incomplete response to ESA is iron deficiency. In the iron-replete patient with an inadequate response to ESA, the following conditions should be evaluated and treated, if reversible:

1. Infection/inflammation (e.g., access infections, surgical inflammation, AIDS or SLE)
2. Chronic blood loss
3. Osteitis fibrosa
4. Aluminum toxicity
5. Hemoglobinopathies (e.g., alpha and beta thalassemias, sickle cell anemia)
6. Folate or vitamin B12 Deficiency
7. Multiple myeloma

8. Malnutrition

9. Hemolysis

RATIONALE

The Anemia Work Group notes that:

In pediatric patients on CAPD, peritonitis may exert a protracted suppressive effect on the response to ESA. The pathophysiology of inflammatory reticuloendothelial blockage is gradually being elucidated and may relate to the inhibition of erythropoiesis, mediated by inflammatory cytokines, such as tumor necrosis factor and interleukin-1. An elevated C-reactive protein level, often associated with inflammation and/or infection, has been a predictor of resistance to ESA.

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5) Nutrition in Chronic Kidney Disease Guidelines

Guideline 1: Patient Evaluation of Protein-Energy Nutritional Status

The most valid measures of protein and energy nutrition status in children treated with a maintenance dialysis (Pediatric Evidence or Opinion-Based) include:

- Dietary interview/diary (Pediatric Opinion-Based)
- Serum Albumin (Pediatric Opinion-Based)
- Height and length (Pediatric Evidence- and Opinion-Based)
- Weight/Height Index (Pediatric Opinion-Based)
- Mid-arm circumference and muscle circumference or area (Pediatric Opinion-Based)
- Skin fold thickness (Pediatric Opinion-Based)
- Head circumferences for age 3 years or less (Pediatric Evidence- and Opinion-Based)
- Standard deviation score (SDS or Z score) for height (Pediatric Evidence- and Opinion-Based)

Guideline 2: Management of Acid-Base Status (Pediatric Evidence- and Opinion-Based)

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

Guideline 3: Urea Kinetic Modeling (Pediatric Evidence- and Opinion-Based)

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

Guideline 4: Interval Measurements (Pediatric Evidence- and Opinion-Based)

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

Guideline 5: Energy Intake for Children Treated with Maintenance Dialysis (Pediatric Evidence- and Opinion-Based)

The initial prescribed energy intake for children treated with maintenance hemodialysis or peritoneal dialysis should be at the Recommended Dietary Allowance (RDA) level for chronological age. Modifications should then be made depending

upon the child's response.

Guideline 6: Protein Intake for Children Treated With Maintenance Dialysis (Pediatric Evidence- and Opinion-Based)

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

Children treated with maintenance peritoneal dialysis should have their initial dietary protein intake based on the RDA for their chronological age plus an additional increment based on anticipated peritoneal losses (Pediatric Evidence- and Opinion-Based)

Guideline 7: Vitamin and mineral Requirements (Pediatric Evidence- and Opinion-Based)

The recommended dietary intake should achieve 100% of the Dietary Reference Intakes for thiamin (B1), riboflavin (B2), pyridoxine (B6), vitamin B12, and folic acid. An intake of 100% of the RDA should be the goal for vitamins A, C, E, And K, copper and zinc.

Guideline 8: Nutrition Management (Pediatric Opinion-Based)

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

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

Guideline 9: Nutritional Supplementation for Children Treated with Maintenance Dialysis (Pediatric Evidence- and Opinion-Based)

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

Guideline 10: Recommendations for the Use of Recombinant Human Growth Hormone (hGH) for Children Treated With Maintenance Dialysis (Pediatric Evidence- and Opinion-Based)

Treatment with recombinant hGH in dialysis patients with growth potential should be considered under the following conditions:

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

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6) Evaluation, Classification and Stratification for Chronic Kidney Disease (CKD)

Guideline 1: Definition and Stages of CKD (Pediatric Opinion-Based)

Adverse outcomes of CKD can often be prevented or delayed through early detection and treatment. Earlier stages of CKD

can be detected through routine laboratory measurements.

- The presence of CKD should be established, based on presence of kidney damage and level of kidney function (glomerular filtration rate (GFR), irrespective of diagnosis.
- The stage of CKD should be assigned based on the level of kidney function, irrespective of diagnosis, according to the K/DOQI CKD classification.

Stage	GFR (ml/min/1.73m ²)	Description
1	>90	Kidney damage with normal GFR
2	60-89	Mild CKD
3	30-59	Moderate CKD
4	15-29	Severe CKD
5	<15	Kidney failure or dialysis

Abbreviations: GFR, glomerular filtration rate.

*May be normal for age

RATIONALE

The CKD Work Group states:

The normal level of GFR varies according to age, gender, and body size. It is conventional to adjust GFR to "standard" body size (surface area of 1.73 m²). Among normal adults, the inter-individual coefficient of variation (standard deviation divided by the mean) of GFR (adjusted for body surface area) within the normal population is approximately 120 to 130 (20 to 25) mUmin/1.73 m². Children reach adult values for mean GFR by approximately age 2 years.

Guideline 4: Estimation of GFR (Pediatric Evidence-Based)

Estimates of GFR are the best overall indices of the level of kidney function.

- The level of kidney function should be assessed by estimating the level of GFR from the serum creatinine.
- The serum creatinine concentration alone should not be used to assess the level of kidney function.
- The level of GFR should be estimated from prediction equations that take into account the serum creatinine concentration and some or all of the following variables: age, gender, race and body size.
- Clinical laboratories should provide an estimate of GFR with the results of serum creatinine measurements.
- Autoanalyzer manufacturers and clinical laboratories should calibrate serum creatinine assays using an international standard.
- In general, measurements of creatinine clearance using timed (for example 24-hour) urine collections does not improve the estimate of GFR over that provided by prediction equations.
- In patients with an estimated GFR <15 ml/min/1.73 m², a 24 hour urine sample should be collected for computation of creatinine clearance, KtN urea and estimation of dietary protein intake to aid in the assessment of the need for kidney replacement therapy.

RATIONALE

The CKD Work Group notes that:

Several formulae for estimating GFR in children have been developed. Two of these, the Schwartz formula, and the Counahan-Barratt formulas utilize the proportionality between GFR and height/serum creatinine. The difference between

the constants cited in the Counahan-Barratt and the Schwartz formula has been attributed to the use of different assays to measure creatinine. The Counahan-Barratt formula was developed using a measure of "true" creatinine and GFR by ^{51}Cr -EDTA plasma clearance, while the original Schwartz formula was developed using insulin clearance and creatinine measured by a modified Jaffe reaction, which may have overestimated true creatinine.

While a systematic review of the literature yielded over 40 references examining prediction equations to estimate GFR, only a handful used a gold standard measure of GFR and included more than 50 children. For the Schwartz formula, most studies reported mean differences between estimated and measured GFR. These ranged from -0.4 to 10 mL/min/1.73 m² with SD ranging from 2 to 20 mL/min/1.73 m². The data suggest that the bias of the estimate of the Schwartz formula increases with decreasing GFR.

Studies describing the accuracy of the estimate show that approximately 75% of Schwartz formula estimates of GFR are within 30% of the measured GFR by insulin clearance. Comparable studies of the Counahan-Barratt formula show 70% to 86% of Counahan-Barratt estimates fall within 30% of GFR measured by ^{51}Cr -EDTA.

Although imprecise, the Schwartz and Counahan-Barratt formulae for estimating GFR in children are convenient and practical. Both use height in the estimate, as height is proportional to muscle mass. The constants used in the equations differ, likely related to the different assays to measure creatinine. For a 5-year-old child who is at median (50th percentile) height for age, the serum creatinine corresponding to a GFR of 60 mL/min/1.73 m² is 1.0 mg/dL using the Schwartz formula and 0.8 mg/dL using the Counahan-Barratt formula. This example illustrates that use of both formulas can allow for estimation of kidney function, and even serum creatinine levels < 1.0 mg/dL can be associated with substantially impaired kidney function in small children and adults who have low muscle mass or malnutrition.

Guideline 5: Assessment of Proteinuria (Pediatric Evidence-Based)

Normal individuals usually excrete very small amounts of protein in their urine. Persistent increased protein excretion is usually a marker of kidney damage. The excretion of specific types of protein, such as albumin or low molecular weight globulins, depends on the type of kidney disease that is present. In this guideline, the term "proteinuria" refers to increased urinary excretion of albumin, other specific proteins or total protein. Guidelines for detection and monitoring of proteinuria in adults and children differ due to differences in the prevalence of CKD type.

Guidelines for Adults and Children:

- Under most circumstances, untimed ("spot") urine samples should be used to detect and monitor proteinuria in children and adults.
- It is usually not necessary to obtain a timed urine collection (overnight or 24-hour) for these evaluations in either children or adults.

Guidelines for Adults:

- When screening adults for CKD, albumin should be measured in a random spot urine sample using either an albumin-specific dipstick or the albumin-to-creatinine ratio.
- When monitoring proteinuria in adults with CKD, the albumin-to-creatinine ratio in spot urine samples should be measured.

Guidelines for Children:

- When screening nondiabetic children for CKD, it is preferable to test a first morning spot urine sample using the urine dipstick. A random specimen is acceptable if a first morning specimen is not available. In children with a urine dipstick showing >1+ protein, the total protein-to-creatinine ratio should be measured in a first morning spot urine sample.
- When monitoring proteinuria in children with nondiabetic CKD, the total protein-to-creatinine ratio on first morning urine samples should be measured.
- When screening or monitoring children for diabetic CKD, the albumin-to-creatinine ratio on a first morning urine specimen should be measured.

RATIONALE FOR TYPE OF PROTEIN: CHILDREN WITHOUT DIABETES

The CKD Work Group states:

In children without diabetes, it is preferable to assess proteinuria as total protein, because:

- Total protein detects albumin, which usually is present in large quantities in glomerular diseases of childhood.
- Total protein detects low molecular weight proteins that are present in other types of CKD (non-glomerular diseases) in childhood.

The prevalence of chronic kidney damage due to diabetes and hypertension is far lower in children than in adults. In contrast, the prevalence of kidney disease due to urinary tract abnormalities and congenital tubular disorders is far more common in children than in adults. These latter diseases may be characterized by low molecular weight proteinuria, which would be detected by tests for total urine protein, but not by tests for albumin. Therefore, the CKD Work Group recommends that total urine protein should be measured to detect and monitor kidney damage in most children, one exception being children with diabetes mellitus.

RATIONALE FOR TYPE OF PROTEIN: CHILDREN WITH DIABETES

The CKD Work Group states:

In post-pubertal children with duration of diabetes greater than 5 years, it is preferable to assess proteinuria as albumin because:

- Albuminuria is a more sensitive marker than total protein for CKD due to diabetes.
- In other children with diabetes, it is preferable to assess proteinuria as total protein because:
- Total protein detects albumin, usually present in large quantities, in childhood CKD due to glomerular diseases.
- Total protein detects low molecular weight proteins, which are present in childhood CKD due to non-glomerular diseases

The risk of diabetic kidney disease in children is higher in post-pubertal children with duration of diabetes greater than 5 years than in other diabetic children. For these reasons, the American Diabetes Association recommends screening these children for CKD, using the same algorithm as for adults. Other diabetic children are screened using the same algorithms as for other children.

*Guideline 6: Additional Markers of CKD
(Pediatric Evidence-Based)

Markers of kidney damage other than proteinuria include abnormalities in the urine sediment and abnormalities on imaging studies. Constellations of markers define clinical presentations for some types of CKD. New markers are needed to detect kidney damage that occurs prior to a reduction in GFR.

- Urine sediment should be examined in patients with CKD and individuals at increased risk of developing CKD.
- Imaging studies of the kidneys should be performed in patients with CKD and in selected individuals at increased risk of developing CKD.
- Although several novel urinary markers (such as tubular or low-molecular weight proteins and specific mononuclear cells) show promise of future utility, they cannot be used for clinical decision-making at present.

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7) Assessment of Dyslipidemias

Guideline 1

1.1 All adults and adolescents with CKD should be evaluated for dyslipidemias.

1.2 For adults and adolescents with CKD, the assessment of dyslipidemias should include a complete fasting lipid profile with total cholesterol, LDL, HDL, and triglycerides.

1.3 For adults and adolescents with Stage 5 CKD, dyslipidemias should be evaluated upon presentation (when the patient is stable), at 2-3 months after a change in treatment or other conditions known to cause dyslipidemias; and at least annually

thereafter.

RATIONALE

The Dyslipidemia Work Group notes:

Young adults (20-40 years old) with Stage 5 CKD have at least a 10-fold higher risk for atherosclerotic cardiovascular disease (ACVD) mortality compared to the general population. There are limited data on ACVD in children with CKD. However, ACVD accounts for approximately 23% of deaths in children and adults < 30 years old who started treatment for Stage 5 CKD as children. Recent data from the Pathobiological Determinants of Atherosclerosis in Youth (PDA Y) study provide compelling evidence in the general pediatric population, that initial fatty streaks seen in adolescents develop into atheromatous plaques in young adults. Moreover, this atherosclerotic process is believed to be accelerated in uremia, thus putting children with Stage 5 CKD at high risk for developing ACVD. Indeed, studies of arteries from children with Stage 5 CKD have demonstrated early ACVD changes.

It is important to note that lipid levels in the general population change with age and puberty, and differ by gender. Very low levels at birth increase rapidly in the first year of life to a mean total cholesterol of 150 mg/dL (3.88 mmol/L), LDL 100 mg/dL (2.59 mmol/L), and HDL 55 mg/dL (1.42 mmol/L). From ages 1-12, lipid levels remain fairly constant, and are slightly lower in girls than boys. During puberty, there is a decrease in total cholesterol, LDL, and a slight decrease in HDL in boys. After puberty (i.e., by age 17), cholesterol and LDL increase to adult levels in boys and girls. Boys continue to have a slightly lower HDL than girls. These changes dictate that the definitions of dyslipidemias be different in children and adults. These guidelines define dyslipidemias for children using lipid levels greater than the 95th percentile for age and gender. Treatment thresholds for children do not differ by age and gender, but these thresholds are different from those of adults.

There are few data documenting the prevalence of dyslipidemias in children and adolescents with CKD. A search was conducted for studies published after 1980 that included at least 15 patients and reported data on the prevalence of dyslipidemia in unselected patients with CKD. There were no studies of hemodialysis patients. Children and adolescents on peritoneal dialysis appeared to have a very high prevalence of dyslipidemias. Indeed, 29% to 87% of pediatric peritoneal dialysis patients had LDL > 100 mg/dL (> 2.59 mmol/L). Similarly, 72% to 84% of pediatric kidney transplant recipients had LDL > 100 mg/dL (> 2.59 mmol/L). In a longitudinal study of pediatric kidney transplant patients, the prevalence of hypercholesterolemia declined from 70.4% to 35% at 10 years, with a decrease in hypertriglyceridemia from 46.3% to 15%. This decline in prevalence may reflect reductions in immunosuppressive medications and improved kidney function. Unfortunately, no longitudinal studies have defined the long-term risk of dyslipidemias in children with CKD, particularly as they survive into young adulthood.

Guideline 2

- 2.1 For adults and adolescents with Stage 5 CKD, a complete lipid profile should be measured after an overnight fast whenever possible.
- 2.2 Hemodialysis patients should have lipid profiles measured either before dialysis, or on days not receiving dialysis.

Guideline 3

Stage 5 CKD patients with dyslipidemias should be evaluated for remediable, secondary causes.

RATIONALE

The Dyslipidemia Work Group notes:

Secondary causes of dyslipidemia in children and adolescents include lipodystrophy; idiopathic hypercalcemia; glycogen storage diseases; cystine storage disease; Gaucher disease; Juvenile Tay-Sachs disease; Niemann-Pick Disease; sphingolipidoses; obstructive liver disease such as biliary atresia; biliary cirrhosis; intrahepatic cholestasis; nephrotic

syndrome; anorexia nervosa; progeria; systemic lupus erythematosus; Werner syndrome; and Klinefelter syndrome. These conditions are fortunately rare, and require referral to appropriate tertiary care specialists.

Guideline 5

5.1 For adolescents with Stage 5 CKD and fasting triglycerides >500 mg/dL (>5.65 mmol/L) that cannot be corrected by removing an underlying cause, treatment with therapeutic lifestyle changes (TLC) should be considered.

5.2 For adolescents with Stage 5 CKD and LDL >130 mg/dL (>3.36 mmol/L), treatment should be considered to reduce LDL to <130 mg/dL (<3.36 mmol/L).

5.3 For adolescents with Stage 5 CKD and LDL <130 mg/dL (>3.36 mmol/L), fasting triglycerides >200 mg/dL (>2.26 mmol/L), and non-HDL cholesterol (total cholesterol minus HDL) >160 mg/dL (>4.14 mmol/L), treatment should be considered to reduce non-HDL cholesterol to <160 mg/dL (<4.14 mmol/L).

RATIONALE FOR TREATING VERY HIGH TRIGLYCERIDES

The Dyslipidemia Work Group states:

Evidence that very high triglycerides can cause pancreatitis in children comes from case reports and small series of patients with familial dyslipidemias. The incidence of pancreatitis caused by hypertriglyceridemia in adolescents with CKD is unknown. However, it seems prudent to treat very high triglycerides with TLC, if nutrition is otherwise adequate. The safety and efficacy of lowering triglycerides with fibrates and niacin have not been established in adolescents.

Isolated hypertriglyceridemia in adolescents should be treated with TLC. Cases of triglycerides persistently >500 mg/dL (>5.65 mmol/L) are rare, and they are generally due to an inherited metabolic disorder. Drug therapy, e.g., low-dose fibrates or nicotinic acid, may be warranted. The use of fibrates or nicotinic acid in adolescents has not been well studied; therefore, routine use of these agents cannot be recommended at this time. Patients should be referred, however, to a pediatric lipid specialist for management and to rule out familial hypertriglyceridemia or rare, inherited disorders such as lipoprotein lipase deficiency or apolipoprotein C-II deficiency.

RATIONALE FOR TREATING HIGH LDL AND HIGH NON-HDL CHOLESTEROL

The Dyslipidemia Work Group states:

Atherosclerosis in young adults was first described in 1953. Most recently, the PDA Y study found that 50% of children 10-14 years old had early fatty streaks, and 8% had fibrous plaques, thus confirming that atherosclerosis begins in childhood. Risk factors associated with ACVD in adults are also associated with atherosclerosis in children. In the Bogalusa Heart Study, body mass index, LDL, and systolic blood pressure were associated with atherosclerotic disease of the aorta and coronary vessels of children. Moreover, hypercholesterolemia in children and adolescents persists into adulthood. Recent studies of subclinical ACVD in children with familial hypercholesterolemia found an increase in intimal medial thickness of the aorta and carotid arteries compared to that of healthy young children. Thus, these and other studies in the general population suggest that ACVD begins in childhood, and that dyslipidemia in children may play an important role in the pathogenesis of ACVD. However, in children with CKD, the relationship between dyslipidemia and subsequent ACVD is unknown.

APPROACH TO TRATING HIGH LDL AND HIGH NON-HDL CHOLESTEROL

The Dyslipidemia Work Group states:

Secondary causes of dyslipidemias should be treated first (Guideline 3). Thereafter, for LDL 130-159 mg/dL (3.36-4.11 mmol/L) TLC should be used first. If after 6 months of TLC, LDL is >130 mg/dL (>3.36 mmol/L), then consider pharmacological management. If LDL is >160 mg/dL (>4.14 mmol/L), then consider starting atorvastatin at the same time as TLC.

THERAPEUTIC LIFESTYLE CHANGES

The Dyslipidemia Work Group states:

TLC for children are similar to those recommended for adults. Recent studies in the general population have shown that dietary fat restriction is safe in children. In particular, there have been no adverse effects on growth and development, or nutrition. However, TLC should be used judiciously, or not at all, in children who are malnourished. If TLC has failed after 6 months, and potential secondary causes of dyslipidemia have been ruled out, drug therapy should be considered.

DRUG THERAPY

The Dyslipidemia Work Group states:

There are few studies examining drug treatment of dyslipidemia in children with CKD. However, a limited number of small, randomized, controlled trials in children and adolescents from the general population have found that statins are safe and effective in lowering LDL. In particular, statins do not appear to have adverse effects on growth and development. A few, very small, uncontrolled trials have likewise reported that statins are safe and effective in patients with nephrotic syndrome. Thus, although statins are not approved for use in children and adolescents, and additional studies are needed, preliminary data suggest they are safe and effective. Therefore, statins should be considered for therapy in adolescents with CKD and elevated LDL, or in hypertriglyceridemic adolescents with CKD and increased non-HDL cholesterol. Currently, the only statin approved by the United States Food and Drug Administration (USFDA) for use in children and adolescents is atorvastatin.

For adolescents who do not achieve the desired target with a statin, addition of a bile acid sequestrant can be considered. Bile acid sequestrants appear to be safe and effective in improving dyslipidemias in children. Cholestyramine is approved for use in children by the USFDA. Although bile acid resins are safe in children of all ages, adherence to therapy is often poor due to the high incidence of adverse effects. No dosage adjustment is required in patients with CKD. However, pediatric dosages have not been established. In children 6-12 years of age, doses of anhydrous cholestyramine 80 mg/kg 3 times a day, not to exceed 8 g per day, can be used. Adverse effects are common and include constipation, abdominal discomfort, nausea, flatulence, vomiting, diarrhea, heartburn, anorexia, and indigestion. In children and adults treated with cyclosporine, bile acid sequestrants should probably be administered between cyclosporine doses. Bile acid sequestrant powders are generally mixed with 4-6 ounces of fluid, and several glasses of water between doses are recommended. The fluid recommended with bile acid powders may limit their use in dialysis or CKD patients who have been prescribed strict fluid restrictions. The newer bile acid sequestrant colesevelam has not yet been studied in children, and thus cannot be recommended at this time. Similarly, the phosphate-binding (and lipid-lowering) agent sevelamer hydrochloride has not been studied in children.

Bile acid sequestrants can increase triglycerides, and hypertriglyceridemia is common in children with CKD. Bile acid resins are relatively contraindicated in patients with triglycerides 2:: 200 mg/dL (2:: 2.26 mmol/L), and definitely contraindicated in patients with triglycerides 2:: 500 mg/dL (2:: 5.65 mmol/L). Other potential, long-term adverse effects of bile acid resins include deficiencies of vitamins A, E, and folic acid. In studies with long-term follow-up, a folic acid supplement was required; however, anemia from folate deficiency was not observed. In CKD patients, hyperhomocysteinemia is more common than in the general population, and therefore the potential for adverse effects from folate deficiency caused by bile acid sequestrants is potentially greater. Taken together, these considerations suggest that bile acid resins should be used with caution in children, and close monitoring for adverse effects such as vitamin deficiencies are warranted.

Currently, atorvastatin is the only USFDA-approved statin for children, and it is approved for post-pubertal males with familial hypercholesterolemia. However, more recent data in boys with familial hypercholesterolemia suggest that lovastatin 10-40 mg can safely decrease LDL by 21 % to 36%. Similar results were reported with pravastatin 5-20 mg.

Additional data on long-term safety, especially with respect to growth and nutrition, are needed before statins can be recommended for use in children of all ages.