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DOI: https://doi.org/10.1016/j.semnephrol.2023.151440

Understanding Similarities and Differences in CKD and Dialysis Care in Children and Adults

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Summary

In lower-income settings there is often a dearth of resources and nephrologists, especially pediatric nephrologists, and individual physicians often find themselves caring for patients with chronic kidney diseases and end-stage kidney failure across the age spectrum. The management of such patients in high-income settings is relatively protocolized and permits high-volume services to run efficiently. The basic principles of managing chronic kidney disease and providing dialysis are similar for adults and children, however, given the differences in body size, causes of kidney failure, nutrition, and growth between children and adults with kidney diseases, nephrologists must understand the relevance of these differences, and have an approach to providing quality and safe dialysis to each group. Prevention, early diagnosis, and early intervention with simple therapeutic and lifestyle interventions are achievable goals to manage symptoms, complications, and reduce progression, or avoid kidney failure in children and adults. These strategies currently are easier to implement in higher-resource settings with robust health systems. In many low-resource settings, kidney diseases are only first diagnosed at end stage, and resources to pay out of pocket for appropriate care are lacking. Many barriers therefore exist in these settings, where specialist nephrology personnel may be least accessible. To improve management of patients at all ages, we highlight differences and similarities, and provide practical guidance on the management of children and adults with chronic kidney disease and kidney failure. It is important that children are managed with a view to optimizing growth and well-being and maximizing future options (eg, maintaining vein health and optimizing cardiovascular risk), and that adults are managed with attention paid to quality of life and optimization of physical health.

Keywords: Chronic kidney disease, adult, child, dialysis, dissimilarities

Chronic kidney disease (CKD)[1] represents an irreversible reduction in kidney function characterized by deterioration of glomerular filtration rate[2] and altered fluid and electrolyte homeostasis, as well as endocrine kidney functions (secretion of erythropoietin, vitamin D, and so forth). CKD is defined according to Kidney Disease: Improving Global Outcomes 2012 in stages, depending on the glomerular filtration rate (GFR) and proteinuria.[3] Multiple formulae have been developed to estimate GFR to improve CKD diagnosis; each formula has strengths and weaknesses, and no formula is universally optimal. In adults, after recent recognition that systematic adjustment for race may have disadvantaged people of African origin, the most recent proposed formula (CKD-Epi 2021) has no race correction, but still does not perform optimally.[4,5] In children, the Schwartz formula, revised in 2009, is used commonly in clinical practice, although a newer formula, the CKiD U25 formula, has been suggested to be superior based on its derivation from multiple observations in more than 900 children with CKD, reduction in bias through use of age-dependent constants, and superior predictive performance compared with previous pediatric estimated GFR equations.[6,7] The impact of race also is being considered in children.[8] In younger infants and neonates, the estimation of GFR is more difficult owing to physiologic changes that occur during these developmental periods. The currently available GFR formulae do not include infants younger than 1 year old. There is additional interest in GFR formulas that do not rely on creatinine level (which may be abnormal in individuals with low muscle mass) and use cystatin C instead to yield better approximations of GFR in certain populations.[9]

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Financial disclosure and conflict of interest statements: none.

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0270-9295/ - see front matter

https://doi.org/10.1016/j.semnephrol.2023.151440

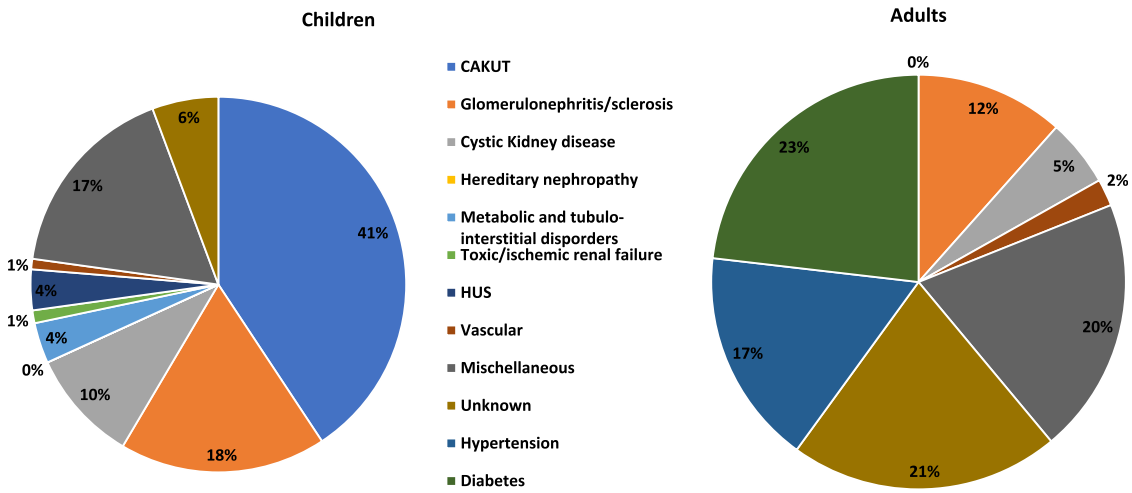

Figure 1. Causes of kidney failure European Renal Registry/European Society of Paediatric Nephrology Registries.[110] Abbreviations: CAKUT, congenital abnormalities of the urinary tract; HUS, Hemolytic Uremic Syndrome. Data were derived from http://www.espn-reg.org[111] and https://www.era-online.org/en/registry.[112]

BURDEN OF CHRONIC KIDENY DISEASE IN ADULTS AND CHILDREN

The CKD burden is increasing in lower-resource settings where an epidemiologic transition is occurring, largely driven by hypertension, diabetes, and obesity in adults (Fig. 1).[10] The burden of infectious diseases such as malaria and human immunodeficiency virus and the lasting impact of acute kidney injury (AKI) adds to the expansion of CKD in these areas. There also now is evidence of CKD hotspots observed most commonly in lower-resource settings (eg, Central America, Sri Lanka, and so forth), likely related to agricultural occupations and contaminated water supplies.[11] Globally, congenital abnormalities of the urinary tract (CAKUT) and other congenital or cystic diseases, followed by glomerulonephritis, are the leading causes of CKD and kidney failure (KF) in children (Fig. 1).[12-14] In neonates, in addition to CAKUT, permanent kidney damage and CKD can result from perinatal insults such as birth asphyxia, exposure to nephrotoxic medications, and sepsis. These neonatal comorbidities can lead to neonatal AKI, associated with risk of future CKD.[15,16]

CKD in children in lower-resource settings tends to be detected late, especially when prenatal ultrasound screening is inaccessible, with as many as 25% of children in these settings first presenting with KF (Table 1).[17] End-stage KF is much less common in children than in adults, with reported incidences of treated KF ranging from 7 to 11.4 per million population in children in the United States, Australia and New Zealand, and Europe compared with estimates of 40 to 570 per million population in adults in Ukraine and Mexico, respectively.[12,18] Data from countries without registries and numbers of untreated individuals are unknown. Given that in adults the prevalence of CKD is relatively consistent between regions at approximately 10%, the more than 10-fold variability in the (reported) incidence of treated KF is more a reflection of variability in access to dialysis and transplantation than true incidence.[19] Importantly, in lower-resource settings, adults reaching KF tend to be up to 2 decades younger than adults reaching KF in higher-income settings, resulting in the loss of potentially economically active individuals from both a family and a societal perspective.[20] Among children and adolescents, the prevalence of CKD may reach 1%, and it has been estimated that worldwide less than 10% of children who require kidney replacement therapy (KRT) receive it.[21] Indeed, a systematic review of access to KRT in children with KF in sub-Saharan Africa found that most children had no access to long-term dialysis or transplantation.[22] For example, for a child in Côte d'Ivoire to receive three hemodialysis (HD) sessions per week, it is necessary to pay 240,000 CFA francs (US $365), or 960,000 CFA francs (US $1,460) per month, which is unaffordable for most.[23] This results in many recorded deaths, 90% of which take place at home owing to abandonment of treatment.[23] Similarly high rates of loss to follow-up evaluation and low retention of children on KRT also reflect multiple socioeconomic barriers faced by families in India and elsewhere.[24,25] Such appalling statistics highlight the need for prevention, early detection, and access to quality treatment for CKD in adults and children everywhere.

CAPACITY FOR CKD CARE

CKD and KF are devastating chronic diseases in children, which have a broad impact on the well-being of the child and their environment.[26] The prime characteristic of childhood is growth and development. Their size,

Table 1. Most Common Causes of Chronic Kidney Disease in Adults and Children

	Children	Adults
Low-resource settings	CAKUT, infections (HIV, malaria), glomerular diseases, agricultural hotspots (contaminated water)	Hypertension, diabetes, glomerular diseases, agricultural hotspots (contaminated water)
High-resource settings	CAKUT, children with chronic diseases (eg, cardiac, oncology, and so forth)	Diabetes, hypertension, polycystic kidneys, glomerular diseases
Comments	More advanced disease at presentation in low-income settings More prenatal diagnoses in high-income settings Availability of genetics in high-income settings Ultrasound for kidney size percentiles: monitor kidney growth Increased risk of low birth weight, preterm birth, AKI, cardiac surgery, and so forth	Screening recommended for high-risk individuals (context-appropriate) Often a disease of the elderly Major impact of diabetes, hypertension Long term risk of CKD after AKI or acute-on-chronic kidney injury

Abbreviations: AKI, acute kidney injury; CAKUT, congenital anomalies of the kidneys and urinary tract; HIV, human immunodeficiency virus.

anatomy, and physiological needs (energetic and metabolic) require a therapeutic approach to CKD in children that is different from adults. In many parts of the world, pediatric nephrology services are scarce and children are managed by adult nephrologists or general pediatricians who may not be fully aware of all the differences in, and scope of, required kidney care. CKD and KF are also very challenging to live with for adults, although more support systems and treatment options tend to be available. Despite the postdoctoral training efforts provided by international societies and certain countries such as South Africa, Senegal, India, and China, the density of nephrologists and pediatric nephrologists in Africa, for example, is still very limited.[27,28] This article focuses on the differences and similarities in managing children and adults with advanced CKD and requiring KRT as a guide for those caring for patients across the age spectrum.

PRIORITIES IN CHRONIC KIDNEY DISEASE

CKD is associated with similar complications in children and adults, which include anemia, mineral bone disorders, metabolic acidosis, arterial hypertension, volume disturbances, and the psychosocial impact of living with a chronic illness. Drivers of poor outcome appear to be similar in higher- and low-resource countries, such as hypertension, which is associated with similar morbidity in children with CKD in the Middle East, Europe, and North America.[29] The special impact of CKD in children is the impact on growth and development, including psychosocial and neurocognitive development, and attention to optimization of growth and changing metabolic demands adds more complexity to the care of children with CKD.[3,30] Important for all patients with CKD, in addition to standard therapy directed at slowing progression, is access to disease-specific therapies, such as immunosuppression for many types of nephritis; therapies to delay cyst progression in polycystic kidney disease; supplements (bicarbonate, sodium, potassium, phosphorus, magnesium, and so forth) for individuals with tubular disorders, such as cystinosis, Lowe's syndrome, Dent's disease, and others; and disease-specific therapies such as cysteamine for cystinosis,[31] lumasiran for oxalosis,[32] and so forth. Some of these therapies remain inaccessible in low-resource settings.

Early Detection and Delaying Progression of CKD

Crucial to best efforts in delaying the progression of CKD is early detection and management. In adults, studies have suggested that screening for kidney disease in high-risk individuals with diabetes, high blood pressure, and cardiovascular disease (CVD) in higher-resource settings is cost effective[33,34] Other high-risk groups such as patients with a history of AKI, infectious diseases, preeclampsia, and a positive family history for cardiovascular and kidney diseases should not be overlooked, especially in high-prevalence regions.[35]

Among children, prenatal ultrasound can be very effective to detect CAKUT early. Standards for the routine use of prenatal ultrasound vary among regions and correlate with country income status. Those with prenatal concern for CAKUT on ultrasound should undergo postnatal testing, including ultrasound and consideration for evaluation by a nephrologist and/or a urologist. CAKUT is discussed further by Lange-Sperandio et al. in this issue. Infants born preterm (before 37 weeks of gestation) and/or with low birth weight (<2,500 g) or small for gestational age should be screened regularly for elevated blood pressure (BP) and CKD (with a minimum of urine albumin and BP measurements) throughout childhood and adulthood.[36-38] Recent studies have reported that evidence of kidney disease may be detected by age 2 years in surviving former extremely premature children.[39] Neonates, infants, and children with a history of AKI, or exposure to nephrotoxic medications or recurrent urinary tract infections, may need evaluation for evidence of permanent kidney damage within a few months.[40] Children with a strong family history of kidney disease also should be considered for screening as

Table 2. General CKD Management Strategies

	Children	Adults
Formulae to estimate eGFR	CKD U25 Schwarz (ethnicity debate in kids?)	CKD-Epi 2021 (flawed, ethnicity debate)
Volume management	Often need to increase fluids with CAKUT, tubular disorders	Often concomitant cardiac dysfunction High-dose diuretics
Blood pressure	Targets by weight, height	Systolic blood pressure < 120 mmHg
Management	Many medications not officially approved for children	May require multiple drugs, Lifestyle changes include healthy food, exercise, no smoking etc
	Lifestyle optimization	Lifestyle optimization
Proteinuria	Control BP, sugar, weight, excessive protein intake (smoking)	Control BP, sugar, weight, excessive protein intake, smoking
	ACEI (ARBs)*	ACEI, ARB
	SGLT2 inhibitors*	SGLT2 inhibitors
Anemia	Erythropoietin, iron	Erythropoietin, iron
	Often depend on transfusion in low-resource settings	Often depend on transfusion in low-resource settings
Nutrition	Infants often require PEG feedings; supplemental formulas	Nutritional supplements
Metabolic acidosis	Bicarbonate (liquid via PEG)	Bicarbonate
PTH	2-4 × ULN Normalization may be beneficial	KDIGO target 2-9 × ULN
Calcium	May need supplemental calcium Need adequate calcium for growth	Excessive calcium intake risk for CVD
Phosphorus	Diet, binders: very difficult in adolescents, processed foods	Diet, binders
Sodium	May require supplementation in tubular disorders	Generally restricted
Potassium	Diet	Diet, K-binding resins and medications
Cardiovascular risk	Risk factor control	Risk factor control Statins, aspirin as indicated
Vascular access planning	Big problem with blood drawing in children, damaging veins Dilemma of central venous port for blood draws may lead to future central vein stenosis	Should protect nondominant arm early on
Planning for transplantation	Pre-emptive living donor ideal Issues around using parents, grandparents? Prioritization on list Minimum size transplant center dependent Very limited availability in low-resource settings (may be only chance for survival)	Pre-emptive living donor ideal Limited by comorbidities Long waiting lists Geography may be limitation Very limited availability in low-resource settings
Comments	High value of multidisciplinary team, including teachers, social workers, psychologists, transplant specialists Caregiver burnout Impact on school, family Avoid AKI	High value multidisciplinary team, including vascular access coordinators, social workers, psychologists, transplant specialists Burnout Impact on work, family Avoid AKI
Online calculators (examples)	NKF (United States) https://www.kidney.org/professionals/kdoqi/gfr_calculator UKidney (United States) https://ukidney.com/nephrology-resources/egfr-calculator Kidney Health (Australia) https://kidney.org.au/health-professionals/egfr-calculator Columbia (United States, varied ethnicities) https://www.columbiamedicine.org/divisions/gharavi/calculators/calc_egfr.php NKF Pediatric (United States) https://www.kidney.org/professionals/kdoqi/gfr_calculatorped Ped(z): pediatric calculator https://pedz.de/de/pedz/main.html	

Abbreviations: ACE, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; ARB, angiotensin-receptor blocker; BP, blood pressure; CKD U25, CKiD Under 25 glomerular filtration rate estimating equation; CKD-Epi, Chronic Kidney Disease Epidemiology Collaboration equation; KDIGO, Kidney Disease: Improving Global Outcomes; NKF, National Kidney Foundation; PEG, percutaneous endoscopic gastrostomy; SGLT2, sodium-glucose cotransporter; ULN, upper limit of normal.

*Studies on the effects in children currently are lacking.

appropriate. The American Academy of Pediatrics recommends an annual measurement of BP in all children age 3 years and older and referral to a nephrologist if there is concern for hypertension.[41]

In terms of delaying the progression of CKD, therapeutic targets are similar for adults and children, including BP control, weight and lifestyle management, control of proteinuria, and use of renin-angiotensin system inhibitors for both adults and children with hypertension and/or proteinuria (Table 2).[3,42] In children, the use of renin-angiotensin system inhibitors such as angiotensin-convertase enzyme inhibitors is associated with desirable antiproteinuric effects and long-term preservation of kidney function.[43] In adults, strong data are accumulating to support use of sodium-glucose cotransporter inhibitors inhibitors in patients with CKD, and despite the current lack of studies, this also is being advocated for selected children.[44,45] BP control is a cornerstone of the management of CKD and is discussed in detail in the article by Karam et al in this issue. In children with renal dysplasia, obstructive uropathy, nephrogenic diabetes insipidus, or other tubulopathies, management of fluid balance is crucial. These children are at high risk of intravascular depletion (which can lead to AKI and rapid progression of CKD) owing to pre-existing polyuria, which results from tubular dysfunction and urinary concentration defects.[46] Consequently, affected infants and children might need a feeding tube to ensure adequate hydration and nutrition to avoid dehydration and growth failure.

In many higher-income settings, low GFR clinics have been established for adults, with multidisciplinary teams, including dieticians, nurses, vascular access teams, social workers, and pharmacists.[47,48] Management by such teams has been associated with better BP and diabetes control, as well as slowing the progression of advanced CKD to KF and delaying the need for dialysis or transplantation. Such teams rarely are available in lower-income settings as resources, and trained allied health workers often are lacking.[28] Children with CKD have even more complex needs, including ensuring psychosocial development, schooling, and growth. Multidisciplinary care therefore is critical to success for these children.[49] At all ages, maximization of urine output is an important goal in advanced CKD to facilitate volume management before and during dialysis. High doses of multiple diuretics may be required to achieve this. In children, even more so than in adults, effective urologic care can play a major role in ameliorating CKD, and CKD progression associated with CAKUT, by relieving urinary tract obstruction and preventing urinary tract infection and renal injury through surgery, bladder care with intermittent catheterization, and preventive antibiotics when appropriate.[50]

A major long-term cause of morbidity and mortality in children and adults with CKD is CVD, which is the leading cause of death in both children and adults with CKD.[51,52] This risk may not always be of immediate concern among pediatric nephrologists, but the antecedents of CVD begin early, and likely are amenable to interventions such as risk factor modification, lipid management, and so forth, which can prolong life in individuals with CKD.[42,53] Concerningly, in adults and children, adherence to clear guidelines for management of CKD and CVD risk is suboptimal.[54,55] Such studies should serve as calls to action in the pediatric and adult nephrology communities to identify barriers to delivery of quality care, and to address these. Although hypertension and persistent proteinuria have been recognized as independent risk factors for progression of CKD for some time, there is accumulating evidence that metabolic acidosis is not only a consequence of, but also may be a contributor to, CKD progression.[56] Multiple clinical trials have supported the link between treatment of acidosis and CKD progression in adults; well-designed clinical trials in children with CKD are not available yet, but the link between acidosis and CKD progression is clear.[57-59] Alkali treatment in children with CKD also can improve linear growth, as is discussed in more detail later in the section on growth and CKD.[59] Management strategies for children and adults with CKD are outlined in Table 2.[42]

Another long-term concern from an adult nephrologist's perspective regarding CKD in children is the frequency of venipunctures performed. Children's veins are small, and unless staff is very experienced, each blood draw may risk destroying veins needed for future dialysis arteriovenous (AV) access in later years. Similarly, placement of indwelling ports or catheters to facilitate repeated blood draws risks central vein thrombosis and stenosis, which may preclude vascular access in the future. How to best tackle this concern is not clear, beyond reducing the frequency of blood draws. Capillary blood draws (finger pricks) are an option in children with CKD, but increase the risk of spurious errors such as pseudohyperkalemia.

Anemia Management

Anemia is an almost universal complication of CKD and typically worsens as GFR declines. It often is multifactorial, owing to reduced erythropoietin production, iron deficiency, and generalized inflammation secondary to chronic uremia. Correction of anemia may be required as early as stage 3 CKD. Treatment of anemia usually requires iron supplementation (parenteral or oral) and erythropoietin administration (intravenous or subcutaneous route), with similar treatment strategies and targets in adults and children.[60] Erythropoietin dosing in both adults and children is initiated per body weight in kilograms and increased as required. The expense of erythropoietin can be a particular challenge in the care of adults,

children, and infants in lower-middle-income countries (LMICs). Intravenous iron often is required to maintain adequate iron stores before and during treatment with erythropoietin to support erythropoiesis. Similar to adults, many pediatric centers use longer-acting erythropoietin stimulating agents (ESA) therapies, especially in infants and younger children who typically are receiving peritoneal dialysis [PD], with the advantage of administration once every 7 to 10 days at home by the caregiver.

In Africa and other low-resource settings, patients reach KF without having been seen at a nephrology consultation.[17,61] As a result, almost 100% of patients are anemic.[62] In most African countries, less than 10% of HD patients are able to receive regular erythropoietin and intravenous iron, therefore oral iron often is used.[22] In addition, several erythropoietin-resistance factors coexist in these patients, whose admission to dialysis has not been planned (hyperparathyroidism, uncontrolled hypertension, and so forth). In a recent report from Africa, typical for most low-resource areas, more than 70% of KF patients required regular transfusion of whole blood.[63] A detailed cross-match of this transfused blood often is not performed. In children or adults in whom kidney transplantation is considered, the risk of developing alloimmunization with donor-specific antibodies in these settings is therefore very high.

CKD-Related Bone and Mineral Disorders

Untreated abnormalities of bone-mineral metabolism lead to CKD−mineral bone disease, which includes abnormalities of serum calcium/phosphorus, bone abnormalities (histologic changes of osteitis fibrosa, osteomalacia, and adynamic osteopathy, as well as rickets and bone deformities in growing children), and soft-tissue calcifications. Increased serum calcium, phosphorous, and/or parathyroid hormone (PTH) levels is associated with increased CKD−mineral bone disease and cardiovascular burden. Reducing dietary phosphate is a challenge for many patients with CKD or who are receiving dialysis. In children in particular, phosphate restriction also can affect the ability to provide sufficient dietary protein for growth. In LMICs when the diagnosis of CKD in infancy is delayed, the first sign of bone involvement may be frank rickets deformities.[64] In adults, given the frequent cardiovascular comorbidities, non−calcium containing phosphate binders are preferred.[65] In children, given the need for calcium for growth, calcium-containing binders frequently are used as long as there is no hypercalcemia because dietary phosphorus restriction limits calcium intake from foods.[66] Adequate caloric and protein intake should be ensured in all infants and growing children who are prescribed a renal diet, especially those who need a low-phosphorus diet to avoid protein-energy malnutrition. For small children who cannot or will not swallow tablets, liquid calcium-containing binders may be the only available options for phosphate-binding. Management of hyperparathyroidism is similar in adults and children (Table 2). The mainstays of treatment include optimization of serum calcium and phosphorus levels, maintaining adequate vitamin 25 hydroxy vitamin D (D-25 OH) stores, and use of calcitriol or active vitamin D analogues as needed.[67] Although there are no clear data on the optimal PTH range, in adults and children the published guidelines set target levels at two to nine times the upper limit of normal.[65] There is, however, some evidence in children that aiming for near-normal PTH levels is associated with better outcomes.[68] Calcimimetics or a parathyroidectomy may be required if hyperparathyroidism persists despite mainstay therapies.[69] Children on dialysis may require a higher dialysate calcium than adults to maintain normal serum calcium levels (Table 3). In lower-resource settings, the high cost of non−calcium phosphate binders (sevelamer, and so forth), calcitriol, vitamin D analogues, and calcimimetics often is prohibitive. According to some African authors, phosphate binders were prescribed in only 28.1% of cases in Senegal and in 30.4% of patients in Chad, with the minority receiving sevelamer (11.9%) and cinacalcet (7.4%).[22,70,71] Patients therefore are at risk of advanced hyperparathyroidism, especially if they also are underdialyzed for economic reasons. Dialysis vintage in children in high-income settings often is short because children are rapidly transplanted, therefore bone disease may be less of a consideration compared with adults, who often require longer periods of chronic dialysis and in whom fractures are common and the ability to comply with optimal treatment is unclear.[65] Management of risk factors (steroid therapy, hyperparathyroidism, immobility, and so forth) and early promotion of bone health (good nutrition, regular exercise, normal vitamin D-25 levels) are key endeavors for all individuals with CKD and KF.

Growth in Children

In children with chronic uremia, slowed growth is a frequent complication.[72] Growth delay is accentuated by early onset of CKD, protein-calorie malnutrition, certain primary diagnoses (eg, tubular disorders, loss of protein in nephrotic syndrome), and comorbid conditions such as genetic abnormalities, cardiac abnormalities, and medications such as steroids.[73] The slowed growth is exacerbated by the metabolic and fluid-electrolyte disorders (metabolic acidosis and hyponatremia), bone abnormalities secondary to hyperparathyroidism, disturbances in growth hormone (GH) secretion, and delayed puberty as consequences of CKD. Children with underlying renal tubular disorders need special attention to their fluid and electrolyte management. In addition to extra electrolytes and minerals, total fluid requirements typically are higher in those infants and children with polyuria. Close

Table 3. Hemodialysis

	Children	Adults
Equipment required	Size-appropriate dialyzers	Standard dialyzers, machines
	Dialyzer size to body surface area	
	Machines that allow blood flow rates <200 and dialysate flow <200	
	Pediatric catheters based on weight	Adult catheters, varying lengths
	Pediatric tubing, different sizes, neonatal/pediatric/adult	Adult tubing, standard size
	Accurate volumetric control: blood volume monitoring (CRIT-LINE) where available	
Starting dose		
Blood flow	3-5 mL/kg per minute	200-250 mL/min
Filter	Based on body size, smaller sizes available	May use smaller filter at start
Blood set	Based on extracorporeal volume	Standard set
	Volume <10% of total blood volume	
	Priming: in certain situations (small children, hemodynamically unstable)	
	Dialysate flow rate, typically at least twice the blood flow rate	
Frequency/time	Start with short duration, daily treatments	Start for 2.5 hours, then daily × 3-4 days, increasing to 4 hours by third or fourth session
Maintenance dose		
Blood flow	Usually 3-5 (can go up to 8 as needed) mL/kg per minute	300-400 mL/min
Filter	Per size	Larger: standard
	Low flux if water not pure	Low flux if water not pure
Blood set	Total extracorporeal blood volume <10% body weight	Standard
Duration/session	Typically 3-4 hours	4 h
Frequency/week	3 times/week	3 times/week
	Nocturnal/home HD offered in some HICs	Nocturnal/home HD offered in some HICs
	High-flux/hemodiafiltration used in some centers	High-flux/hemodiafiltration used in some centers
	Occasionally need 4-5 times/week for good control, growth	Short daily
	Occasionally daily (eg, primary hyperoxaluria)	Nocturnal
Adequacy measure	Clinical: including growth	Clinical
	(KT/V >1.2-1.4)	(KT/V >1.2-1.4)
K bath/target	Pre-HD <6 mmol/L	Pre-HD <6 mmol/L
Bicarb bath/target	Pre-HD >20 mmol/L	Pre-HD >20 mmol/L
Dry weight assessment*	Clinical (account for growth)	Clinical
	BNP	BNP
	Ultrasound: inferior vena cava diameter, lung water	Ultrasound: inferior vena cava diameter, lung water
	CRIT-LINE where available	CRIT-LINE in selected patients
Ideal interdialytic weight gain	10% Body weight	2 kg
	Diuretics continue if needed, if urine output	Diuretics continue if urine output
Maximum UF	Usually <10 mL/kg per hour (can go up to 13 mL/kg per hour in select situations)	As tolerated (maximum, 1,000 mL/h)
	If IDWG excessive, longer duration/more frequent short dialysis	
Access	Ideal: AVF > AVG > catheter; tempered by availability of resources/personnel	Ideal: AVF > AVG > catheter
	Catheter often used	
	Smallest catheter 7F for adequate flow	Catheter may be used in older, frail patients with limited life-expectancy
	CVC: more common in younger children, short time to transplant	Ultrasound mapping often in HICs
	AVF: minimal vein and artery dimensions Brachiocephalic/radiocephalic	
	Ultrasound mapping often in HICs	
Anticoagulation	LMWH, heparin: dose based on body weight	LMWH, heparin: standard dosing
Nutrition	Intradialytic nutrition used occasionally; protein restriction avoided	Fluid, potassium, phosphate restriction
	PEG feeds at night	
Comments	Disruptive for school, psychosocial development	High cost in low-resource settings, often dialyze less frequently
	Situational factors: high cost, out-of-pocket expenses, caregiver burden, lack of availability of pediatric dialysis in low-resource settings	Situational factors: high cost, out-of-pocket expenses for all components of care

Abbreviations: AVF, arteriovenous fistula; AVG, arteriovenous graft; BNP, brain natriuretic peptide; HD, hemodialysis; HIC, high-income country; IDWG, interdialytic weight gain; KT/V, clearance x time/volume; LMWH, low-molecular-weight heparin; PEG, percutaneous endoscopic gastrostomy; UF, ultrafiltration.

*Also applies to peritoneal dialysis.

monitoring of fluid supplementation and electrolyte/mineral balance remain crucial for maintenance of growth and normal development of those children. Uremia is also a state of GH and insulin-like growth factor-1 resistance, with poor growth despite normal serum GH and insulin-like growth factor-1 levels and evidence of suboptimal cellular responses to these growth factors mediated by uremia.[73] Slowed growth can lead to anxiety and depressive disorders in children. Growth hormone treatment with improved height is associated with an improved quality of life.[74] The optimization of growth is facilitated by a multidisciplinary approach that involves dieticians and other specialists (such as endocrinologists, psychologists, and social workers), which is relatively routine in high-income settings.[73] GH treatment is almost nonexistent in lower-income settings. Nutrition is a crucial component of CKD treatment and plays an important role in growth, This is discussed in detail in the accompanying article in this issue by Iygenar et al.

PREPARING FOR DIALYSIS

Much attention is being paid to the importance of shared decision making in choosing the optimal treatment strategy for KF (HD or PD dialysis, conservative kidney management, transplantation), especially in adults.[75] For most individuals in higher-resource settings the choice is a personal one; some choose HD because they prefer not to take on the responsibility of home dialysis, others choose PD or home HD because they wish to retain maximal independence, may live remotely, work full-time, and so forth. Among the elderly or those with many comorbidities, supportive care without dialysis is a reasonable alternative, at times with improved survival, and often with improved quality of life compared with dialysis.[75,76] In children, PD often is preferred because this usually is less intrusive in their daily lives, permits greater participation in school and other activities, may be associated with overall lower cardiovascular risks compared with HD, and can be done at night with automated PD (APD).[77,78] In countries where resources are limited, PD-first policies have been instituted to reduce overall costs and to increase the number of people who can be dialyzed.[79] Optimally, these discussions about dialysis are held before a patient reaches KF to permit time for decision making, but also time to prepare the patient in terms of vascular or peritoneal access, transplant workup, identification of living donors, and so forth.

In children, dialysis choice also is based on child age and weight at the start of dialysis. PD is the treatment of choice in infants and young children who weigh less than 8 kg.[49] In high-resource settings, newer HD machines designed for infants and younger children may be used while a PD catheter is placed surgically and the child waits to heal.[80] Around the world, particularly in the United States and Europe, nearly 80% of children with CKD begin KRT with dialysis.[81] If resources are available, transplantation should be the treatment of choice everywhere because it delivers the best outcomes.[82] Although preemptive transplantation is ideal from the standpoint of avoiding dialysis-associated morbidities and decreasing overall costs, it is performed in only 20% of children in high-income settings, and transplantation overall is rare in children in low-income settings.[81,83] Challenges to transplantation in low-income settings include cost; lack of infrastructure and necessary technical and immunologic expertise; alloimmunization of patients during dialysis because of repeated blood transfusions; inability to monitor drug levels, viral loads, and donor-specific antibodies in a timely manner; and a lack of knowledge, fear, or lack of legislation to permit kidney donation.[84-86] Transplantation in adults and children is discussed in detail in the accompanying article by Dechu et al.

In practice, in lower-income countries, treatment for CKD often is late, and may be initiated under difficult conditions in patients with decompensated uremia.[17,87] Patients are not prepared for dialysis both psychologically and medically. The majority of children and adults in lower income settings are diagnosed KF without having been seen by a specialist (pediatrician or nephrologist) and KRT is required urgently. If resources are available, either provided by the state, or, more commonly, paid out of pocket by the patient/family, patients may begin dialysis, usually HD, and in 90% of cases with a temporary catheter.[27] Counseling on kidney disease, dietary habits, and day-to-day management often only are begun during dialysis. Those who cannot afford dialysis often leave the hospital and likely die.[22] Globally, it is estimated that, at most, half of those who need dialysis actually receive it and are able to continue long term, and this may be worse for children.[21,88] In lower-resource settings, pediatric nephrology services are scarce and when dialysis is indicated, few children have access to it.[22,89,90] The pediatric population on dialysis in lower-resource settings consists mostly of adolescents who are dialyzed in adult units. In Senegal, for example, the average age of children receiving dialysis was 13.92 $\pm$ 3.67 years,[91] in Pakistan, similarly the mean age was 10.55 $\pm$ 3.2 years.[92] Families in India and Pakistan, similar to most LMICs, make many sacrifices to maintain children on dialysis, even where dialysis may be provided for free, because the related financial and social costs of moving, job losses, provision for other family members, loss of education for siblings, and so forth are very high.[24,92]

When dialysis is not available or not chosen, it is important that supportive care is provided to manage symptoms and optimize quality of life. Although this topic has received much attention in adults, more literature and shared expertise is emerging also for children.[93-95]

ADULTS AND CHILDREN ON HEMODIALYSIS

Basic differences between adult and pediatric HD are outlined in Table 3. For adults, the standard HD prescription is 4 hours three times per week, although a systematic review has shown that in settings where resources are stretched, twice-a-week dialysis may be tolerated by many patients.[96] Increasingly, incremental dialysis is being suggested for adults, especially at the start of dialysis.[97] This strategy requires close patient follow-up, and may improve quality of life and reduce the overall costs of dialysis. Prior guidelines have suggested AV access was the best option for all patients, however, especially in patients with reduced life expectancy, a shared decision may be reached to continue dialysis with a tunneled (internal jugular) venous catheter.[98] In lower-income settings such as sub-Saharan Africa and Asia, HD often is initiated under emergency conditions using femoral and jugular central venous catheters. If the first catheter is provided by the hospital in many countries, a second catheter is often at the patient's expense. Temporary catheters are used for long periods, leading to more infectious and thrombotic complications.[99] AV fistula surgery is not universally available owing to a shortage of trained surgeons and is expensive.[100] Management of fistula complications is also a real challenge under these circumstances. In high-resource settings, HD in infants and children is the second preferred KRT modality after PD. HD typically is performed when there is a contraindication to PD or when the psychosocial setting of the child prohibits PD. In adolescents, in whom psychosocial issues are heightened, and adherence is even more of a challenge, HD may be chosen to ensure adequacy of therapy. Although an AV fistula or conduit is the preferred choice in children and adolescents, other factors (small vessels for vascular access in smaller children, likely transplantation in a few months from a donor, and so forth) may lead to choice of a tunneled HD catheter for HD access.

For a child, an appropriate-size tunneled HD catheter typically is placed in the internal jugular vein (first choice), femoral vein (second choice), or subclavian vein (last choice). Catheter size is chosen based on patient weight, although small catheters often are not available in low-resource settings and adult catheters may be used to save a life. AV fistulae can be considered as the ultimate dialysis access goal for older children and adolescents, but a tunneled catheter usually is needed until an AV fistula is performed and ready to use. HD is associated with major limitations in children, mainly related to vascular access issues. The smallest HD catheter that can support adequate blood flow and clearance (usually at least 7F) cannot be placed successfully and securely in children who weigh less than 8 kg. The catheter size compared with the extracorporeal circuit volume makes HD less suitable for infants and younger children owing to the risk of hemodynamic instability and more frequent blood loss

In adults, dialysis blood sets and filter sizes are relatively standard, although some controversy exists regarding the value of hemodiafiltration compared with standard HD.[101] In children, the extracorporeal blood volume that is tolerated during dialysis is dependent on body weight and has a ceiling value. This optimally requires smaller pediatric dialyzers and blood tubing, which is not available everywhere, especially where dedicated pediatric dialysis facilities do not exist. Under such circumstances, to minimize precipitating hypovolemia at the start of dialysis in children when using larger dialyzers/blood sets, and/or because of severe anemia often present as a result of late presentation, the first connection to the HD machine often is performed by priming with isogroup isoRh whole blood, not leukocyte-free or platelet-free. This necessary compromise increases the risk of blood-related accidents, allo-immunization, and the occurrence of acute pulmonary edema during the first HD sessions because patients often already are volume overloaded. In all settings, low-molecular weight heparins are the most prescribed for anticoagulation during HD because they have the advantage of requiring a single injection rather than unfractionated heparin, which requires continuous infusion during the session.

Volume removal in adults who have cardiovascular instability, autonomic neuropathy from diabetes, or vascular disease may be challenging. Target weight gain ideally should not exceed 2 kg between sessions. This can be very challenging for some patients. Larger volume removal may necessitate longer sessions or additional sessions. In children, volume removal should not exceed 13 mL/kg per hour to avoid rapid fluid shifts, which, if happening repeatedly, can lead to myocardial stunning and worsen cardiovascular outcomes. More frequent dialysis may be required for volume control or at times in very large patients. Reimbursement for additional HD sessions in a week is challenging even when dialysis is covered by the health system and may be unaffordable if paid for out of pocket.

ADULTS AND CHILDREN ON PERITONEAL DIALYSIS

The basic differences between adult and pediatric PD are outlined in Table 4. A tunneled cuffed Tenckhoff catheter is required for PD, ideally placed days to weeks before PD is to be initiated, to permit healing of the surgical site and avoid leaks.[102] Catheters may be placed surgically in the operating room or at the bedside by radiologists or interventional nephrologists.[103] Outcomes appear similar, but waiting time, costs, and the break-in period of the catheter seem improved when experienced nephrologists place the catheters. Catheter exit sites

Table 4. Peritoneal Dialysis

	Children	Adults
Equipment required	Pediatric size Tenckhoff catheters: based on body size/weight Minilaparotomy/laparoscopic insertion Omentectomy typically performed	Tenckhoff catheter: standard size Minilaparotomy/laparoscopic insertion
	Exit site facing down/laterally Challenges with stomas, PEG tubes	Exit site facing down/laterally
	CAPD/pediatric APD sets/machines	CAPD/APD sets/machines
Starting dose	Ideally wait until catheter is healed: typically 2 weeks (if possible) If needed -> bedrest	Ideally wait until catheter is healed, if not -> bed rest
Fill volume	10-20 mL/kg May be difficult to instill small volumes in infant CAPD Unfractionated heparin often added to minimize clotting	500-1,000 mL Unfractionated heparin often added to minimize clotting (500 IU/L)
Number of exchanges (CAPD)	Minimum 3-4 Adjust to use whole bag (avoid waste)	Minimum 3-4 Icodextrin often used for long dwell
Number of exchanges (cycler)	4-5 in larger child/adolescent High number in infants/smaller children (12-15/day)	4-5
	Mixture of short cycles for urea/potassium clearance, long cycles for phosphate clearance	Cycle length adjusted for clearance, UF
Glucose concentration	As low as possible	As low as possible
Calcium concentration	High 1.75 mmol/L	Normal 1.25 mmol/L
Maintenance dose		
Fill volume	30-50 mL/kg or 1,100-1,400 mL/m^2 Measurement of intraperitoneal pressure controversial	2,000 mL (sometimes more)
Number of exchanges (CAPD)	4-5 in larger child/adolescent High number in infants/smaller children (12-15/day)	4-5
	Mix short and long exchanges for maximal use of bags, fluid control	Often with icodextrin for longer night dwell
Number of exchanges (cycler)	10-15 Last fill as required, small volume at least (to reduce catheter trauma)	4-6 Last fill often with icodextrin, day dwell
	Mixture of short cycles for urea/potassium clearance, long cycles for phosphate clearance	Cycle length adjusted for clearance, ultrafiltration Extra manual exchange during day sometimes needed
Glucose concentration	As low as possible	As low as possible
Calcium concentration	High 1.75 mmol/L	Normal 1.25 mmol/L
Adequacy measure	Clinical Peritoneal equilibration test younger children: more likely to be high transporters	Clinical Peritoneal equilibration test
	(Kt/V urea) Residual renal function/urine output	(Kt/V urea) Residual renal function/urine output
Nutrition	Optimize protein intake for growth Often need to account for PD protein losses with additional protein intake Phosphate restriction May require potassium supplementation	Monitor serum albumin level In some patients may need to account for PD protein losses Phosphate restriction May require potassium supplementation Fluid restriction
Comments	Ideally PD overnight, stop early enough in am so child can get to school on time In low-resource settings CAPD more often than APD Cost of therapy out of pocket Lack of facilities and disposables High caregiver burden	High likelihood of requiring daytime dwell In low-resource settings CAPD more often than APD Cost of therapy out of pocket Lack of facilities and disposables

Abbreviations: APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis; PD, peritoneal dialysis; PEG, percutaneous gastrostomy; UF, ultrafiltration.
*Assess dry weight as for hemodialysis.

should face laterally or downward in both adults and children to reduce the risk of exit site infections.[104] Challenges in children arise if the child also has a percutaneous feeding tube because this may limit the location of the exit site. Worldwide, morbidity and outcomes on PD are very much related to comorbidities in higher-income as well as lower-resource regions.[105] PD has been suggested as the dialysis modality of choice in lower-resource settings because it is presumed to be less expensive; this, however, is not universally the case. PD does require more effort from the patient/family and thus uptake of PD globally is far lower than HD in adults.[106] Acute starts on PD are possible and can be facilitated by use of acutely placed tunneled catheters and a well-planned and structured approach, with bed rest and low fill volumes for several days.[107] PD also can be initiated incrementally with fewer exchanges per day or lower fill volumes, which may be increased over time as needed.

PD can be performed as either continuous ambulatory peritoneal dialysis (CAPD) using a Y-set connection system or as automated peritoneal dialysis (APD). Advantages and disadvantages are highlighted in Table 4. At the very beginning of PD in children, the volumes of dialysate infused must be very small to avoid leaks, on the order of 5 to 10 mL/kg in newborns and 10 to 20 mL/kg in infants and older children. The increase in dialysate volume in small patients should be gradual until the typical full PD volume is reached according to the child's size (30-50 mL/kg or 1,100-1,400 mL/m^2).[108]

In adults, the starting prescription for CAPD is generally three to four exchanges of 2 liters per day. The CAPD bags are manufactured in 2 liter quantities because of this. Very large adults may require more than 2 liters, which is more easily achievable using the cycler because the bags are 5 liters. The starting prescription for APD is five to six cycles of 2 liters per night, with or without a daytime dwell. Standard lactate-based solutions containing 1.36%, 2.27%, and 3.86% dextrose are used. Icodextrin and amino acid−based solutions may be used in selected cases to manage fluid overload or malnutrition, but these significantly increase the cost. The dialysis prescription then is adjusted according to the patients' individual clinical status, peritoneal membrane clearance, and ultrafiltration characteristics.

In children, the number of exchanges during CAPD typically varies from three to five exchanges per day with an isotonic dialysate and the lowest dextrose content tolerated. A challenge is how to manage the exchanges without disrupting school attendance. As with many equipment and supply considerations, in LMICs simple supplies such as 1-liter PD bags or 500-mL PD bags for infants and toddlers often are difficult to acquire. Adult CAPD bags are 2 liters, therefore, in children for example, two rapid exchanges can be performed from a single bag in the morning and another bag in the evening, followed by longer dwells during the day and night (ie, four to six exchanges from two 2-liter PD bags). When a child needs more than five exchanges per day or in the event of loss of residual diuresis, recourse to APD is essential. APD exchanges are made using a cycler and with 10 to 15 nocturnal sessions over 8 to 12 hours every day, generally with a dry abdomen during the day. If necessary, the dose of dialysis can be increased by adding a last fill during the day. Cycle length can be varied to ensure small-molecule clearance and ultrafiltration (shorter dwells) and phosphate removal (longer dwells). Children tend to be high transporters and therefore in comparison with adults require more exchanges with shorter dwell times for full efficacy. This is best achieved using APD. Fewer exchanges with CAPD in children may be associated with significant volume overload. Close attention must be paid to serum sodium levels because of sodium sieving (with rapid exchanges) and/or sodium loss (with longer dwells), which occur more frequently in children

Adults usually are their own caregivers, children mostly rely on others who must be trained. PD requires good understanding and motivation from patients and caregivers alike, and experienced staff are critical to success. The glucose load from PD can contribute to weight gain in both adults and children. Abdominal fullness, however, also may reduce appetite and food intake, which may worsen growth and nutrition, especially in children. Children generally require a higher calcium dialysate than adults because of ongoing growth and a tendency to develop hypocalcemia. The main risk of PD is peritonitis, the risk of which increases with the number of times the catheter must be accessed in a day. In CAPD, the catheter is accessed before and after each exchange; in APD, the catheter is accessed only at the start and at the end of the session. Careful exit site care and hygiene are key. Young children may not understand the need to keep the catheter site clean and therefore require more vigilance to avoid infections. Children and adults with peritonitis may require more frequent exchanges and/or higher-glucose solutions to maintain ultrafiltration.[109] Patients and families must be well trained and retrained with each episode of peritonitis, as described elsewhere.[109]

PD worldwide remains the most commonly used modality of kidney replacement therapy in children. PD is especially well suited for children because this can be done in children of almost any size, at home and at night, leading to less disruption of school and other social activities, and permits greater intake of fluid and nutrition. Care must be taken with some activities such as swimming or exercise to avoid catheter injuries or infections.

CONSERVATIVE KIDNEY MANAGEMENT

conservative kidney management is a realistic option for anyone with end-stage kidney disease, but comes most

often into question among the frail and elderly. Such a decision should be arrived at after careful shared consideration of all therapeutic options.[75] In children, some programs do not believe in dialysis as a destination therapy for those who are not eligible for transplantation. In these cases, careful discussion with the family and supportive and palliative care are imperative.[95]

CONCLUSIONS

The burden of CKD is increasing globally. The holy grail would be to diagnose each individual early enough to implement therapeutic and lifestyle interventions that would interrupt or delay the progression to KF. This may be possible (but not yet achieved) in robust health systems, but in many lower-resource settings, adults and children with CKD remain undiagnosed until very late. In these regions there is often a dearth of nephrologists, especially pediatric nephrologists, and therefore individual physicians often find themselves caring for patients with CKD and KF across the age spectrum. The basic principles of managing CKD and providing dialysis are similar for adults and children, however, given the differences in body size, in leading causes of KF (CAKUT in children versus diabetes in adults), and in nutrition and growth, nephrologists must understand the relevance of these differences and have an approach to provide appropriate dialysis to each group. It is important that children are managed with a view to optimizing growth and well-being and maximizing future options (eg, maintaining vein health and optimizing cardiovascular risk), and that adults are managed with attention paid to quality of life and optimization of physical health.

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