

Persistent Renal Disease

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This chapter will outline principles for the nutritional management of children with both acute and chronic disturbances of renal function. A decline in glomerular filtration rate (GFR) is common to both disorders, which results in altered renal physiologic functions. The impairment of nitrogenous waste-product excretion and altered regulation of water, electrolyte, and acid-base homeostasis may challenge the provision of optimal nutrition. The discussion will begin with the nutritional management of acute renal failure (ARF), which is defined by a rapid decline in GFR. Given the extreme physiologic abnormalities that may accompany severe ARF, the nutritional care of the critically ill child will be emphasized. The discussion will then focus on the care of children with chronic kidney disease (CKD), who are at increased risk for malnutrition and growth impairment. Noting the shared issues faced by children with chronic renal insufficiency (CRI) and those on maintenance dialysis, the nutritional management of these children will be discussed together. The nutritional care of children who have received renal transplantations will then be reviewed. As the range of clinical manifestations of both acute and chronic renal failure is broad, the need for individualized nutritional management is emphasized throughout.

ESTIMATION OF GFR

GFR is equal to the sum of the filtration rates of all functioning nephrons and reflects functioning renal mass. Estimation of GFR allows clinicians to determine the severity and course of both acute and chronic disturbances of renal function and permits anticipation of necessary changes in therapy, including adjustments of nutritional support. The “gold standard” for measurement of GFR is an inulin clearance. Despite being accurate, performance of an inulin clearance is cumbersome and rarely employed in routine clinical practice. Alternatively, creatinine clearance based on a timed urine collection is readily available. However, the collection itself is inconvenient, prone to error, and impractical in children who are not toilet trained.

Estimation of GFR based on serum creatinine is both convenient and easy to perform. The accuracy of this estimation in pediatric patients can be

improved by using predictive equations that take into account the patient’s height, age, and gender. Recent guidelines provided by the National Kidney Foundation (NKF) recommend estimation of GFR from predictive equations,¹ and the Schwartz formula has gained widespread clinical use in North America (Table 1).^{2,3,4} Given the tubular secretion of creatinine, the Schwartz formula tends to overestimate GFR, and this overestimation increases with decreasing GFR.^{5,6} If an exact measurement of GFR is necessary, this can be determined by an inulin clearance or the clearance of other filtration markers such as radioactive and nonradioactive iothalamate, iothexol, ⁵¹Cr-ethylenediaminetetra-acetic acid (EDTA), and Tc 99m-diethylenetriaminepentaacetic acid (DTPA). However, using predictive formulas such as the Schwartz calculation is usually sufficient in general practice.

ACUTE RENAL FAILURE

ARF is defined by a rapid deterioration in GFR resulting in impairment of nitrogenous waste-product excretion. Depending on the severity of the insult, disturbances in waste excretion may be accompanied by impairment of acid–base homeostasis and loss of water and electrolyte regulation. In mild cases, nonoliguric ARF may be asymptomatic and only be detected when serum laboratory studies are performed. When severe, oliguric ARF may result in significant derangements of electrolyte and volume balance and necessitate the initiation of renal replacement therapy.

The etiology of ARF appears to be changing with advancement of medical and surgical practice, and this trend is most apparent in tertiary care centers. In referral centers, ARF due to primary renal disease is now less frequent than failure secondary to ischemia, drug toxicity, or sepsis in children. This was illustrated in a retrospective study from a large pediatric tertiary center, which reviewed the course of 254 episodes of ARF in 248 children during the period of January 1998 and June 2001.⁷ Approximately two-thirds of these children had underlying comorbid conditions. Only 7% of cases of ARF were due to primary renal disease, and the most common causes of ARF were renal ischemia (21%), nephrotoxic agents (16%), and sepsis (11%). As in adults, the reported mortality for children with ARF is high, reaching 30 to 40% and is greatest for those who require dialysis.^{8–11} Preexisting or hospital-acquired malnutrition has been identified as a contributing factor to the poor outcome of severe ARF,¹² and therefore providing adequate nutrition should be viewed as a crucial element in the therapeutic effort.

To provide nutritional support necessitates the provision of volume, either in the form of enteral feeds, intravenous nutrition, or a combination of both. If ARF is accompanied by anuria or oligoanuria (urine flow <0.5 to 1 mL/kg/h), nutrition will be limited or volume status will be aggravated unless renal replacement therapy is initiated. The modality of renal replacement therapy is chosen based on the clinical status of the patient and the expertise of the center. Options for renal replacement therapy include peritoneal dialysis (PD) and hemodialysis, and hemodialysis may be performed on an intermittent or continuous basis. For hemodynamically stable patients with ARF, intermittent hemodialysis is typically performed daily for 2 to 4 hours, depending on the size of the patient. During the several-hour treatment, ultrafiltration of the daily fluid requirement in addition to any other desired fluid removal is attempted as hemodynamically tolerated. If the patient is hemodynamically unstable, continuous renal replacement therapy (CRRT) allows for gradual ultrafiltration of fluid and is the modality of choice in such patients. Two commonly used modalities of CRRT are continuous venovenous hemodiafiltration (CVVHD) and continuous

Table 1 Estimation of GFR by the Schwartz Formula

$C_{cr} = k \times L/S_{cr}$
C_{cr} = creatinine clearance in mL/min/1.73 m ²
K = proportionality constant
L = length (cm)
S_{cr} = serum creatinine (mg/dL)
k values:
– Full-term babies during first year of life = 0.45
– Children greater than 1 yr and adolescent girls = 0.55
– Adolescent boys = 0.7

Adapted from references 2–4.

venovenous hemofiltration (CVVH). CVVHD uses primarily diffusive with added convective clearance, whereas CVVH uses solely convective clearance.

ARF: Energy Metabolism and Requirements

Careful assessment of energy requirements in children with ARF is essential. Inadequate caloric provision will result in poor protein retention, and excessive nutrition increases the risk for metabolic derangement and fluid excess. Total energy requirements include resting energy expenditure, energy needed for physical activity, and diet-induced thermogenesis. In patients with uncomplicated ARF, energy expenditure has been shown to be comparable to healthy subjects as measured by indirect calorimetry.¹³ ARF associated with sepsis or multiorgan dysfunction results in increased energy expenditure, and the increase in expenditure is believed to be proportionate to the underlying process leading to the critical illness.¹⁴ One study of critically ill adult patients compared the energy expenditure of patients who required dialysis for severe ARF to those who had normal or only moderately impaired renal function. All of the patients demonstrated increased energy expenditure due to their critical illness, though there was significant individual variation. The measured energy expenditure was greater for those who required only supportive measures when compared to those who required dialysis with average hypermetabolism measured at 42% and 28%, respectively. It was proposed that ARF reduced energy demand secondary to diminished renal metabolic activity.¹⁵

Given the significant clinical variability, predicting the energy requirements of critically ill patients remains a great challenge. The use of indirect calorimetry allows nutrition to be tailored to the needs of the individual patient and is the preferred method when available. When assessment by indirect calorimetry is not possible, energy expenditure can be estimated by one of the calculations for predicting energy requirements. The reader is referred to Chapter 11 for further reading regarding the use and limitations of these calculations.

The general recommendation for adult patients with ARF is that energy provided be tailored to the individual patient and not exceed 130% of the patient's resting energy expenditure.^{13,16–18} Pediatric data and guidelines for energy requirements in ARF are lacking, and assessment should address individual needs. Pediatric patients who are relatively well and not oliguric are unlikely to have increased energy requirements, and those who are critically ill will have increased expenditures. A group of critically ill pediatric patients on CRRT were provided calories 20 to 30% above their resting energy expenditures based on indirect calorimetry.¹⁴ Despite providing this nutritional care, positive nitrogen balance was often not met. For practical purposes, it is reasonable to start at the recommended dietary caloric intake for an aged-matched healthy child and

adjust as clinically indicated based on predictive equations or indirect calorimetry. Nutrition regimens should be modified to account for obligatory caloric delivery when dextrose containing intravenous fluids and dextrose containing dialysate solutions are used.

Hyperglycemia is not uncommon in critically ill patients with ARF. The potential for altered carbohydrate metabolism must be considered given that standard nutrition provides the majority of calories from dextrose, and patients on dialysis are delivered additional dextrose from dialysate. Hyperglycemia is a consequence of both accelerated hepatic gluconeogenesis and insulin resistance. Increased hepatic gluconeogenesis results from conversion of amino acids released during protein catabolism.¹⁹ Additionally, the kidney plays a direct role in glucose homeostasis, which is regulated by insulin.²⁰ Critically ill patients with ARF may demonstrate insulin resistance as evidenced by higher blood glucose and insulin concentrations.^{21,22} During acute renal injury, insulin resistance may be more likely given the loss of the kidney as a major target organ for insulin action. The consequences of insulin resistance and hyperglycemia have been shown to be significant. Both were associated with increased mortality in critically ill adults with ARF.²² In addition, reports indicate that critically ill infants and children who demonstrated sustained hyperglycemia suffered a 3-fold increase in mortality over those with well-controlled glycemia.²³ By employing a strategy of strict glycemic control with intensive insulin therapy to maintain blood glucose level between 80 and 110 mg/dL, the morbidity and mortality among adult patients in a surgical intensive care unit were significantly reduced.²⁴ Given the association of hyperglycemia with increased complications and worse prognosis, efforts to maintain normoglycemia should be made.

ARF: Protein Metabolism and Requirements

ARF is a state of increased catabolism, which parallels the severity of the underlying illness. During metabolic stress, counterregulatory hormones and cytokines are produced with subsequent release of large amounts of glucose, fatty acids, and amino acids from the body's stores. The catabolism of skeletal muscle allows for the generation of glucose, which is the preferred substrate for the brain, red blood cells, and renal medulla. This stress response is an effective short-term adaptation, though a prolonged response is maladaptive and can result in reduction of lean body mass.

Studies evaluating critically ill adults with ARF have reported high protein catabolic rates of 1.4 to 1.8 g/kg/d.^{18,25,26} Virtually all nitrogen arising from amino acids liberated during protein degradation is converted to urea, and the extent of protein catabolism may be assessed by calculating urea nitrogen appearance (UNA). In dialysis patients, UNA equals the sum of the urea in the dialysis ultrafiltrate, urine, and the change

in the body nitrogen pool. The UNA was studied in a group of critically ill children with anuric ARF maintained CRRT and measured to be >180 mg/kg/d.²⁷ This compares to a mean UNA of 103 mg/kg/d in well children on stable PD.²⁸ Increased protein catabolic rate was confirmed in a subsequent report of critically ill pediatric patients on CVVH and CVVHD with a mean UNA of 291 and 245 mg/kg/d, respectively. Nitrogen balance, defined as the difference between nitrogen intake and UNA, was often negative in these patients despite the provision of 1.5 g/kg/d of protein.¹⁴

If the care of a patient with ARF requires dialysis, the modality of dialysis must be considered when determining protein requirements. Hemodialysis leads to nitrogen loss, as amino acids and small peptides are filtered across the dialysis membrane.^{29,30} During continuous dialysis, there will be continuous nitrogen loss. A study to compare amino acid losses between CVVHD and CVVH in children was undertaken by Maxvold and colleagues.¹⁴ CVVH provides clearance solely by convection, as compared to clearance by CVVHD, which is primarily diffusive. With the exception of glutamic acid, individual free amino acid clearances were greater on CVVH than on CVVHD, though over the 48-hour period of the study, there was no significant difference in daily loss of amino acid when comparing the two modalities. Amino acid losses by dialysis clearance represented 12% and 11% of daily protein intake on CVVH and CVVHD, respectively. PD can result in significant protein losses through the dialysis effluent, and the degree of protein loss varies inversely with the body surface area of the child. Peritoneal protein loss when assessed in children on chronic PD was highest in infants (277 ± 22 mg/kg/d) and lowest in children who were above 50 kg (91 ± 15 mg/kg/d).³¹

Currently, a few studies have attempted to define protein or amino acid requirements for adult patients with ARF, and no studies exist for pediatric patients. Protein requirements in children are dependent on age and severity of illness. A child with uncomplicated ARF (not critically ill) should be provided protein in the amount recommended for age with adjustment to provide ongoing needs. While protein intake is increased, electrolytes, acid-base balance, and uremia should be assessed daily. Protein requirements in children who are critically ill will be increased, though data specific to ARF are lacking. Protein should be provided based on recommendations for critically ill children and adjusted for individual needs. The American Society for Parental and Enteral Nutrition (ASPEN) has put forth recommendations for protein intake and estimated protein losses for children with ARF supported with dialysis (Table 2).³² Adjustment of protein intake should be made to maintain blood urea nitrogen (BUN) >40 mg/dL and <80 mg/dL, if clinically appropriate. Few studies are available that allow estimation of optimal protein to energy ratio in critically ill children, though provision of 10 to 20% of total energy as protein is often reasonable.

Table 2 Recommended Protein Intake and Estimated Protein Losses During Dialysis Therapy for Acute Renal Failure

Age (weight range)	RDI	Estimated PD Losses	Estimated HD Losses	Estimated CRRT Losses	Daily Protein Intake Goal
Infant age < 2 yr (≤ 10 kg)	1.6–2.2	2.0–4.0	0.5–1.0	2.0–3.0	2.0–6.0
Small child age 1–6 yr ($> 10 \leq 25$ kg)	1.0–1.2	2.0–3.0	0.5–1.0	2.0–3.0	1.0–3.0
Older child age 7–14 yr ($> 25 \leq 40$ kg)	0.8–1.2	1.0–2.0	0.5–1.0	2.0–3.0	1.0–2.0
Adolescent age 15–21 yr 0.8–1.0 (> 40)	0.8–1.2	1.0–2.0	0.5–1.0	2.0–3.0	1.0–2.0

Adapted from reference 32.
Values are expressed as grams of protein/kg/d.
CRRT = continuous renal replacement therapy; HD = hemodialysis; PD = peritoneal dialysis; RDI = recommended dietary intake for normal children.

ARF: Micronutrient Requirements

Trace-element requirements in ARF are not clearly defined. Most recommendations for requirements in ARF are extrapolated from data in patients with chronic renal failure. In addition, many of the findings regarding trace element metabolism in ARF may represent the effect of the acute phase response and not necessarily reflect specific effects induced by ARF. As trace elements have small molecular weights and critical illness results in altered protein binding, hemodialysis may alter trace element homeostasis. In vitro data have shown that trace elements are cleared during CVVH, including selenium, chromium, copper, and zinc.³³ The ultrafiltration rate, or rate of convective fluid removal, was a significant factor affecting clearance. However, the assessments of losses in patients on CRRT have been variable.^{34,35} Variations likely stem from differences in patient population, CRRT method, and assays employed. One study confirmed removal of copper, selenium, and zinc.³⁶ As selenium is cofactor for the antioxidant glutathione peroxidase enzymes, impaired defense against antioxidant stress is of concern. Further studies are needed to determine trace-element requirements in renal failure. For patients on parenteral nutrition (PN), standard supplements of trace elements should be provided.

Recommendations for vitamin supplementation during ARF are provided by the ASPEN guidelines.³² Additional water-soluble vitamins should be administered if the patient is on hemodialysis to replace expected losses. Supplementation with folate, B₁₂, pyridoxine, thiamine, and riboflavin is recommended. Vitamin C is metabolized to oxalate, which can accumulate in patients with CKD. Oxalate accumulation has not been adequately studied in ARF. Supplementation of vitamin C should not exceed the dietary reference intake (DRI) (see Appendix II, Table II-1). Fat-soluble vitamins may accumulate in CKD, as they are not removed with dialysis. Little data

regarding fat-soluble vitamins in ARF are available, though deficiencies, with the exception of vitamin K, have been reported.³⁷ ASPEN guidelines recommend supplementation of fat-soluble vitamins if the duration of ARF is limited (ie, <2 weeks).³²

ARF: Electrolyte Considerations

ARF predisposes the patient to electrolyte and acid-base disorders, including hyperkalemia, hyperphosphatemia, hypocalcemia, and acidosis. Full discussion of electrolyte physiology in the setting of normal and altered renal function is beyond the scope of this chapter. A limited discussion is provided to serve as a basis for nutritional planning.

Given the potential for life-threatening arrhythmias, hyperkalemia is a dreaded consequence of ARF. Potassium is the most abundant intracellular cation, with less than 2% of total body potassium present in the extracellular fluid. As potassium is primarily renally excreted, decreased GFR and renal tubular damage may result in significant hyperkalemia. In addition to decreased excretion, hyperkalemia may result from transcellular shift induced by acidosis and increased extracellular load secondary to enhanced cell turnover, hemolysis, and transfusion of red blood cells. Therefore, potassium should be withheld during evolving ARF until acceptable potassium homeostasis is assured. If significant hyperkalemia results (≥ 6.0 mEq/L), treatment with a potassium exchange resin (ie, sodium polystyrene sulfonate) should be considered. If dialysis is initiated, potassium clearance should be anticipated if the dialysate contains no or little potassium. While on CRRT, potassium will be cleared continuously. If clinically appropriate, potassium salts may be added to the dialysate (typically up to 3 mEq/L) to mitigate the tendency for hypokalemia.

Similar to hyperkalemia, hyperphosphatemia is a common complication of oliguric and anuric renal failure. Phosphorus is the major

intracellular anion with less than 1% present in the extracellular space. Serum phosphorus occurs in two forms, organic and inorganic. The inorganic fraction is the principal circulating form and routinely assayed for clinical use. When GFR is within the normal range and renal tubular function is intact, approximately 80 to 90% of serum inorganic phosphorus is filtered, and typically more than 80% of filtered phosphorus is reabsorbed. In ARF, hyperphosphatemia may cause hypocalcemia as a result of calcium-phosphate precipitation, which typically begins when the calcium \times phosphorus product is greater than 70. Treatment of hyperphosphatemia includes restricting phosphorus intake and administering oral phosphate binders with enteral feeds. If needed, nutritionally complete formulas designed for acute and chronic renal failure are available and have lower phosphorus content. These formulas include Similac PM 60/40 (Ross Products) for infants and Suplena (Abbott) for children and adults (see Appendix III, Table III-1). Calcium carbonate and calcium acetate are commonly used phosphorus binders and will provide supplemental calcium, which will be beneficial if hypocalcemia is present.

ARF: Routes of Nutrition

After estimating the nutritional needs of a child with ARF, the next challenge is to determine the appropriate route of nutrition. If allowable, enteral nutrition is the preferred method of support. Proposed benefits of enteral nutrition include intestinal trophism, reducing bacterial translocation, stimulation of the immune system, and cost effectiveness.^{38–41} Early initiation of enteral nutrition was shown to reduce septic complications in adult surgical patients when compared to PN⁴² and was well tolerated in critically ill pediatric patients.⁴³ A specific benefit of enteral feeds is the potential for providing concentrated nutrition, which minimizes fluid intake.

Though enteral feeds are preferred, they may not be tolerated in critically ill patients. The underlying illness and need for vasoactive medications may compromise gastrointestinal perfusion. An additional concern in the setting of ARF is the detrimental effect of uremia on gastrointestinal motility. However, nasogastric feeds were well tolerated when applied carefully to a population of adult patients with ARF without significant increase in major gastrointestinal complications.⁴⁴ To decrease the risk of aspiration and improve tolerance of feeds when gastric emptying is delayed, transpyloric feeds should be considered. When critically ill children with and without ARF were compared, continuous transpyloric feeds were associated with increased gastrointestinal complications, including abdominal distension and excessive gastric residue. However, transpyloric feeds were overall effective and well tolerated.^{45,46}

If enteral feeds are initiated, both standard formulas and formulas appropriate for decreased renal function are available. Feeds should be

initiated with hypo- or normocaloric formula at low rates of 0.5 to 1 mL/kg/h with gradual increase to normal caloric delivery for age over 36 to 48 hours as tolerated. Gastric residuals and abdominal exams should be monitored closely with advancement.⁴⁶ If the patient is volume restricted, the rate should be increased to the target volume and then gradually fortified using modular components to meet nutritional needs (Table 3). To optimize digestibility, similar proportions of fat, protein, and carbohydrate as in the base formula should be used. In patients on CRRT, amino acid and small peptide losses may challenge the ability to supply adequate protein enterally. If indicated, administration of 10% amino acids can be provided to achieve desired goals.⁴⁴

In critically ill patients with ARF, enteral feeds often cannot meet nutritional needs. PN combined with enteral support or total parental nutrition may be necessary. A balanced PN regimen usually provides 10 to 20% of total calories by amino acids, 50 to 60% of calories by dextrose, and 20 to 30% by lipid emulsion. Modification of PN should be performed based on amino acid losses and dextrose absorption from dialysis therapies. Electrolyte composition should be guided by regular assessment of the patient's laboratory studies.

CHRONIC KIDNEY DISEASE

CKD is defined as kidney damage based on persistent structural or functional abnormalities, which may be associated with reduced or normal GFR. In children, CKD arises more commonly from congenital than acquired renal disease. When reviewing registry data of children with CRI, the most common primary diseases were obstructive uropathy (21.6%), renal aplasia, hypoplasia, and dysplasia (17.6%), and reflux nephropathy (8.4%).

Focal segmental glomerulosclerosis, an acquired glomerulopathy, accounted for 8.7% of cases.⁴⁷

When kidney damage is significant, there is a progressive loss of functioning nephron mass leading to end-stage renal disease (ESRD). To avoid or delay this outcome, providing supportive measures to retard progression should be provided. Critical measures to be taken include treating hypertension and reducing proteinuria when proteinuria is significant. In 2002, the Kidney Disease Outcomes Quality Initiative (K/DOQI) of the NKF put forth definition criteria and a classification scheme defining the stages of CKD (Table 4). Given the importance of early detection and intervention, guidelines to facilitate the detection of kidney disease in children and adults were provided and have been summarized.^{1,48} When compared to adult onset CKD, persistent kidney disease during childhood poses unique challenges, including growth impairment. Despite advances in medical management, growth in children with CKD remains suboptimal.

Data regarding growth of children with CKD are provided by the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS). NAPRTCS is a research effort, which studies the clinical course and natural history of children with CRI (GFR <75 mL/min/1.73 m²), on maintenance dialysis, and after renal transplantation with the ultimate goal of improving care. Review of the registry reveals little change in the mean height standard deviation score (HtSDS) of children enrolled between 1994 and 2001. Analysis of data in 1996, 1998, and 2001, revealed a relatively static mean HtSDS of -1.5 (1,725 patients),⁴⁹ -1.4 (3,863 patients),⁵⁰ and -1.4 (4,666 patients),⁵¹ respectively. A recent analysis of the NAPRTCS registry reviewed the stature of children with CKD and included data submitted through January of 2004. Defining severe growth delay as HtSDS of less than -1.88, 36.9% of children were found to have severe

Table 4 Stages of Chronic Kidney Disease

Stage	Description	GFR (mL/min/1.73 m ²)
1	Kidney damage with normal or increased GFR	≥ 90
2	Kidney damage with mildly decreased GFR	60–89
3	Moderately decreased GFR	30–59
4	Severely decreased GFR	15–29
5	Kidney failure	< 15 (or dialysis)

Adapted from reference 1.

Chronic kidney disease is defined as either kidney damage or GFR < 60 mL/min/1.73 m² persisting for 3 months or more. Kidney damage is defined as pathologic abnormalities or makers of damage, including abnormalities in blood or urine tests or imaging studies.

growth impairment at entry. There was a strong correlation with worsening renal function and short stature at entry. The mean HtSDSs for children with creatinine clearance of 10 to 25 mL/min/1.73 m² and greater than 50 mL/min/1.73 m² were -1.92 and -0.89, respectively.⁵²

The youngest children with CKD comprise the most vulnerable population at risk for severe growth deficiency. In the healthy state, growth rate is rapid during the first 2 years of life. It is during this critical time that the most significant loss of height potential can occur. The European Study Group for nutritional treatment of chronic renal failure in childhood identified that infants with early onset chronic renal failure had already lost approximately 1 SD of height during fetal life and another standard deviation lost by the third postnatal month.⁵³ This finding was consistent with reported average birth length of -0.74 SDS in 12 infants with chronic renal failure.⁵⁴ Multivariate analysis of the NAPRTCS registry revealed that infants with congenital renal disease who entered with a low estimated GFR had the most severe growth attenuation.⁵²

Though the etiology of growth failure is multifactorial, inadequate nutrition will adversely affect growth outcome.^{55,56} In addition to impacting somatic growth, malnutrition is clearly associated with increased morbidity and mortality in children with CKD. Serum albumin has been identified as a surrogate marker for nutritional status, though levels may reflect factors such as inflammation, hemodilution, and glomerular loss. Due to nutritional concerns, the K/DOQI Nutritional Guidelines recommend including serum albumin as part of the routine nutritional assessment of maintenance dialysis patients.⁵⁷ In the adult population, hypoalbuminemia at dialysis initiation and during the maintenance of chronic dialysis has been shown to be predictive of future mortality.^{58,59,60} The same association of hypoalbuminemia with increased risk for mortality has been found in pediatric patients.⁶¹ When serum albumin was

Table 3 Nutrient Content of Selected Modular Products*

Modular Product (Manufacturer)	Energy (kcal)	Protein (g)	Fat (g)	Carb (g)	Na (mg)	K (mg)	P (mg)
Carbohydrate (per 100 g)							
-Moducal (Mead Johnson)	375	0	0	95	70	5	Trace
-Polycose (Ross Products)	380	0	0	95	110	10	12
Fat (per 100 mL)							
-Canola oil	813	0	92	0	0	0	0
-Microlipid (Mead Johnson)	449	0	51	0	0	0	0
Carbohydrate and fat (per 100 g)							
-Duocal (SHS International)	492	0	73	22	≤ 20	≤ 5	≤ 5
Protein (per 100 g)							
-Beneprotein (ReSource)	357	86	0	0	214	500	286

Adapted from reference 11.

Carb = carbohydrate; K = potassium; Na = sodium; P = phosphorus.

*For the most current nutrient content, see product labels.

analyzed in over 1,700 pediatric patients at initiation of dialysis, each -1 g/dL difference in albumin was associated with a 54% higher risk of death. This finding was independent of the causes of CKD and other potentially confounding variables. This study also found that HtSDS was inversely associated with mortality risk and consistent with previous findings of growth failure and mortality.^{62,63}

CKD: Spontaneous Nutritional Intake

Several studies have demonstrated altered spontaneous nutritional intake in children with CKD, underscoring the importance of nutritional counseling in the management of these children. An Italian study reviewed 4-day weighed dietary records from 50 children with creatinine clearance of 15 to 65 mL/min/1.73 m² and 93 healthy controls.⁶⁴ The mean energy intake was 76 to 88% of the recommended dietary allowance (RDA) in children with CKD compared with 90 to 93% in healthy subjects. Protein intake was also 33% lower in children with CKD with intake of 1.6 to 2.7 g/kg/d compared with 2.1 to 3.1 g/kg/d in healthy controls. Other studies have confirmed decreased caloric intake in children with CKD, though protein intake has been high. The energy intake of 15 children with moderate renal insufficiency in Spain was evaluated and expressed as percentages of international recommendations. Mean energy and protein intakes were 87% and 223%, respectively.⁶⁵ Foreman and colleagues assessed nutrient intake in children with CRI and found that the mean caloric and protein intake were 80% and 153% of the RDA, respectively.⁶⁶ The caloric intake decreased with increasing age, though the caloric intake was normal when factored by body weight. There was no relationship found between the degree of renal insufficiency and caloric or protein intake.⁶⁶ However, other studies have demonstrated decreased energy intake with increasing severity of renal insufficiency.^{65,67}

The etiology of decreased spontaneous energy intake in children with CKD is unclear, though altered cytokine levels are likely significant. The effect of inflammation and cytokines on appetite and cachexia in CKD has recently been reviewed.^{68,69} It has been suggested that the term malnutrition is misapplied in CKD, and cachexia more accurately describes the process.⁷⁰ Cachexia is typified by loss of body weight in which muscle mass is replaced by fatty tissue and is associated with declining serum proteins. Anorexia combined with increased metabolism of fat and lean mass leads to cachexia. Leptin is produced by adipocytes and exerts sustained inhibitory effect on food intake while increasing energy expenditure. Leptin is cleared from the circulation by glomerular filtration and then undergoes degradation in the renal tubules.⁷¹ Circulating concentrations of cytokines such as leptin, tumor necrosis factor- α , and interleukins 1 and 6 are elevated in CKD and correlate with the degree of cachexia.^{72,73} Further studies are

needed to elucidate the underlying mechanisms of inflammation-associated cachexia in CKD.

CKD: Supplemental Feedings

The difficulties associated with feeding infants and young children with CKD are well recognized and may result from refusal of feeds, gastroesophageal reflux (GER), and vomiting.⁷⁴ As nutritional intake may be suboptimal in children with CKD, the use of supplemental enteral feedings has been studied and recently reviewed.⁷⁰ Given that growth velocity is maximal in infancy and predominantly dependent on nutrition, most studies have focused on the younger child. An early study by Brewer noted improved growth in a group of infants and small children (<10 kg) on PD who received nasogastric feeds. The weight SDS (WtSDS) and HtSDS improved in 11 and 10 of 14 patients, respectively.⁷⁵ At Great Ormond Street Hospital for Children, nasogastric and gastric feeds were initiated in 35 children up to age 5 years with GFR < 26 mL/min/1.73 m². The aim of supplemental feedings was to provide at least 100% of estimated average requirement for energy and 100% of the reference nutrient intake for protein for height age. The benefit was most apparent in the 0 to 2-year age group ($n = 26$) with improved mean WtSDS from -3.1 at the initiation of feeds to -1.4 at 2 years. Improvement in HtSDS was also significant with mean Ht SDS -2.9 at initiation and -2.1 at two years.⁷⁶ A subsequent report from the same unit studied the growth outcome of 81 children who presented with chronic renal failure (GFR < 20 mL/min/1.73 m²) in the first 6 months of life. Supplemental enteral feeds were commenced in 81% of patients when growth became subnormal. The mean HtSDS was within the normal range at 1 year of age and continued to improve thereafter.⁷⁷ Other studies have supported improvement in growth with supplemental feeds.^{78,79,80}

In addition to ensuring sufficient energy and protein intake, the effect of providing supplemental sodium and water to young children with polyuric, salt-wasting forms of chronic renal failure was studied. It was proposed that these children experience growth delay due to chronic intravascular depletion and negative sodium balance, and that the provision of low-caloric density, high-volume, sodium-supplemented feeds would promote normal growth. The treatment group consisted of 24 children diagnosed with polyuric renal insufficiency (<65 mL/min/1.73 m²) in the first year of life and were compared to a historical population control and a literature control. The nutritional therapy prescribed consisted of formula diluted with water to a caloric density of 0.3 to 0.5 kcal/mL and supplemented with 2 to 4 mEq of sodium per 100 mL of formula. The average energy intake for the treatment group was 104 kcal/kg/d (102% RDA), and the average protein intake was 2.45 g/kg/d (153% RDA). None of the children received growth hormone (GH). The treatment group maintained their height SDS at 1 and 2 years, with a net gain of height SDS

of 0.15 during the 2 years. The change in height SDS by regression analysis was significantly greater in the treatment group than in the control groups.⁸¹

Though supplemental feeds resulted in improved growth in some studies, others have not demonstrated the same benefit. Several studies have shown stabilization of linear growth without significant catch-up growth.^{82,83} Abitbol and colleagues studied 12 infants with congenital renal insufficiency and provided controlled feeding regimens starting at 3 months of age. Six of these infants received supplemental nasogastric or gastric tube feedings. The average energy intake was 95% RDA with average protein intake of 141% RDA. The study revealed that the major height deficit was incurred during the first 6 months of life, as the length SDS fell from -0.7 at birth to approximately -1.9 at 6 months. There was no catch-up growth noted as indicated by the length SDS of -2.0 at 24 months.⁵⁴ The only multicenter experience comes from the NAPRTCS survey, which reviewed the impact of supplemental feedings on growth and mortality in children < 6 years of age at dialysis initiation. Questionnaires were completed on 137 patients, 70% of whom received supplemental feedings and outcome was compared to those who did not receive supplements. Significantly more children prior to 2 years of age were given supplemental feedings when compared to children initiating dialysis from 2 to 5 years ($\sim 80\%$ vs 41%). Despite supplemental feedings, there was no difference in height and weight, and height and weight SDS did not improve over time with supplementation. In addition, mortality was unaffected.⁸⁴

Though inadequate nutrition will negatively impact growth in children with CKD, the variable response to nutritional support highlights the complexity of growth impairment in these patients. Alterations in the GH/insulin-like growth factor-1 (IGF-1) axis independently affect growth in the uremic milieu. Although serum GH and IGF-1 levels are usually normal or high in growth-retarded children with CKD, uremic serum has high IGF-1-binding capacity which results in low IGF-1 bioactivity.⁸⁵ In conjunction with optimal medical and nutritional management, recombinant human growth hormone (rhGH) therapy significantly improves linear growth.⁸⁶⁻⁸⁸ Despite evidence of efficacy and safety, only 22.2% of growth-impaired children which entered into the NAPRTCS CRI registry were receiving rhGH at their 12-month visit.⁴⁷ Recommendations for evaluation and treatment of growth failure in children with CRI have been published and include recommendations for rhGH therapy.⁸⁹ Secondary hyperparathyroidism and chronic metabolic acidosis are additional factors that impair growth. To optimize the utilization of nutrition for growth and response to GH, appropriate correction of secondary hyperparathyroidism and metabolic acidosis is critical.

Supplemental feedings are an accepted standard of practice in the care of children with CKD who do not meet the RDA for energy and

protein. Studies thus far identify younger children as the group most likely to need this support, and the choice of nasogastric versus gastric feedings depends on the needs and comorbidities of the individual patient. Complications associated with nasogastric and gastrostomy feedings include emesis, exit-site infection, and leakage. Additional risks for patients on PD include peritonitis. It is prudent to provide supplementation in children who demonstrate inadequate intake or decline in growth, though prospective studies defining the optimal approach to nutritional supplementation are needed.

CKD: Assessment of Nutritional Status

The importance of nutritional status has been emphasized in numerous clinical practice guidelines for care of patients with CKD.^{57,90} Nutritional status is a complex concept, and no single measurement is comprehensive. Therefore a multistaged evaluation of body composition is necessary. Measurements of nutritional parameters are complicated in CKD given the potential for fluid overload and possible abnormalities in the distribution of fat and lean tissue. Children with chronic renal failure and after renal transplantation have been found to have discordant body composition with relatively high fat mass and low lean mass.⁹¹ Additionally, assessment methods recommended for children with CKD were developed in healthy children, and the validity may be limited in CKD. A comprehensive review has been published summarizing the methods recommended for nutritional assessment of children with CKD and details the advantages and disadvantages of these methods.⁹²

The most recently published *K/DOQI Clinical Practice Guideline for Nutrition in Chronic Renal Failure* addresses the protein-energy nutritional status for children receiving maintenance dialysis. The recommended measures include an assessment of dietary intake, serum albumin, and anthropometric measurements. In addition, K/DOQI guidelines recommend measurement of the protein equivalent of nitrogen appearance

(PNA) for children maintained on PD, which allows estimation of protein intake.⁵⁷ The measures and suggested frequency are summarized in Table 5. Reflecting growth challenges faced by the younger child, the frequency of measurement is increased in children <2 years. These guidelines outline the minimum frequency of assessment, and more frequent assessment may be appropriate and should be tailored to the individual patient. In particular, infants and children with comorbid conditions in addition to ESRD may need more frequent monitoring.

Though there is strong evidence that children with mild to moderate CRI are at risk of growth impairment,^{65,67,93,94} there are no formal guidelines available for pediatric patients with CRI prior to the onset of ESRD. In the absence of guidelines, it has been recommended that the same assessment for children with ESRD be undertaken in children with CRI, though the frequency of assessment is guided by the degree of insufficiency and should be individualized.⁹² Infants in particular are at high risk of malnutrition and may benefit monthly evaluation regardless of the degree of insufficiency.

Nutritional Management of CKD

The following will detail nutritional management and guidelines for children with CRI, on maintenance dialysis, and after renal transplantation. To avoid repetition, the dietary management of children with CRI and on maintenance dialysis will be discussed together. A separate discussion of the nutritional management of patients after renal transplantation will follow. Tables 6 and 7 outline nutrient recommendations for children with CRI and on maintenance dialysis, respectively. Modifications should be made based on individual response or clinical need, such as suboptimal growth or catabolic stress due to acute illness. In general, the use of chronological age is recommended for determining requirements. However, when chronological and height age are significantly different (ie, height <2%), basing requirements for energy and protein on height age

may be more appropriate to promote improved growth and “catch-up” growth.

To increase energy intake and improve compliance, dietary modifications for children are typically less restrictive than those prescribed to adults. Dietary guidelines for adults often recommend specific amounts of a restricted nutrient, such as a “2 g sodium diet.” In pediatrics, restrictions are imposed only when clinically indicated and usually take the form of a “low-nutrient X diet” with education on which foods are high or low in that nutrient. Clinical indications for restriction include hypertension and edema, which would warrant the recommendation for a low sodium diet. Guidance is provided to substitute or avoid that food. The specified amount of nutrients provided in Tables 6 and 7 can be used as a general references. Depending on the response to the diet, the restriction can be liberalized or tightened.

If available, the support of a renal dietician is indispensable in optimizing the dietary management of children with CKD. The modification of food and fluid intake proves to be a great challenge for many. Every child with CKD and appropriate family member or caretaker should receive nutrition counseling based on individual needs. In addition to addressing the specifics of the renal disease process, the education level and social influences of the family must be considered when counseling is provided. The dietary care plan requires ongoing modification based on the changes in the child’s age, nutritional status, renal function, treatment modality, and medication regimen. Depending on the disease time course, a renal dietician may support an individual through the various stages of renal insufficiency, maintenance dialysis, and renal transplantation. Families need continual guidance and support to establish and consistently enforce prescribed dietary guidelines. Nutritional specialists can ease the burden of restrictions and increase the likelihood of success by providing practical suggestions for modifying or replacing favorite foods or fluids.

NUTRITIONAL MANAGEMENT OF CRI AND MAINTENANCE DIALYSIS

CRI and Maintenance Dialysis: Energy Requirements

Energy requirements for children with CRI and on maintenance dialysis have been based on requirements for healthy children, as there is lack of evidence to suggest that these children have increased needs. Therefore, the initial prescribed energy intake for infants, children, and adolescents with CKD should be the DRI for chronologic age (see Appendix II, Table II-5). Adequate energy intake is not only critical to allow optimal growth but prevents the utilization of protein stores as an energy source. Energy-malnourished children may require additional energy to restore normal growth and allow “catch-up” growth if possible.

Table 5 Suggested Nutritional Parameters and Minimum Schedule of Measurements for Children on Dialysis

Parameter	Minimal Interval	
	Age < 2 yr	Age ≥ 2 yr
Length	Monthly	Not applicable
Standing height	Not applicable	3–4 mo
Head circumference	Monthly	3–4 mo until age 36 mo
Estimated dry weight	Monthly	3–4 mo
Weight/height index	Monthly	3–4 mo
Height SD score	3–4 mo	Monthly
Serum albumin	Monthly	Monthly
Skinfold thickness	No agreement	3–4 mo
Midarm anthropometric measures	3–4 mo	3–4 mo
Dietary interview	Monthly	3–4 mo
Urea kinetic modeling	3–4 mo	3–4 mo

Adapted from reference 57.
mo = months; SDS = standard deviation score.

Table 6 Daily Nutrient Recommendations for Children with Chronic Renal Insufficiency

Nutrient	Infant		Toddler	Child	Adolescent	
	0–6 mo	7–12 mo	1–2 yr	3–8 yr	9–13 yr	14–18 yr
Energy (kcal/kg/d)						
Boys	95	80–85	85–90	85–90	60–65	50–55
Girls	85–90	75	80–85	80–85	60	45
Protein (g/kg/d)	1.5	1.1–1.5	0.9–1.1	0.8–0.95	0.8–0.95	Boys: 0.75–0.85 Girls: 0.7–0.85
Sodium:	If clinically appropriate, no restriction necessary. If edema or HTN: no salt shaker and avoid salty foods (restrict to ~1–3 mEq/kg/d)					
Potassium	If hyperkalemia develops, avoid foods with high potassium content (restrict to ~1–3 mEq/kg/d)					
Calcium	100% of the DRI Monitor total calcium load, including calcium derived from phosphate binders					
Phosphorus	Consider low phosphorus formula if serum levels are elevated despite use of phosphate binders		≤400–600 mg/d when serum levels are elevated		≤600–800 mg/d when serum levels are elevated	
Vitamins	If needed, supplement to 100% of DRI. Supplement with Vitamin D metabolite if needed to prevent hyperparathyroidism and renal osteodystrophy.					
Minerals	If needed, supplement to 100% of DRI. Iron supplementation will be needed if receiving erythropoietin therapy.					

Adapted from reference 110.

Table 7 Daily Nutrient Recommendations for Children on Maintenance Dialysis

Nutrient	Infant		Toddler	Child		Adolescent	
	0–6 mo	7–12 mo	1–3 yr	4–6 yr	7–10 yr	11–14 yr	15–18 yr
Energy (kcal/kg/d)	110	100	105	90	70	Boys: 55 Girls: 50	Boys: 45 Girls: 40
Protein (g/kg/d)						Boys: 1.4 Girls: 1.4	Boys: 1.3 Girls: 1.2
HD Patients	2.6	2.0	1.6	1.6	1.4		
PD patients	2.9–3.0	2.3–2.4	1.9–2.0	1.9–2.0	1.7–1.8	Boys: 1.7–1.8 Girls: 1.7–1.8	Boys: 1.4–1.5 Girls: 1.4–1.5
Sodium	In general, no salt shaker and avoid salty foods. For infants and small children, sodium supplementation may be needed due to losses from dialysis.						
Potassium	Avoid foods with high potassium content (restrict to ~1–3 mEq/kg/d).						
Calcium	100% of the DRI.						
Phosphorus	Consider low phosphorus formula if serum levels are elevated despite use of phosphate binders.		≤400–600 mg/d		≤600–800 mg/d		
Vitamins	If needed, supplement to 100% DRI for thiamin, riboflavin, pyridoxine, folic acid, and vitamin B ₁₂ , and 100% RDA for vitamins A, C, E, and K. Supplement with vitamin D metabolites to prevent secondary hyperparathyroidism and renal osteodystrophy.						
Minerals	If needed, supplement to 100% of the DRI for copper and zinc. Iron supplements will be needed while on erythropoietin therapy.						

Adapted from reference 110.

DRI = daily recommended intake; RDA = recommended daily allowance.

Achieving energy goals for infants and toddlers can be challenging due to anorexia and GER, and supplemental feedings may be necessary to achieve intended goals. Oral supplementation is preferred, though tube feedings may be necessary. Tube feeds can be provided via nasogastric, gastrostomy, or gastrojejunostomy tubes and be infused by intermittent bolus or continuous infusion.^{95,96} To encourage daytime oral intake and provide oral stimulation, continuous overnight feeds are generally preferred. Infants and toddlers who have been supported with tube feedings may experience oral

feeding dysfunction and need the counseling of a multidisciplinary feeding team.^{97,98}

Management of CRI and maintenance dialysis may require volume restriction if urine output is low. Volume restriction is most problematic if intake of solid nutrition is low due to age or oral aversion. If volume restriction is indicated, fortification of feeds to increase caloric density will be necessary. Caloric density may be increased gradually by 2 to 4 kcal/oz increments up to 60 kcal/oz as needed,⁹⁹ and the tempo of fortification will depend on individual tolerance. Both breast

milk and commercial formulas may be fortified. It is not advisable to increase the energy density of formula by concentration alone due to the increased sodium, potassium, phosphorus, and overall renal solute load. Carbohydrate and fat modular products, or a combination of both, can be added to achieve the desired caloric density. See Table 3 for the nutrient content of selected modular products. Readily available oils such as canola, corn, or safflower may be used for fat supplementation. The benefit of fat modular products is the process of emulsification, which prevents

the fat from separating out of the formula during continuous feeds. When making a formula with increased energy density, an attempt should be made to preserve the proportionate distribution of energy from carbohydrate, protein, and fat as in the base formula.

For older children, minimizing the number of restrictions as allowable by metabolic balance will increase the likelihood of achieving energy goals. Individuals with poor appetites may respond to small, frequent meals and snacks. Energy can be added to foods by adding heart-healthy oils or margarines, creams, syrups, or carbohydrate modules. Low-calorie or calorie-free drinks should be restricted. If the child does not meet energy requirements, supplemental nutrition should be provided. As for infants, oral supplementation is preferred, though tube feedings may be required. Nonrenal pediatric feedings designed for children older than 1 year have relatively high phosphorus and potassium content, which may result in electrolyte disturbance. Nutritionally complete renal formulas designed to be energy dense, high or low in protein, and low in electrolytes including phosphorus may be given to children older than 1 year. Suplena (Ross Products) is designed for the predialyzed patient and Nepro (Abbott) is intended for patients on maintenance dialysis (see Appendix III, Table III-2). Serum magnesium should be monitored if used in younger children, as the magnesium content is higher in adult renal products than in infant or pediatric formulas.

Energy intake and requirement issues specific to PD include early satiety or anorexia due to the pressure exerted by the indwelling dialysate volume and the effect of glucose absorption.^{100,101} When calculating energy intake, intraperitoneal dialysate glucose absorption should also be considered. Approximately 7 to 10 kcal/kg/d are absorbed by children on CAPD.¹⁰² If the need for tube feeds is anticipated, placement of gastrostomy or gastrojejunostomy tubes should be performed well before initiating PD. Allowing sufficient time to heal will reduce technical challenges, such as leakage of dialysate at the site of tube placement.

Protein Requirements

Care for patients with CRI emphasizes supportive measures for the benefit of retarding disease progression. There has been concern that higher protein intake would induce intraglomerular hypertension and hyperfiltration injury and hasten progression of kidney disease. Given the finding that a low-protein diet was able to slow the deterioration of renal function in rodent studies,^{103,104} prospective clinical studies prescribing low-protein diets were conducted in both adults¹⁰⁵⁻¹⁰⁸ and children.¹⁰⁹ The results of prospective clinical studies in adults were contradictory. Overall the progression rate was not significantly influenced by protein restriction over a period of 2 to 3 years, though a low-protein diet postponed the development of uremic symptoms and start of dialysis for patients with advanced renal failure. In the pediatric study, a low-protein diet of 0.8 to 1.1 g/kg/d

was provided for 2 to 3 years. This diet did not affect the rate of decline in creatinine clearance or adversely affect growth.

Given the current lack of evidence that a low-protein diet provides renal protection, children with CRI should be prescribed protein intake according to the DRI (see Appendix II, Table II-4). Requirements are increased by significant proteinuria, catabolism due to intercurrent illness, and use of glucocorticoids. Inadequate protein intake will impact body composition with reduction of lean mass and limit growth. Even if protein intake exceeds recommended levels, protein malnutrition may occur if overall energy intake is low. Protein intake may exceed recommended levels if serum urea and phosphate remain acceptable. Goals in CRI should focus on avoiding excessive protein intake, which may exacerbate uremia or hyperphosphatemia. It has been advocated that approximately 60 to 70% of protein should be of high biological value,¹¹⁰ which will minimize urea production by reusing circulating nonessential amino acids for protein maintenance. Regardless, emphasis should be placed on palatability of the protein form to optimize intake. Modular protein products are available if needed (Table 3).

For children undergoing maintenance PD, protein intake must provide at least 100% DRI plus an allowance for replacement of transperitoneal losses of protein and amino acids. Transperitoneal protein losses demonstrate significant variability, and an inverse correlation between body surface area and peritoneal protein loss has been demonstrated. Infants were shown to have nearly 2-fold greater peritoneal protein losses per meter square body surface area than older children weighing more than 50 kg.³¹ In addition, transperitoneal protein losses were twice as great in patients requiring maintenance PD due to steroid-resistant nephrotic syndrome when compared to children without nephrotic syndrome.¹¹¹ Given the significant variability in losses, regular assessment of growth, serum albumin, and urea levels is essential to determine if adjustment in protein intake is necessary.

For children undergoing chronic hemodialysis, the K/DOQI recommends the RDA for age and an additional increment of 0.4 g/kg/d for dialysis protein losses to achieve positive nitrogen balance.⁵⁷ Future revisions to the K/DOQI nutrition guidelines will need to consider the newer DRI for protein intake (DRI). Regular assessment of predialysis urea levels may allow assessment of protein intake, though other clinical factors affecting BUN must be considered. A predialysis BUN greater than 70 to 80 mmol/L may indicate excessive protein intake. However inadequate dialysis, recirculation of blood, and increased catabolism will also increase the predialysis BUN. Alternatively, persistently low predialysis BUN of <20 mmol/L may indicate inadequate protein intake.

Vitamin and Micronutrient Requirement

Little is known about specific vitamin requirements in children with CKD, underscoring the need for

further study. It has been recommended that intake be the same as for normal children.⁷⁰ When intake is considerably less than recommended, vitamin supplementation is indicated. Children on dialysis have additional risk for vitamin deficiency due to losses of water-soluble vitamins through dialysis. The K/DOQI guidelines recommend that dietary intake should achieve 100% of the DRI for thiamin (B₁), riboflavin (B₂), pyridoxine (B₆), vitamin B₁₂, and folic acid. An intake of 100% RDA for vitamins A, C, E, and K, copper, and zinc is also recommended (see Appendix II, Tables II-1 and II-2).⁵⁷ When studied, the dietary intake of vitamins in children on PD was lower than the RDA, and supplementation resulted in intakes that exceeded recommended amounts.¹¹²⁻¹¹⁴ Routine assessment of dietary intake should be performed before providing supplements. If supplements are indicated, infants and small children may be given liquid or chewable multivitamin preparations and additional folic acid dosed for age. Older children and adults may be provided B complex vitamins containing folic acid, such as Nephrocaps (Fleming & Company) and NephroVite (R&D Laboratories, Inc.). Excessive amounts of vitamin A and vitamin C should be avoided. Excessive vitamin A can lead to hypercalcemia,¹¹⁵ anemia, and hyperlipidemia. Vitamin C is metabolized into oxalate, which is renally excreted. Excessive vitamin C may result in elevated oxalate levels and complications of retention.¹¹⁶

In CKD, the need for vitamin D supplementation should be assessed regularly. The most active form of vitamin D is 1,25-dihydroxycholecalciferol (1,25[OH]₂D₃), and the enzymatic step of 1 α -hydroxylation occurs in the kidney. With progressive renal insufficiency, secondary hyperparathyroidism and defective bone mineralization may ensue due to inadequate 1,25(OH)₂D₃ levels. Secondary hyperparathyroidism can begin as early as stage 2 CKD. An early study of renal osteodystrophy in 29 children with moderate to severe CRI found that PTH levels were elevated in all children with GFR < 45 mL/min/1.73 m². "Early" renal osteodystrophy characterized by elevated PTH but normal serum chemistries detected in one quarter of the patients.¹¹⁷

Recent guidelines recommend assessment of 25-cholecalciferol (25[OH]D₃) in CKD stages 2 to 4 and supplementation with vitamin D₂ (ergocalciferol) if the level is <30 ng/mL. In stage 5 CKD, supplementation with ergocalciferol will not be effective, as this cannot be converted to the active form. If indicated based on serum levels of PTH and vitamin D metabolites, supplementation with activated vitamin D should be provided. Calcitriol is commonly used, with recommended initiation doses in CKD stages 2 to 4 of 0.05 μ g every other day for infants <10 kg, 0.1 to 0.15 μ g/d for children 10 to 20 kg, and 0.25 μ g/d for children <20 kg. For children with CKD stage 5, recommended initial calcitriol dosing ranges from 0.0075 to 0.025 μ g/d given three times per week, depending on serum PTH level.¹¹⁸ If the child is on maintenance hemodialysis, intravenous calcitriol may be provided at dialysis sessions. Due to potent effect on intestinal calcium absorption,

calcitriol treatment can induce hypercalcemia and preclude its use at therapeutic doses. Newer vitamin D analogues have been developed which minimize intestinal calcium and phosphorus absorption while suppressing PTH levels as effectively as calcitriol.^{119,120} Currently available active vitamin D sterols with less hypercalcemic effect include paracalcitol and doxercalciferol, though only paracalcitol has been studied in children.^{121,122}

Adjustment of active vitamin D sterol dosing should be made to achieve target PTH levels for CKD stage. In CKD stage 5 (GFR <15 mL/min/1.73 m²), recommendations are to adjust supplementation to keep PTH levels 200 to 300 pmol/L.¹¹⁸ A potential risk of active vitamin D sterol therapy is subnormal bone formation. Excessive doses of calcitriol may suppress osteoblastic activity, and care should be taken to avoid excessive reduction in PTH levels, as this may be associated with adynamic bone disease.¹²³

Children with CKD are at risk for anemia secondary to erythropoietin deficiency and iron deficiency. The introduction of recombinant erythropoietin (rHuEPO) therapy in 1988 provided a highly effective treatment in correcting anemia associated with CKD.¹²⁴ Iron deficiency is the most common factor that limits the response to rHuEPO, and children on rHuEPO usually require large amounts of supplemental iron. For children on maintenance hemodialysis, it is strongly recommended that iron be given intravenously. For children who are predialysis or on maintenance PD, iron may be provided either orally or intravenously. Dosing of iron supplementation is guided by serum ferritin and transferrin saturation.¹²⁵

Hyperhomocysteinemia is associated with folate deficiency and has been identified as an independent risk factor for cardiovascular disease in adults with chronic renal disease.^{126,127} Hyperhomocysteinemia has also been found in children with CKD, though a clear relation to vascular disease remains to be seen.¹²⁸ When children with and without CKD were studied, plasma homocysteine levels were found to increase with deterioration of renal function. Hyperhomocysteinemia was found in 5.2% of controls, 35.7% of nondialyzed CKD, and 86.6% of children with ESRD on dialysis. Folate levels were also lower in patients than controls.¹²⁹ When children on PD and hemodialysis were provided folic acid supplementation of 2.5 mg daily, plasma homocysteine concentrations were significantly reduced.¹³⁰ Currently there is no standard for monitoring homocysteine levels in children with CKD. Guidelines recommend that dietary intake for folic acid should achieve 100% the RDI. If dietary intake of folic acid is inadequate, supplementation should be considered.

Electrolyte Disturbances

Electrolyte disturbances commonly seen in CKD include hyperphosphatemia, hypocalcemia, and hyperkalemia. Though serum levels of sodium are typically within normal range, the inability to maintain sodium homeostasis will have significant clinical effect. Kidney disease associated

with sodium retention may result in hypertension and edema. Alternatively, sodium losses from urine wasting in polyuric kidney disease or losses from dialysis effluent may require sodium supplementation to ensure normal serum concentration and adequate growth. Dietary restrictions of electrolytes may pose significant challenges to the child and family and contribute to inadequate energy intake overall. Restrictions should be applied only when indicated.

Hyperphosphatemia in CKD can lead to significant morbidity due to metastatic calcification, secondary hyperparathyroidism, and renal osteodystrophy. More commonly seen when GFR falls <50 mL/min/1.73 m², hyperphosphatemia contributes to secondary hyperparathyroidism by lowering the serum ionized calcium, inhibiting the production of 1,25(OH)₂D₃, and directly stimulating PTH secretion. Therefore normal levels of serum phosphorus should be maintained to prevent renal osteodystrophy and poor growth. Guidelines recommend that dietary phosphorus intake be restricted to the DRI (see Appendix II, Table II-2) for age when the serum PTH is above the target range for the stage of CKD and the serum phosphorus is within the normal range for age. Phosphorus intake should be restricted further if both the serum PTH and phosphorus levels are elevated.¹¹⁸ In children who require phosphorus restriction, intake of milk, milk products, eggs, nuts, dried beans, peanut butter, whole grains, chocolate, and other high-phosphorus containing foods should be limited. Restriction of dietary phosphorus can challenge efforts to achieve adequate protein intake, as protein and phosphorus are often found in the same foods. Animal proteins have relatively favorable phosphorus to protein ratios when compared to the ratios in eggs, dairy products, legumes, and lentils. If supplementation with formula is indicated, children and adults may be provided Nepro (Ross Products) and Suplena (Ross Products), which are formulated for patients who are predialysis and on maintenance dialysis, respectively (see Appendix II, Table II-5).

In addition to limiting dietary phosphorus, intestinal absorption of phosphorus can be decreased with the use of phosphate binders. Options for phosphate binders include both calcium-based (calcium acetate, calcium carbonate) and noncalcium-, nonmetal-containing binders (sevelamer hydrochloride, lanthanum carbonate). Aluminum-containing binders are available, but long-term use has resulted in retention and toxicity.¹³¹⁻¹³³ First-line therapy for hyperphosphatemia in children is often a calcium-based binder, and calcium acetate results in less calcium absorption than calcium carbonate. However, children who receive calcium-based binders may experience hypercalcemia with associated risks of joint, vessel, and soft tissue metastatic calcification.¹³⁴ Sevelamer hydrochloride has been shown to be effective and safe when studied in pediatric populations and is associated with less hypercalcemia.¹³⁵⁻¹³⁷ Lanthanum carbonate has not been studied in children. The only phosphate binder readily available in a liquid or powdered

form is calcium carbonate, limiting the options for small children and infants. Recently, methods to prepare sevelamer hydrochloride oral suspension have been published.¹³⁸

In formula-fed infants with CRI or on maintenance dialysis, it is our center's practice to attempt feeds with standard formulas and use phosphate binders when indicated. Good Start Supreme (Nestle Clinical Nutrition) has a lower phosphorus content compared to other standard cow's milk-based formula. Should hyperphosphatemia develop and persist despite prescription of phosphate binders, a low-phosphorus formula such as Similac PM 60/40 (Ross Products) may be provided. The calcium content of Similac PM 60/40 is lower than that of standard infant formulas (see Appendix III, Table III-1). Therefore ensuring adequate calcium intake is critical to promote normal bone mineralization. When indicated, calcium supplementation should be provided. Recommended tolerable upper limit of calcium intake for children less than 1 year has not been determined. In children older than 1 year and adults, dietary and supplemental calcium intake should not exceed 2.5 g/d. The calcium content of phosphate binders should be included in the daily calcium intake.

As with the development of hyperphosphatemia, progressive decline in kidney function predisposes to hyperkalemia. However, hyperkalemia does not typically occur in early stages of CKD due to adaptive changes of individual nephrons as GFR declines. When hyperkalemia develops and persists, high potassium-containing foods should be limited. Unfortunately many high-postassium foods are favored by children and include potato products, tomato products, bananas, oranges, and chocolate. If necessary, potassium exchange resins, such as sodium polystyrene sulfonate can be prescribed. Formula-fed infants with significant CKD may require scheduled doses of sodium polystyrene sulfonate daily, though this may be met with increased spitting, aversion, sorbitol-induced diarrhea, and enteral tube obstruction. Methods to lower the potassium content of formula by pretreatment of the formula with sodium polystyrene sulfonate have been published. This resulted in $62 \pm 2.6\%$ reduction of potassium content, though the sodium content of the formula was disproportionately increased ($234 \pm 37\%$). The disproportionate effect was due, in part, to exchange for calcium and magnesium.¹³⁹ Increased sodium content was seen in a subsequent report of formula pretreatment with sodium polystyrene sulfonate.¹⁴⁰ Should similar methods be employed, the potential complications of increase sodium intake and electrolyte abnormalities should be monitored for.

Sodium balance is directly linked to volume status. Kidney disease characterized by oliguria or anuria typically requires sodium and fluid restrictions to avoid clinical signs of volume excess, such as hypertension and edema. Children at risk for sodium retention are directed to limit dietary intake, including salty snacks, processed luncheon meats, canned soups, and packaged entrees. Food from fast food restaurants should also be limited.

Prior to the initiation of maintenance dialysis, diuretics may be used to improve sodium balance. After the initiation of maintenance dialysis, children continue to limit sodium intake, especially if hypertension is present. Infants on PD may require sodium supplementation due to sodium losses during dialysis coupled with the relatively low sodium concentration found in formula. To avoid hyponatremia and ensure adequate extracellular volume, sodium supplements may be needed (ie, 3 to 5 mEq/kg/d) with close monitoring of electrolytes, volume balance, and growth.¹⁴¹

NUTRITIONAL MANAGEMENT AFTER RENAL TRANSPLANTATION

Renal transplantation is recognized as the preferred treatment for children with Stage 5 CKD, as restoration of normal renal physiologic function can greatly improve the child's quality of life. If the renal allograft functions well, normalization of fluid and dietary intake is allowed. Children often have improvement in appetite after transplantation, though immunosuppressive drugs may cause nausea, vomiting, constipation, diarrhea, or anorexia. These symptoms are typically treated symptomatically. The following section will discuss growth and metabolic disorders after renal transplantation. General guidelines for nutritional management will follow. If the renal allograft has decreased function, principles of nutritional care for children with chronic renal insufficiency should be applied.

Growth After Kidney Transplantation

Though growth typically improves after transplantation, many children demonstrate suboptimal growth overall.¹⁴²⁻¹⁴⁴ During the first years following successful renal transplantation, infants and younger children may display "catch-up" growth; however accelerated growth is often not maintained thereafter. In older children catch-up growth is generally not observed and targeted final adult height is not achieved. Impairment of growth is multifactorial and includes corticosteroid use and decreased renal function. With each 1 mg/dL increase in serum creatinine, a 0.17 decrease in height SDS was observed.¹⁴² To date, strong effort is being made to introduce steroid-sparing regimens utilizing early dose reduction, withdrawal, or avoidance of steroids.^{145,146} If growth is poor, initiation of GH should be considered, weighing the potential benefits of improved linear growth with stimulatory effects upon leukocyte function.^{147,148} Analysis of the NAPRTCS database comparing growth and allograft function in transplant recipients would suggest that this therapy is effective and safe.¹⁴⁹ In addition to poor linear growth, children may demonstrate discordant body composition with relatively low lean mass, high fat mass, and increased central adiposity after renal transplantation.⁹¹ Given the association of truncal obesity with increased cardiovascular morbidity in adults, this may suggest additional lifetime risks in these pediatric patients.

Hyperlipidemia After Renal Transplantation

Hyperlipidemia is a common and significant disorder after renal transplantation and occurs in up to 70% of adult recipients.^{150,151} A known cause of cardiovascular disease, hyperlipidemia leads to increased morbidity and mortality in adult transplant recipients, a population which is already burdened with numerous cardiovascular risks.¹⁵² Children also have a high incidence of lipid abnormalities after renal transplantation, reported in as many as 50% of children.¹⁵³ Though well documented in adults, the cardiovascular effects of hyperlipidemia in children are not currently known.^{154,155} In addition to potential cardiovascular risks, there is growing concern that hyperlipidemia may promote allograft injury with increased risk of chronic transplant nephropathy and graft failure.^{156,157}

Known risk factors for hyperlipidemia in adult renal transplant recipients include renal dysfunction, hypoalbuminemia, pretransplant hyperlipidemia, family history of hyperlipidemia, obesity, and specific diseases resulting in ESRD.¹⁵⁸ When risk factors for hypercholesterolemia or hypertriglyceridemia were studied in pediatric recipients, only pretransplant hyperlipidemia, increased years since transplantation, and reduced GFR correlated.¹⁵³ A subsequent study confirmed pretransplant hyperlipidemia to be a significant risk factor for the development of lipid abnormalities after transplantation.¹⁵⁹ Immunosuppressive medications have also been associated with dyslipidemias, in particular steroids,^{150,160} calcineurin inhibitors,^{161,162} and sirolimus.^{163,164} When comparing calcineurin inhibitors, the incidence of hyperlipidemia appears to be higher in patients receiving cyclosporine (CsA) than those receiving tacrolimus.^{151,165,166} A longitudinal study of pediatric renal transplant recipients demonstrated that the prevalence hyperlipidemia declined from 1 to 10 years posttransplant, and this was thought to be due to the reduction of immunosuppressive therapy. Elevated total cholesterol and total triglycerides declined from 70 to 35% and 46 to 15%, respectively.¹⁶⁷

Children who receive renal transplants are at increased risk for hyperlipidemia, and this risk will be lifelong given the current therapeutic options of dialysis or transplantation for treatment of ESRD. It is standard practice to monitor serum lipids after renal transplantation. Should hyperlipidemia develop, dietary modifications to reduce the intake of saturated fats should be employed. Delucci and colleagues offered the Step II American Heart Association diet (no more than 30% of total calories from fat, no more than 7% of calories from saturated fatty acids) to pediatric renal transplant patients with hyperlipidemia. Of 22 eligible patients, only 12 children were willing to participate. After 12 weeks of the diet, total cholesterol and LDL cholesterol declined modestly by 11% and 14%, respectively.¹⁶⁸ When the practical benefit of lifestyle change is limited, pharmacologic treatment should be considered. Lipid-lowering agents such as HMGCoA-reductase inhibitors, or "statins" have been used

in pediatric renal transplant recipients with success.^{159,169-171} However, these studies were small and larger controlled studies are needed to more clearly define efficacy and risk.

Diabetes Mellitus After Renal Transplantation

Hyperglycemia and posttransplant diabetes mellitus (PTDM) are well-known complications of solid-organ transplantation. The reported incidence of PTDM in pediatric renal transplant recipients ranges from 2 to 10%,¹⁷²⁻¹⁷⁴ and the risk for development of PTDM is associated with the immunosuppression regimen prescribed. Both corticosteroids and calcineurin inhibitors are known to affect carbohydrate metabolism. Corticosteroids alter carbohydrate metabolism by impairing peripheral utilization of glucose, elevating plasma glucagon concentration, and increasing gluconeogenesis.¹⁷⁵ CsA and tacrolimus have been shown to inhibit insulin secretion from beta cells.^{176,177} When tacrolimus became widely prescribed in adult renal transplantation, the rate of acute rejection decreased and renal allograft outcomes improved. However, there was an increased incidence of side effects, particularly of diabetes mellitus.^{165,178}

Initial pediatric studies and reports also demonstrated that tacrolimus-based immunosuppression regimens increased the risk for PTDM when compared with CsA-based regimens.¹⁷⁹ The odds ratio for PTDM was 9.1 (95% CI 1.1 to 76.0, $p = .04$) for tacrolimus use at PTDM diagnosis compared to CsA.¹⁷³ However, as the use of tacrolimus has become more widespread, optimal dosing has targeted lower trough levels, and the incidence of PTDM has decreased. More recently, a large European multicenter study comparing the efficacy and safety of tacrolimus with microemulsion CsA found no difference in the incidence of PTDM (3% in tacrolimus and 2.2% in CsA).^{172,180} Other reported risk factors for PTDM in pediatric renal transplantation include family history of type 2 DM, hyperglycemia in the 2 weeks after transplantation, and African-American race.^{173,179} Increased weight or body mass index was not identified as a risk factor.

In 2001, NAPRTCS published a report of 36 children who developed PTDM after renal transplantation.¹⁷⁹ The majority of patients (63.6%) presented within the first 6 months of transplantation. The diagnosis was most frequently made by the detection of hyperglycemia on routine laboratory follow-up (64%). Three patients (9%) presented with diabetic ketoacidosis. The development of PTDM was a transient disorder in the majority, as less than one-third of patients remained on insulin therapy at follow-up. Another analysis of 16 children who developed PTDM noted that for patients who presented early after transplantation (mean 0.3 years), the disorder was more likely to be transient. Those who presented later (mean 2.7 years) were more likely to have persistent PTDM. The authors proposed that the transient

course reflects insulin resistance due to acute stress on beta-cell function and initial exposure to high doses of corticosteroids, and the persistent course reflects permanent beta-cell injury. They questioned as to whether permanent injury in some resulted from long-term exposure to tacrolimus or CsA.¹⁷³

Nutritional Management After Renal Transplantation

For children who have well-functioning renal allografts, macronutrient intake should be guided by recommendations for healthy children. Energy requirements and intake should generally match that for the normal population. However, if the immunosuppressive regimen includes corticosteroids, this may increase appetite and result in excessive energy intake. Up to 12% of transplanted children become obese,¹⁸¹ and efforts to control total energy intake may be necessary. In addition, if hyperglycemia or PTDM develops, intake of simple carbohydrates should be adjusted. When considering protein requirements, some have recommended providing 1 to 1.5 times the DRI for the first 3 months after transplantation.¹¹⁰ This is due to the catabolic effect of surgery and glucocorticoid therapy, if steroids are provided. Should the posttransplant course be relatively unremarkable, reducing protein intake to the DRI after approximately 3 months is appropriate. With respect to fat intake, if hyperlipidemia develops, dietary modification of fat intake remains the first line of therapy. If patients have an insufficient result from dietary modification, pharmacologic intervention should be considered.

Recommendations for micronutrient intake after renal transplantation are also based on the recommended intake for healthy children, though there are some specific considerations. Multivitamin supplementation is generally not necessary after successful renal transplantation. When corticosteroids are used for immunosuppression, calcium intake should meet 100% of the DRI (see Appendix II, Table II-2). Supplementation may be necessary for those who are unable to achieve adequate dietary intake. Sodium restriction should be applied to patients who develop hypertension after transplantation. Hypertension after transplantation may result from corticosteroid and calcineurin inhibitor use and often improves or resolves as immunosuppressant doses are decreased to maintenance levels.

The most recent NAPRTCS data report that the 5-year graft survival for living donor and deceased donor renal transplantation are 85.1% and 76.9%, respectively.⁴⁷ Renal allograft function decreases over time due to many factors including acute rejection episodes, chronic rejection, and effects of nephrotoxic agents. If a child has a renal transplant with decreased function, nutritional therapy should be based on guidelines for nutrition in the setting of CRI.

SUMMARY

Acute and chronic disturbances of kidney function require a well-developed nutritional plan. Providing adequate and appropriate nutrition should be viewed as a critical element in the care of these children, as inadequate nutrition may negatively impact outcome, growth, and development. Alterations in renal function and clinical status during the disease course require repeated evaluations and adjustments of the nutritional care plan. If available, the assessment and counseling provided by a renal dietician is an indispensable resource for the child, caregivers, and clinicians.

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