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Chronic Kidney Disease in Children

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Overview

Practice Essentials

Chronic kidney disease (CKD) is characterized by an irreversible deterioration of renal function that gradually progresses to end-stage renal disease. During the past 2 decades, the incidence of CKD in children has steadily increased.[1]

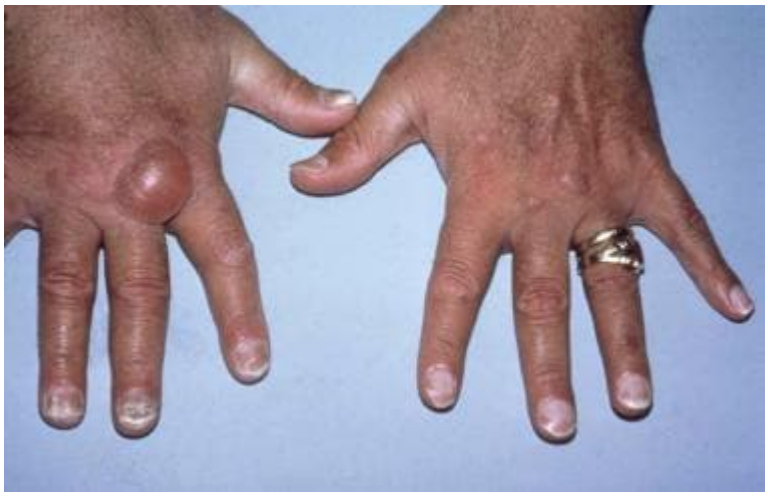
Signs and symptoms

CKD is asymptomatic in its earliest stages (stage I and stage II), although urinalysis findings or blood pressure may be abnormal. As CKD progresses to more advanced stages, signs and symptoms greatly increase. Polydipsia and nocturia (secondary to a reduced capacity to concentrate the urine) may be some of the earliest symptoms that suggest CKD in an otherwise healthy-looking child who has tubulointerstitial kidney disease.

The signs and symptoms in advanced CKD may include the following:

- Anemia
- Anorexia, nausea, vomiting
- Bone disease (termed osteodystrophy)
- Cardiovascular disease
- Hyperkalemia
- Hypertension
- Metabolic acidosis
- Volume overload

The image below illustrates several uremia-related cutaneous disorders.



Hands of a transfusion-dependent patient on long-term hemodialysis. Several uremia-related cutaneous disorders are visible. The pigmentary alteration results from retained urochromes and hemosiderin deposition. The large bullae are consistent with

either porphyria cutanea tarda or the bullous disease of dialysis. All nails show the distal brown-red and proximal white coloring of half-and-half nails.

See Presentation for more detail.

Diagnosis

Initial testing in a child with suspected CKD must include an examination of the urine and estimation of the glomerular filtration rate. Anemia is an important clinical finding in CKD, and a complete blood cell count is an important investigation both in the initial evaluation and the subsequent follow-up in affected children.

Imaging studies such as ultrasonography and radionuclide studies help in confirming the diagnosis of CKD and may also provide clues to its etiology.

See Workup for more detail.

Management

Treatment of chronic kidney disease should include the following:

- Specific therapy based on diagnosis
- Evaluation and management of reversible causes of renal dysfunction
- Prevention and treatment of complications of decreased kidney function (eg, anemia, bone disease, cardiovascular manifestations, hypertension, growth failure)
- Evaluation and management of comorbid conditions
- Slowing the loss of kidney function
- Preparation for kidney failure therapy
- Replacement of kidney function with dialysis and transplantation if signs and symptoms of uremia are present
- Management of complications

See Treatment for more detail.

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Background

Chronic kidney disease (CKD) and renal failure (RF) have been recognized as significant medical problems for most of the last 2 centuries and, until relatively recently, were uniformly fatal. Scientific and technologic improvements during the second half of the 20th century provided renal replacement therapy as a life-sustaining option for many individuals who otherwise may have died. The impact of these medical advancements has been remarkable.

Chronic kidney disease is characterized by an irreversible deterioration of renal function that gradually progresses to end-stage renal disease (ESRD). Chronic kidney disease has emerged as a serious public health problem. Data from the United States Renal Data System (USRDS) show that incidence of kidney failure is rising among adults and is commonly associated with poor outcomes and high cost.[1] Moreover, in the past 2 decades, the incidence of chronic kidney disease in children has steadily increased, with poor and ethnic minority children disproportionately affected.[1]

Children, adolescents, and young adults constitute less than 5% of the end-stage kidney disease (ESKD) population, and their 10-year survival ranges from 70% to 85%.[1, 2] Although children represent only a small proportion of all patients with CKD, affected children pose unique challenges to the health care system and to their providers, who must address not only the primary renal disorder, but the many extrarenal manifestations of CKD that complicate management.[3, 4] Most importantly, the development of ESRD compromises the life expectancy of affected patients, with an age-specific mortality rate for children receiving dialysis that is 30 to 150 times higher than for healthy peers.

The major health consequences of chronic kidney disease include not only progression to kidney failure but also an increased risk of cardiovascular disease. Evidence-based clinical practice guidelines support early recognition and treatment of chronic kidney disease–related complications to improve growth and development and, ultimately, the quality of life in children with this chronic condition. Appropriate pediatric care may reduce the prevalence of this complex and expensive condition.

Definition of chronic renal disease

The definition and classification of chronic renal disease may help identify affected individuals, possibly resulting in the early institution of effective therapy. To achieve this goal, the Kidney Disease Outcomes Quality Initiative (KDOQI) working group of the National Kidney Foundation (NKF) defined chronic kidney disease as "evidence of structural or functional kidney

abnormalities (abnormal urinalysis, imaging studies, or histology) that persist for at least 3 months, with or without a decreased glomerular filtration rate (GFR), as defined by a GFR of less than 60 mL/min per 1.73 m2."[2, 3, 4]

Note, however, that the above definition is not applicable to children younger than 2 years, because they normally have a low GFR, even when corrected for body surface area. In these patients, calculated GFR based on serum creatinine can be compared with normative age-appropriate values to detect renal impairment.

See also Chronic Renal Failure, Renal Failure, Chronic and Dialysis Complications,Dermatologic Manifestations of Renal Disease, Renal Transplantation (Medical), and Perioperative Management of the Patient With Chronic Renal Failure.

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Etiology and Pathophysiology

The chief causes of chronic kidney disease (CKD) in children include the following:

- Obstructive uropathy
- Hypoplastic or dysplastic kidneys
- Reflux nephropathy
- Focal segmental glomerulosclerosis as a variant of childhood nephritic syndrome
- Polycystic kidney disease, autosomal-recessive and autosomal-dominant varieties

The distribution of causes varies with age. Whereas congenital anomalies of the kidney and urinary tract predominate in younger patients, glomerulonephritis is the leading cause in children older than 12 years of age.

Despite the diverse etiologies, once chronic kidney disease develops, the subsequent response of the failing kidney is similar. The kidney initially adapts to damage by increasing the filtration rate in the remaining normal nephrons, a process called adaptive hyperfiltration. As a result, patients with mild chronic kidney disease often have a normal or near-normal serum creatinine concentration. Additional homeostatic mechanisms (most frequently occurring within the renal tubules) permit the serum concentrations of sodium, potassium, calcium, and phosphorous and total body water to also remain within the reference range, particularly among those with mild to moderate stages of chronic kidney disease.

Adaptive hyperfiltration, although initially beneficial, appears to result in long-term damage to the glomeruli of the remaining nephrons, which is manifested by pathologic proteinuria and progressive kidney insufficiency. This irreversibility appears to be responsible for the development of end-stage kidney failure among persons in whom the original illness is either inactive or cured.

Although the underlying problem that initiated chronic kidney disease often cannot be treated primarily, extensive studies in experimental animals and preliminary studies in humans suggest that progression in chronic renal disease may be largely due to secondary factors that are unrelated to the activity of the initial disease. These include anemia, osteodystrophy, systemic and intraglomerular hypertension, glomerular hypertrophy, proteinuria, metabolic acidosis, hyperlipidemia, tubulointerstitial disease, systemic inflammation, and altered prostanoid metabolism. This common sequence of events in diverse types of chronic kidney disease is the basis for the common management plan for children with chronic kidney disease, irrespective of the etiology.

A prospective multicenter cohort study by Greenberg et al that assessed long-term kidney outcomes after pediatric cardiac surgery (between one and 18 months of age) reported that at follow-up after cardiopulmonary bypass, 17% of the 131 children in the study (22 children) had hypertension and 18% (21 children) had chronic kidney disease.[5]

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United States statistics

Based on data from the North American Pediatric Renal Transplant Cooperative Study (NAPRTCS) chronic renal insufficiency (CRI) database, 5651 patients aged 2-17 years were entered into this voluntary listing and had an estimated glomerular filtration rate (eGFR) of less than 75 mL/min per 1.73 m2.[6] In the past 2 decades, the incidence of the disease has steadily increased among all ethnic groups.

In a National Health and Nutrition Examination Survey (NHANES) on the prevalence of chronic kidney disease (CKD) in adolescents aged 12-18 years, the authors observed that the prevalence of persistent albuminuria was similar between 1988

and 2014 and ranged from 3.29% to 3.26%. However the prevalence of both reduced and low eGFRs was higher in the most recent study period.[7]

International statistics

Globally, the prevalence of CKD stage II or lower in children is reported to be approximately 18.5-58.3 per million children. Disease prevalence is much lower than that in adults; in a study from India, children constituted 5.3% of all patients with chronic kidney disease seen in a referral hospital.[8] Data from the ItalKid study reported a mean incidence of 12.1 cases per year per million in the age-related population (age range, 8.8-13.9 y) and a prevalence of 74.7 per million in this population.[9] However, underreporting due to lack of recognition may suggest an even higher prevalence in children.

Sexual, racial, and age differences in incidence

In the United States, the incidence and rate of progression to end-stage renal disease (ESRD) are equal in both sexes, although obstructive uropathies are more common in males.

ESRD rates in Black individuals are 2.7 times higher than in White individuals, which may be due to genetic susceptibility; other factors may include socioeconomic problems and limited access to medical care. Such factors may result in the delivery of excessive numbers of low birth weight (LBW) babies, partially accounting for the observed increased incidence of ESRD, because chronic kidney disease is more common with increasing prematurity and survivorship.

Choi et al found that rates of ESRD among Black patients exceeded those among White patients at all levels of baseline eGFR.[10] Similarly, mortality rates among Black patients were equal to or higher than those among White patients at all levels of eGFR. Risk of ESRD among Black patients was highest at an eGFR of 45-59 mL/min/1.73 m2, as was the risk of mortality.[1]

The frequency of chronic kidney disease increases with age and is much more common in adults than children. Among children, chronic kidney disease is more common in children older than 6 years than in those younger than 6 years. The percentages in the NAPRTCS cohort were 19% in children aged 0-1 years; 17% in those aged 6-12 years; 33% in children aged 2-5 years; and 31% in those older than 12 years.[6]

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Genetics

Chronic kidney disease (CKD) is a heterogeneous disease, with possibly both genomic and environmental contributory factors. Various studies have shown a high CKD heritability (30-75%).

Genome-wide association studies (GWAS) and GWAS meta-analyses have identified several genetic loci, including variants in UMOD, SHROOM3, solute carriers, and E3 ubiquitin ligases. However, these genetic markers do not account for all the susceptibility to CKD, and other factors must contribute to the missing heritability.

A shorter telomere length has been associated with renal dysfunction and CKD progression, although most studies include small numbers of cases with variable findings. Copy number variants (CNVs) have been linked to congenital anomalies of the kidney and urinary tract, posterior urethral valves, nephronophthisis, and immunoglobulin A nephropathy. The A3243G mutation in the MT-TL1 gene has been associated with focal segmental glomerulosclerosis.

Only one GWAS has found associations between X chromosome and renal function (rs12845465 and rs5987107). No loci in the Y chromosome have reached genome-wide significance. Although additional biomarkers have been investigated in less common suspects such as telomeres, CNVs, mitochondrial DNA, and sex chromosomes, hidden heritability in CKD remains unexplained.[11]

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Prognosis

Once chronic kidney disease (CKD) occurs, progression to end-stage renal disease (ESRD) appears certain. In a study by Warady et al, hypoalbuminemia, hypertension, dyslipidemia, male gender, anemia, nephrotic range proteinuria, dyslipidemia at baseline, hyperphosphatemia, and lower values for glomerular filtration rate (GFR) at baseline were predictors of rapid progression.[12] However, the rate of progression depends on the underlying diagnosis, on the successful implementation of secondary preventive measures, and on the individual patient.

About 70% of children with chronic kidney disease develop ESRD by age 20 years. Children with ESRD have a 10-year survival rate of about 80% and an age-specific mortality rate of about 30 times that seen in children without ESRD. The most common cause of death in these children is cardiovascular disease, followed by infection. Of the deaths due to cardiovascular causes,

25% were attributed to cardiac arrest (cause uncertain), 16% to stroke, 14% to myocardial ischemia, 12% to pulmonary edema, 11% to hyperkalemia, and 22% to other cardiovascular causes, including arrhythmia. Data from the Australia and New Zealand (ANZ) registry revealed that the risk of death was associated with the year in which renal replacement therapy was initiated, the age of patients at the start of that therapy, and the type of dialysis used.[13]

Once the estimated glomerular filtration rate (eGFR) declines to less than 30 mL/min per 1.73 m2 and the child has stage IV chronic kidney disease, the child and the family should be prepared for renal replacement therapy. The family should be provided with information related to preemptive kidney transplantation, peritoneal dialysis, and hemodialysis. When preemptive transplantation is not an option, the choice between the 2 forms of dialysis is generally dictated by technical, social, and compliance issues, as well as family preference. Peritoneal dialysis is much more common in infants and younger children.

Patients on long-term dialysis have a high incidence of morbidity and mortality. Preemptive renal transplantation should be the goal of management in these children.

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Patient Education

Children with chronic kidney disease and their families should receive education about the importance of compliance with secondary preventative measures, natural disease progression, prescribed medications (highlighting their potential benefits and adverse effects), diet, and types of long-term renal replacement modalities.

Information related to preemptive kidney transplantation, peritoneal dialysis, and hemodialysis should be provided to the family once the child's estimated glomerular filtration rate (eGFR) declines to less than 30 mL/min per 1.73 m2 and the child has stage IV chronic kidney disease.

For patient education information, see Chronic Kidney Disease and Kidney Transplant.

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Presentation

History and Physical Examination

Chronic kidney disease (CKD) is asymptomatic in its earliest stages (stage I and stage II), although urinalysis findings or blood pressure may be abnormal. As chronic kidney disease progresses to more advanced stages, signs and symptoms greatly increase.

Polydipsia and nocturia (secondary to a reduced capacity to concentrate the urine) may be one of the earliest symptoms that indicate a diagnosis of chronic kidney disease in an otherwise healthy-looking child who has tubulointerstitial kidney disease.

The signs and symptoms in advanced chronic kidney disease may include the following:

- Volume overload
- Hyperkalemia
- Metabolic acidosis
- Hypertension
- Anemia
- Bone disease (termed osteodystrophy)
- Cardiovascular disease
- Anorexia, nausea, vomiting

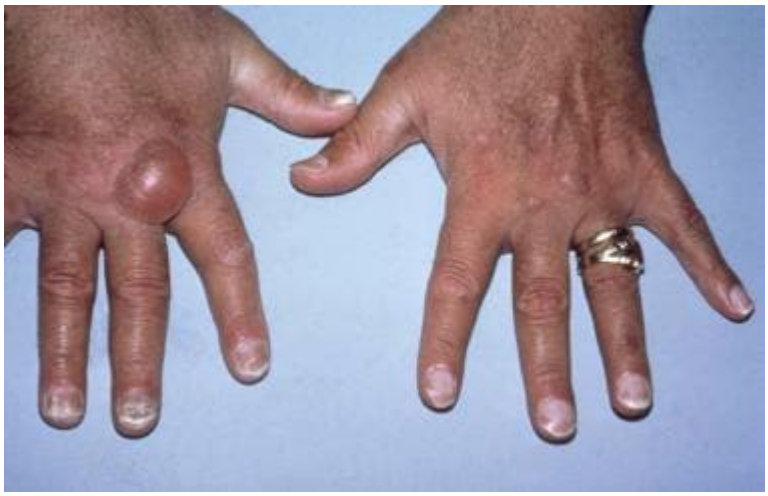
The absolute serum levels of blood urea nitrogen (BUN) or creatinine do not directly correlate with the development of these symptoms; however, estimated glomerular filtration rate (eGFR) seems to be associated with a stronger correlation.

The physical findings vary depending on the severity of kidney failure and can range from an absence of any physical findings to the presence of one or more of the following:

- Anemia
- Short stature
- Hypertension
- Osteodystrophy
- Cardiac abnormalities (eg, left ventricular hypertrophy [LVH], pericarditis)
- Peripheral neuropathy
- Central nervous system (CNS) abnormalities (eg, ranging from loss of concentration and lethargy to seizures, coma)

Approximately 50-100% of patients with end-stage renal disease (ESRD) also have at least one dermatologic condition. In addition, uremia and conditions associated with renal replacement therapy often give rise to numerous and, often, relatively unique cutaneous disorders. These dermatologic manifestations of renal disease may be divided into 3 general associated with ESRD, uremia, or renal transplantation. Discussion of the common cutaneous disorders in renal disease is beyond the scope of this article; see Dermatologic Manifestations of Renal Disease.

The image below illustrates several uremia-related cutaneous disorders.



Hands of a transfusion-dependent patient on long-term hemodialysis. Several uremia-related cutaneous disorders are visible. The pigmentary alteration results from retained urochromes and hemosiderin deposition. The large bullae are consistent with either porphyria cutanea tarda or the bullous disease of dialysis. All nails show the distal brown-red and proximal white coloring of half-and-half nails.

A population-based, case-control study with 1994 patients with childhood CKD and 20,032 controls sought to determine the association of childhood CKD with prenatal risk factors, including birth weight, maternal diabetes mellitus, and maternal overweight/obesity. The prevalence of CKD was 126.7 cases per 100,000 births. The study concludes that low birth weight, maternal gestational diabetes mellitus, and maternal overweight/obesity associated significantly with obstructive uropathy. The data suggested that prenatal factors may impact the risk of CKD. The authors add that future studies are needed to determine if modification of these factors could reduce the risk of childhood CKD.[14]

Staging

The Kidney Disease Outcomes Quality Initiative (KDOQI) recommended the following classification of chronic renal disease by stage[4, 15] :

- Stage I disease is defined by a normal glomerular filtration rate (GFR) (> 90 mL/min per 1.73 m2) and persistent albuminuria
- Stage II disease is characterized by a GFR of 60-89 mL/min per 1.73 m2 and persistent albuminuria
- Stage III disease is characterized by a GFR of 30-59 mL/min per 1.73 m2
- Stage IV disease is characterized by a GFR of 15-29 mL/min per 1.73 m2
- Stage V disease is characterized by a GFR of less than 15 mL/min per 1.73 m2 or end-stage renal disease (ESRD)

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Diagnostic Considerations

Unexplained anemia or short stature is sometimes the only presentation in a child with chronic kidney disease (CKD). A high index of suspicion is required for early diagnosis.

Differential Diagnoses

- Acute Kidney Injury
- Chronic Glomerulonephritis
- Diabetic Nephropathy
- Nephrosclerosis
- Rapidly Progressive Glomerulonephritis

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Workup

Workup

Approach Considerations

Initial testing in a child with suspected chronic kidney disease (CKD) must include an examination of the urine and estimation of the glomerular filtration rate (GFR). An important aspect of this initial evaluation is the determination of disease duration. Although the distinction between acute, subacute, and chronic kidney disease or failure is arbitrary, the differential diagnosis can frequently be narrowed if the disease duration is known. This assessment is best performed by comparing the current urinalysis or plasma creatinine concentration (PCr) with previous results, if available.

Imaging studies such as ultrasonography and radionuclide studies help in confirming the diagnosis of chronic kidney disease and may also provide clues to its etiology.

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CBC Count and Serum Chemistry Studies

Anemia is an important clinical finding in chronic kidney disease (CKD), and a complete blood cell (CBC) count is an important investigation both in the initial evaluation and the subsequent follow-up in these children. Anemia may indicate the chronic nature of the renal failure in the absence of any other obvious causes and may also be a clue to the underlying cardiovascular disease.[16]

Serum chemistry testing provides a valuable diagnostic tool both in the initial diagnosis and in the subsequent follow-up in these children. Blood urea nitrogen (BUN) and serum creatinine assessments are the most important tests. Estimation of the serum sodium, potassium, calcium, phosphorus, bicarbonate, alkaline phosphatase, parathyroid hormone (PTH), and cholesterol and fractionated lipid levels are important in the treatment and prevention of various chronic kidney disease–related complications.

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Urine Studies

Urine examination is perhaps the most important test and should be considered a part of the physical examination in all children being screened or evaluated for chronic kidney disease (CKD). It can be performed at the bedside or in the clinic using a fresh urine sample.

Urine dipstick and microscopy

An initial evaluation consists of a multitest detection strip (dipstick) test, followed by urine microscopy. The dipstick is a quick method of screening and detecting proteinuria, hematuria, and pyuria and provides an estimate of the specific gravity (urine-concentrating capacity).

Urine microscopy is performed on a centrifuge-spun urine specimen to look for red blood cells (RBCs), white blood cells (WBCs), and casts. Most children with chronic kidney disease have broad hyaline casts. Characteristic findings on microscopic examination of the urine sediment may suggest a diagnosis other than chronic kidney disease. As an example, the presence of muddy-brown granular casts and epithelial cell casts is highly suggestive of acute tubular necrosis, whereas RBC casts would suggest an acute nephritic process.

Proteinuria and albuminuria analysis

The most appropriate, practical, and precise method for estimation of proteinuria in children is to calculate the protein-to-creatinine ratio in a spot urine specimen. Patients with a positive dipstick test finding (1+ or greater) should undergo quantitative measurement (protein-to-creatinine ratio or albumin-to-creatinine ratio) within 3 months to confirm proteinuria. When postpubertal children with diabetes mellitus of 5 or more years' duration are screened, albumin should be measured in a spot urine sample using either albumin-specific dipstick or albumin-to-creatinine ratio testing.

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Novel Biomarkers

Although elevated serum creatinine and proteinuria are the most frequently utilized biomarkers of chronic kidney disease (CKD), creatinine and proteinuria increase relatively late in the course of kidney damage and progression in CKD. Novel biomarkers may identify children with the earliest stages of injury and repair, before proteinuria or serum creatinine identifies irreversible injury and nephron loss.

Because CKD progression involves multiple processes in the kidney, it is unlikely that one biomarker will best predict glomerular filtration rate (GFR) decline. It is likely that panels of biomarkers that leverage the additive properties of each individual biomarker will be the most useful clinical tools in identifying risk of CKD progression in children. A panel of biomarkers that represent the multifactorial pathophysiologic mechanisms leading to CKD progression, including tubulointerstitial injury, fibrosis, inflammation, and repair, may prove useful for predicting GFR decline in children.

A study showed that urine neutrophil gelatinase-associated lipocalin (NGAL) predicted CKD progression, but this biomarker did not significantly improve on a clinical model of CKD risk factors, including estimated glomerular filtration rate (eGFR) and proteinuria. However, tumor necrosis factor receptor 1 (TNFR1) and tumor necrosis factor receptor 2 (TNFR2) had a strong association with progression to end-stage renal disease (ESRD) even after controlling for albuminuria and eGFR.[17]

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Estimation of Glomerular Filtration Rate

The glomerular filtration rate (GFR) is equal to the sum of the filtration rates in all of the functioning nephrons; thus, estimation of the GFR gives a rough measure of the number of functioning nephrons. A reduction in GFR implies progression of the underlying disease.

The Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines state that estimates of GFR are the best overall indices of the level of kidney function.[4] The reference range of GFR in young adults is 120-130 mL/min per 1.73 m2. However, the reference range of estimated GFR (eGFR) is much lower in early infancy, even when corrected for body surface area, and subsequently increases in relationship to body size for as long as 2 years. Hence, the eGFR ranges that are used to define the 5 CKD stages apply only to children aged 2 years and older (see Staging). The eGFR can be estimated from the constant k, plasma creatinine concentration (PCr) (in mg/dL), and body length (L) (in cm) according to the Schwartz formula, as follows:

- GFR = (k X L) / PCr

The value of k is different at different ages:

- k = 0.4 for preterm infants),
- k = 0.45 for full-term infants
- k = 0.55 for those aged 2-12 years in children and adolescent girls

- k = 0.7 years in adolescent boys

Therefore, all children with chronic kidney disease should have an eGFR calculated. This should be calculated from the Schwartz (or Counahan-Barratt prediction) equation in children, because it is convenient, reasonably precise, and practical. The constants used in the equations differ slightly, likely related to the different assays to measure creatinine.

Creatinine clearance estimates are difficult and imprecise, because they require 24-hour urine collections, which may be incomplete for various reasons. It is a known fact that estimation of GFR or creatinine clearance from serum creatinine critically depends on calibration of the serum creatinine assay, specific to the expected lower levels found in children without chronic kidney disease.

For young adults, the Chronic Kidney Disease in Children study (CKiD) formula underestimates eGFR, whereas the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula overestimates eGFR. Averaging results from the 2 formulas provided an eGFR similar to an iohexol GFR. Cystatin C–based equations do not outperform the creatinine-based formulas in the general population and are therefore not recommended for routine assessment of kidney function but may be considered for special clinical situations in which patients have reduced muscle mass.[18]

Plasma cystatin C concentration

Because of the problems with changes in creatinine production and secretion, other endogenous compounds have been evaluated in an effort to provide a more accurate estimation of GFR. Perhaps the most promising is cystatin C, a low–molecular-weight protein that is a member of the cystatin superfamily of cysteine protease inhibitors. Cystatin C is produced by all nucleated cells, and its rate of production is relatively constant and is unaltered by inflammatory conditions or changes in diet. The plasma cystatin C concentration may correlate more closely with the GFR than with the PCr.

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Ultrasonography

Ultrasonography is a commonly used radiographic technique in patients who present with kidney disease because of its safety, its ease of use, and the information this modality provides. Because obstruction is a readily reversible disorder, all patients who present with acute or chronic failure of unknown etiology should undergo ultrasonography, the modality of choice to assess possible obstructive disease. Although less sensitive than computed tomography (CT) scanning in initially revealing a renal mass, ultrasonography can be useful in differentiating a simple benign cyst from a more complex cyst or a solid tumor. This technique is also commonly used to screen for and to diagnose types of polycystic kidney disease.

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Radionuclide Studies

Early detection of renal scarring is possible with radioisotope scanning with 99m (99m)-technetium dimercaptosuccinic acid (DMSA). This imaging modality is more sensitive than intravenous pyelography (IVP) in detecting renal scars and is considered the criterion standard for diagnosing reflux nephropathy, if present.

Voiding cystourethrography

Voiding cystourethrography can be performed with a radionuclide tracer study and is used to detect vesicoureteral reflux.

Retrograde or anterograde pyelography

Antegrade or retrograde pyelography may be used to better diagnose and relieve urinary tract obstruction; however, the use of pyelography for the diagnosis of obstruction has largely been supplanted by ultrasonography and computed tomography (CT) scanning. Nonetheless, antegrade or retrograde pyelography may be indicated when the clinical history is highly suggestive (unexplained acute renal failure with a bland urine sediment in a patient with known pelvic malignancy) despite ultrasonography and CT scanning findings being negative for hydronephrosis (because of possible ureteral encasement). Consultation with a pediatric urologist is suggested if antegrade or retrograde pyelography is considered.

Skeletal survey

A skeletal survey is useful in evaluating for secondary hyperparathyroidism, a component of osteodystrophy, as well as for bone-age estimation before starting or in continuation of growth hormone therapy.[19]

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Kidney Biopsy and Histologic Features

A renal biopsy is commonly performed in patients with suspected glomerulonephritis or vasculitis and in those with otherwise unexplained chronic kidney disease (CKD) or acute kidney failure. If a child has small shrunken kidneys, a kidney biopsy is often unnecessary to establish a diagnosis of chronic kidney disease.

In advanced stages of chronic kidney disease, irrespective of the underlying etiology, the findings often consist of segmental and globally sclerosed glomeruli and tubulointerstitial atrophy, often with tubulointerstitial mononuclear infiltrates.

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Treatment

Approach Considerations

Patients with chronic kidney disease (CKD) should be evaluated to determine the following:

- Diagnosis (type of kidney disease)
- Comorbid conditions (such as hyperlipidemia)
- Severity, which based on level of kidney function
- Complications, related to level of kidney function
- Risk for loss of kidney function
- Risk for cardiovascular disease

Treatment of chronic kidney disease should include the following:

- Specific therapy based on diagnosis
- Evaluation and management of reversible causes of renal dysfunction
- Prevention and treatment of complications of decreased kidney function (eg, anemia, bone disease, cardiovascular manifestations, hypertension, growth failure)
- Evaluation and management of comorbid conditions
- Slowing the loss of kidney function
- Preparation for kidney failure therapy
- Replacement of kidney function with dialysis and transplantation if signs and symptoms of uremia are present
- Management of complications

Evaluation of reversible causes of renal dysfunction

Every physician caring for patients with chronic kidney failure must determine the various factors or clinical states that may have aggravated or exacerbated the degree of kidney failure. Once these factors are corrected or reversed, the severity of kidney failure may improve, and kidney function may return to stable basal level of function. The common reversible causes include volume depletion, drugs (nonsteroidal anti-inflammatory drugs [NSAIDs], contrast agents), infection, and congestive heart failure.

Retarding progression of renal disease

In adults with chronic kidney disease, interventions to slow the progression of kidney disease that have been proven to be effective include strict blood pressure control and angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor–blocker (ARB) therapy, lipid lowering therapy, and correction of anemia. In these patients, aggressive goals are recommended for both proteinuria and blood pressure. In addition, antihypertensive therapy is used for both renal protection and cardiovascular protection, because chronic kidney disease is associated with a marked increase in cardiovascular risk.

Consultations

According to the recommendations of the Pediatric Work Group of Kidney Disease Outcomes Quality Initiative (KDOQI) for chronic kidney disease (CKD), all children with evidence of CKD should be referred to a pediatric nephrologist for consultation and comanagement.[4]

Transfer

Patients with any complications require transfer to a center with a pediatric nephrology unit where acute dialysis can be performed if required.

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Anemia Management

The presence of anemia 1 month after dialysis initiation is associated with an increased risk of prolonged hospitalization and death in pediatric patients. The beneficial effects of treating anemia with erythropoietin in patients who are dialysis-dependent include the improvement of cardiac status, exercise capacity, cognitive function, and quality of life. Recombinant human erythropoietin (rHuEPO) has been used for chronic kidney disease (CKD)–associated anemia since 1986. Based on the Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines, the recommended target hemoglobin-to-hematocrit (Hgb/Hct) ratio is 11-12 g/dL / 33-36%.[20]

Iron supplementation is essential to ensure an adequate response to erythropoietin. This is targeted to maintain a transferrin saturation level of 20% or higher and serum ferritin level of 100 ng/dL or higher in children with chronic kidney disease. The pediatric dose of oral iron is 2-3 mg/kg/d divided in 2-3 doses.

Oral iron is best absorbed when ingested without food or other medications. The percentage of iron absorbed orally is affected by the iron salt form (eg, ferrous sulfate, ferrous gluconate), the amount administered, the dosing regimen, and size of iron stores. Foods that enhance iron absorption include protein from meat and vitamin C. Foods that may inhibit absorption include unrefined grains, soy, coffee, cocoa, herb teas, red wine, calcium, and some proteins (eg, soy, eggs, casein).

Intravenous iron may be necessary for maintenance treatment of anemia associated with CKD. Intravenous iron products that are FDA-approved for use in children include iron dextran (DexFerrum, InFed), iron sucrose (Venofer), and ferric gluconate (Ferrlecit).

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Management of Bone Disease

Children with stage II chronic kidney disease usually have no signs or symptoms of bone abnormalities. However, these children may have evidence of abnormalities on laboratory testing (eg, decreased serum calcitriol [1,25 dihydroxyvitamin D] and elevated serum parathyroid hormone [PTH]). Counsel the child and family about chronic kidney disease and its impact on bone metabolism. The importance of laboratory monitoring should be emphasized, and future interventions to prevent renal osteodystrophy should be discussed. Subtle signs of renal osteodystrophy begin to be observed when the glomerular filtration rate (GFR) decreases to 50% of the reference range (stage III disease).

The 2 major types of bone disease commonly encountered in patients with chronic kidney disease before maintenance dialysis include enhanced bone resorption (osteitis fibrosa) and osteomalacia/rickets. As chronic kidney disease advances to end-stage renal disease (ESRD), adynamic bone disease may also be found. Mild forms of these derangements in bone metabolism may be observed in the early stages (eg, stage II) and may become more severe as kidney function deteriorates.

Serum concentrations of calcium, phosphate, and PTH should be measured on an ongoing basis in all children with chronic kidney disease, even those with mild disease who often have evidence of abnormalities in bone metabolism. Vitamin D insufficiency and deficiency are very prevalent in pediatric patients across all stages of chronic kidney disease, particularly in nonwhite and obese patients, and may contribute to growth deficits during the earliest stages of chronic kidney disease.[21]

For calcium and phosphorus measurements, the Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines recommend monthly measurements in stage V disease, whereas PTH measurements should be obtained at least every 3 months.[4, 15] Early detection of bone metabolic abnormalities ensures that therapeutic interventions can be initiated, thereby preventing or minimizing renal osteodystrophy.

According to the KDOQI clinical practice guidelines for pediatric osteodystrophy, phosphate binders are recommended if phosphorus or intact PTH levels cannot be controlled within the target range despite dietary phosphorus restriction.[4, 15] Calcium-based phosphate binders are effective in lowering serum phosphorus levels and may be used as the initial binder

therapy, but total calcium uptake should be rechecked.[22] The serum levels of corrected total calcium should be maintained within the reference range for the laboratory used. The serum calcium-phosphorus product should be maintained at less than 55 mg2/dL in adolescents.

Serum PTH concentration is inversely correlated with renal function and is almost always elevated when the GFR falls below 60 mL/min per 1.73 m2. Although the optimal serum PTH values in children with chronic kidney disease are uncertain, the KDOQI guidelines recommend targeted levels of serum intact PTH in stage V disease to be 200-300 pg/mL.[4, 15]

Patients with serum levels of intact PTH of more than 300 pg/mL may be treated with active vitamin D sterols to maintain PTH levels at about 2-4 times the reference range.

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Management of Cardiovascular Manifestations

Cardiovascular disease (CVD) is the major cause of mortality in both adults and children on long-term dialysis and in adults after kidney transplantation. The prevalence of coronary artery disease (CAD) and left ventricular hypertrophy (LVH), which are precursors of cardiovascular disease mortality and morbidity, is high. The prevalence of congestive heart failure (CHF), which is an independent predictor of death in chronic renal disease, is also high. Treatment strategies should include identification and treatment of modifiable risk factors for cardiovascular disease such as smoking, obesity, hypertension, hyperlipidemia, hypertriglyceridemia, anemia, hypercalcemia, and hyperphosphatemia.

Both hypertension and anemia are associated with LVH in chronic renal disease. Treatment of each condition causes regression of LVH in chronic renal disease.

Homocysteine levels are elevated in chronic kidney disease, and elevated homocysteine levels are associated with cardiovascular disease. The effect of dietary fortification with folic acid on homocysteine levels in chronic kidney disease is unknown.

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Hyperlipidemia Management

The Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines on dyslipidemias recommend that all children as well as adults with chronic kidney disease should be evaluated for dyslipidemia.[4, 15] The patients should be evaluated with a complete fasting lipid profile, including total cholesterol, LDL, high-density lipoprotein (HDL), and triglycerides at presentation, and should be evaluated annually thereafter or 2-3 months after a change in treatment or other conditions known to cause dyslipidemia. Elevated levels of total and low-density lipoprotein (LDL) cholesterol are associated with cardiovascular disease in chronic renal disease.

There is a lack of conclusive data, and thus controversy exists, regarding the risks and benefits of systematic treatment of dyslipidemia in children with chronic renal disease.[23] The National Cholesterol Expert Panel on Children (NCEP-C) treatment guidelines should be followed for children with chronic kidney disease (stages I-IV) and prepubertal children on dialysis. The approach for pubertal children with stage V chronic kidney disease is similar to that for adults, but higher thresholds are used for treating LDL and non-HDL cholesterol. Recommendations for adolescents are discussed in detail elsewhere.

Hepatic 3-methylglutaryl coenzyme A reductase inhibitors (statins), fibrates, plant stanols, bile acid–binding resins, and dietary manipulation are options for individualized treatment.

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Hypertension Management

Hypertension is a highly significant and independent predictor for progression of chronic kidney disease (CKD) in children.[24] It has been reported that at least 38% of children with chronic kidney disease in the United States receive antihypertensive therapy.[25] Hypertension has also been found to be a predictor of mortality in children with CKD.[26]

The optimal target blood pressure for children with chronic renal failure is recommended to be below the 90th percentile for age. Treatment of even mild hypertension is important in patients with chronic renal failure to protect against both progressive renal failure and cardiovascular disease, which is markedly increased in even moderate chronic renal disease.

Treatment of hypertension in children, with and without chronic kidney disease, is based on 3 factors: (1) degree of blood pressure elevation, (2) the presence of cardiovascular risk factors, and (3) the presence of end-organ damage. Additionally, the initial antihypertensive agent may be selected based on cause of chronic kidney disease and age.

Angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) have an additional benefit in at least some patients with chronic renal disease, slowing the rate of progressive renal injury, independent of the activity of the underlying disease.

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Metabolic Acidosis Management

The kidneys play a critical role in acid-base homeostasis by excreting an acid load (produced by cellular metabolism and skeletal growth in children) and preventing bicarbonate loss in the urine. An increasing tendency to retain hydrogen ions has been observed among patients with chronic kidney disease (CKD), eventually leading to a progressive metabolic acidosis. In children, overt acidosis is characteristically present when the estimated glomerular filtration rate (eGFR) is less than 30 mL/min per 1.73 m2 (stage IV).

The acidosis in chronic kidney disease in children can be associated with an increased or normal anion gap. Guidelines recommend maintaining a serum bicarbonate level of 22 mmol/L. If necessary, the authors recommend supplementation with sodium bicarbonate, started at 1-2 mEq/kg/d in 2-3 divided doses; the dose is titrated to the clinical target.

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Management of Growth Disruption

Disruption of the hypothalamic-pituitary growth hormone axis contributes to the growth hormone–resistant state in uremia. Long-term growth hormone treatment in children with chronic kidney disease (CKD) induces catch-up growth, and most patients may achieve normal adult height if treatment is initiated before end-stage renal disease (ESRD).[27] A Cochrane review of 16 studies yielded similar results finding that recombinant human growth hormone (rhGH) increased height in children with CKD by about 4 cm after 1 year and by an additional 2 cm after 2 years of treatment compared with no treatment.[28]

In children who have received a kidney transplant and fulfil the above growth criteria, we recommend initiation of growth hormone (GH) therapy 1 year after transplantation if spontaneous catch-up growth does not occur and steroid-free immunosuppression is not a feasible option. GH should be given at dosages of 0.045-0.05 mg/kg per day by daily subcutaneous injections until patients have reached their final height or until renal transplantation.[29]

Based on the Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines, treatment with rhGH should be considered under the following conditions[4, 15, 29] :

- Children whose height for chronologic age varies by more than 2 negative standard deviation scores (SDS)
- Children whose height velocity for chronologic age varies by more than 2 negative SDS
- Children with growth potential documented by open epiphyses
- No other contraindication for recombinant hGH use

Additionally, the following nutritional and metabolic imbalances should be corrected before use of recombinant hGH:

- Insufficient intake of energy, protein, and other nutrients
- Acidosis
- Hyperphosphatemia (correct serum phosphorus level to < 1.5 times the upper limit for age)
- Secondary hyperparathyroidism

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Dietary Management

Dietary management is of paramount importance in children with chronic kidney disease (CKD). These patients have an altered metabolic milieu due to deranged kidney function. The challenge for pediatricians is to optimize the growth and development of children in this setting.

Nutritional management is one of the most important components of care for children with CKD that can improve key outcomes. Aggressive control of hypertension; correction of metabolic acidosis, water, and electrolyte abnormalities; and preventing

episodes of acute on chronic kidney injury appear to constitute the most promising strategies. Effective dietary support requires the coordinated team efforts of a pediatric nephrologist, a pediatric renal dietitian, a social worker, the primary care provider, and the family.

In a cross-sectional study of dietary intake assessed by food frequency questionnaire (FFQ) in the North American Chronic Kidney Disease in Children (CKiD) prospective cohort study, children in the CKiD cohort were found to consume more sodium, phosphorus, protein, and calories than recommended. The gap between actual consumption and recommendations indicates a need for improved nutritional counseling and monitoring.[30]

The challenge for both pediatricians and dietitians is to make the diet interesting and palatable in order to ensure compliance. The goal is not only to add years to life but also to add life to years.

Energy

Energy requirements should meet at least the recommended dietary allowance (RDA) for normal children of same height age.

If protein-energy malnutrition (PEM) is present, protein and energy requirements need to be increased further to improve weight gain and linear growth. Calorie intake should be enough to enhance the efficiency of protein (protein-sparing effect) and to prevent the patient from lapsing into a catabolic state. Poor intake is common in these patients due to anorexia, nausea, and dietary restrictions.

When use of chronologic age does not account for the growth disruption, height age should be the basis for energy estimation. Supplementation can be used as per requirement (enteral or parenteral nutrition as needed).

Protein

Protein is required to maintain positive nitrogen balance for growth and maintain body protein turn over. The protein intake must be carefully controlled, avoiding protein malnutrition from an excessively restricted diet while avoiding toxicity from nitrogenous waste products from an excessively generous diet.

The diet should include 1.1-1.2 g/kg/d protein, with 60-70% protein from high biologic value origin. High biologic value proteins are of utmost importance, because they are beneficial in promoting muscle anabolism and decreasing muscle wasting.

Protein restriction is not recommended in children, because it has not been shown to influence the decrease in renal function in children with chronic kidney disease.

Phosphorus and calcium

As the glomerular filtration rate (GFR) progressively declines, excretion of phosphate decreases, and, hence, serum phosphorus levels increase. Because of this process, care must be taken for the following:

- Dietary phosphorus restriction
- Regular phosphate binders with the meals

The elemental calcium intake recommended for pediatric patients with chronic kidney disease is as follows:

- Age 1-10 years: 500-600 mg/d
- Age 11-18 years: 800-1000 mg/d

High amounts of phosphorus affect growth in children and, if the levels are high over a long period, may cause renal osteodystrophy. Prolonged elevation of serum calcium and phosphorus levels leads to vascular calcification. The daily elemental calcium requirement is about 80-100 mg/kg/d.

Potassium

The potassium requirement should be individualized depending on the serum potassium levels. Approximately 1600-2400 mg of potassium can be given.

Close watch should be kept on the potassium levels, and modifications can be made accordingly. Hyperkalemia may occur due to excessive intake of high-potassium foods, catabolism, and other causes. Leaching of pulses and vegetables should be suggested if the child is hyperkalemic.

Special attention should be given if the child is anuric.

Daily bowel movements are important, because the gastrointestinal route accounts for as much as 30% of potassium excretion in patients with chronic renal failure.

Sodium and fluid

No added salt (NAS) and restriction of salty snacks is recommended. The allowance of salt depends on the presence of edema, hypertension, and administration of sodium-containing medications. Salt intake should be kept to less than 2400 mg/d.

If the child is hypertensive and edematous, further restriction of salt and fluid is emphasized. However, exceptions include diseases in which sodium is lost in the urine (salt-losing nephropathies).

Once these children progress to dialysis or opt for kidney transplantation, a dietician should be consulted again, because the dietary requirements change.

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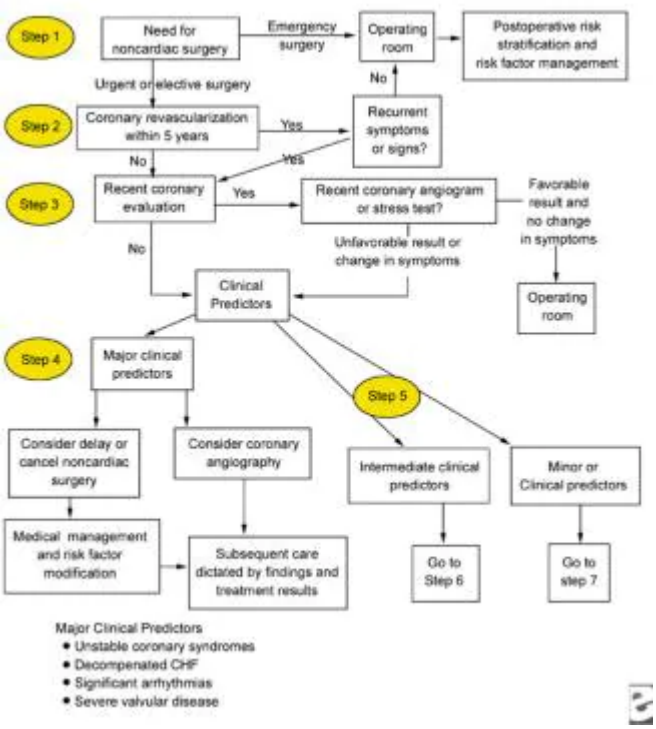
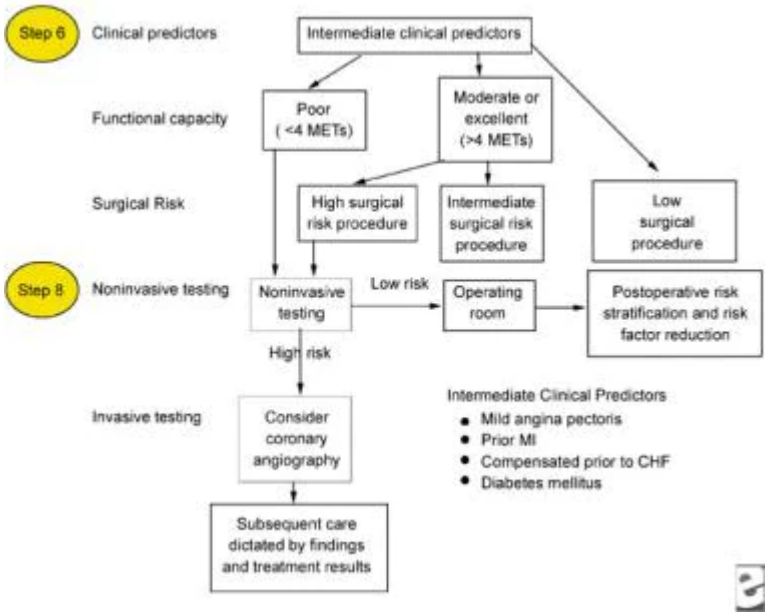
Surgical Intervention

Surgical intervention is often recommended in children with obstructive uropathy to relieve acute kidney failure due to initial or recurrent obstruction. These children should be provided follow-up because, despite surgical intervention, they have persistent underlying chronic kidney disease (CKD). In those children who opt for hemodialysis, an arteriovenous fistula needs to be created by the vascular surgery team as an access for hemodialysis.

The following images depict diagrams of major, intermediate, and minor predictors that may be used in the perioperative management of patients with chronic renal failure.



Major clinical predictors to be used for the perioperative management of a patient with chronic renal failure. CHF = congestive heart failure.



Intermediate clinical predictors to be used for the perioperative management of a patient with chronic renal failure. CHF = congestive heart failure; METs = metabolic equivalents of task; MI = myocardial infarction.

Minor clinical predictors to be used for the perioperative management of a patient with chronic renal failure. ECG = electrocardiogram; METs = metabolic equivalents of task.

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Long-Term Monitoring

All children with chronic kidney disease (CKD) require regular follow-up on an outpatient basis in a dedicated chronic kidney disease clinic until initiation of long-term renal replacement therapy. This involves a multidisciplinary team approach that involves the nephrologist, primary care physician, renal dietitian, nurse, and social worker. They should work in close coordination with the primary pediatrician or family physician.

Monitor calcium, phosphate, parathyroid hormone (PTH), and vitamin D levels on an ongoing basis in all children with chronic kidney disease, even those with mild disease who often have evidence of abnormalities in bone metabolism. There is a high prevalence of vitamin D insufficiency and deficiency across all stages of pediatric chronic kidney disease, particularly in nonwhite and obese patients, which may contribute to growth deficits during the earliest stages of this disease.[21]

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Medication

Medication Summary

Some medications (eg, nonsteroidal anti-inflammatory drugs [NSAIDs]) and radiocontrast agents are contraindicated in children with chronic kidney disease (CKD) because of the risk of deterioration of kidney function. Dose modification is required for a wide variety of drugs belonging to different categories.

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Iron salts

Class Summary

Iron salts are used to replenish iron stores. The body stores iron in compounds called ferritin and hemosiderin for future use in the production of hemoglobin. Iron absorption is a variable of the existing body iron stores, the form and quantity in foods, and the combination of foods in the diet. The ferrous form of inorganic iron is more readily absorbed.

Ferrous sulfate (Feosol, MyKidz Iron, Fer-Iron)

Ferrous sulfate is a source of iron for hemoglobin synthesis in the treatment of anemia of chronic renal failure. This agent is used with erythropoietin to prevent iron stores depletion. Oral solutions and chewable tablet formulations of ferrous iron salts are available for use in pediatric populations.

Sodium ferric gluconate complex (Ferrlecit, Nulecit)

Sodium ferric gluconate complex is used to treat microcytic hypochromic anemia due to iron deficiency when oral administration is unfeasible or ineffective as well as to replenish iron stores in individuals on erythropoietin therapy who cannot take or tolerate oral iron supplementation.

Iron sucrose (Venofer)

Iron sucrose is a polynuclear iron (III) hydroxide in sucrose for intravenous use. This agent contains no preservatives or dextran polysaccharides. Iron sucrose is FDA-approved for anemia associated with CKD in children aged 2 or older who are dependent on hemodialysis, those not dependent on hemodialysis, or who are on peritoneal dialysis and are stabilized on erythropoietin therapy.

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Colony Stimulating Factors

Class Summary

Colony-stimulating factors are used to stimulate blood cell production. Endogenous erythropoietin stimulates red blood cell (RBC) hematopoiesis. Recombinant human erythropoietin (epoetin alfa) and darbepoetin stimulate erythropoiesis in anemic conditions.

Epoetin alfa (Epogen, Procrit)

Epoetin alfa stimulates the division and differentiation of committed erythroid progenitor cells and induces the release of reticulocytes from the bone marrow into the blood stream.

Darbepoetin alfa (Aranesp)

Darbepoetin alfa stimulates the division and differentiation of committed erythroid progenitor cells and induces the release of reticulocytes from the bone marrow into the blood stream.

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Phosphate binders

Class Summary

Phosphate binding agents are indicated if phosphate elevation is uncontrolled by dietary phosphate restriction. Calcium phosphate binders are typically the initial therapy for hyperphosphatemia. Calcium supplements and calcitriol may also possibly be used for hypocalcemia.

Calcium acetate (Eliphos, PhosLo)

Calcium acetate is indicated for the treatment of hyperphosphatemia secondary to chronic renal failure. This agent combines with dietary phosphorus to form insoluble calcium phosphate, which is excreted in feces. One caplet or tablet of calcium acetate 667 mg is equivalent to 169-mg elemental calcium (ie, 1 g calcium acetate equivalent to 250-mg of elemental calcium).

Calcium carbonate (Caltrate, Tums, Alcalak)

Calcium carbonate is used to treat hyperphosphatemia in chronic renal failure. This agent combines with dietary phosphorus to form insoluble calcium phosphate, which is excreted in feces. Calcium carbonate is also indicated for hypocalcemia. Calcium carbonate 1 g is equivalent to 400 mg of elemental calcium.

Sevelamer (Renagel, Renvela)

Sevelamer is indicated to reduce serum phosphorous in patients with end-stage renal disease (ESRD). This agent binds dietary phosphate in the intestine, thus inhibiting its absorption as well as reduces the incidence of hypercalcemic episodes in patients on hemodialysis compared with patients receiving calcium acetate treatment.

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Vitamin D Analogues

Class Summary

Hyperparathyroidism is treated with calcitriol or other active vitamin D analogues. These drugs may also be used to treat hypocalcemia.

Calcitriol (Rocaltrol, Calcijex, Vectical)

Calcitriol is a primary active metabolite of vitamin D-3. This agent increases calcium levels in serum by promoting absorption of calcium in the intestines and retention in the kidneys. Calcitriol decreases excessive serum phosphatase levels and parathyroid levels as well as decreases bone resorption.

Calcitriol should be used in patients with renal failure who are unable to convert the inactive prohormone forms to the active metabolite. This agent is available in oral and parenteral formulations. This active form of vitamin D is used in cases of proximal renal tubular acidosis (pRTA) as multitherapy with large quantities of alkali and potassium supplementation and is also used to suppress parathyroid production and secretion in secondary hyperparathyroidism and for treatment of hypocalcemia in chronic renal failure by increasing intestinal calcium absorption.

Paricalcitol (Zemplar)

Paricalcitol, an active form of vitamin D, is formed through the removal of the 19th carbon group and modifications to the side chain of calcitriol, thus reducing the calcemic effect. This agent has been reported to suppress parathyroid hormone (PTH) without significant impact on calcium, phosphorus, or calcium-phosphorus product. Paricalcitol increases calcium levels in serum by promoting absorption of calcium in intestines and retention in kidneys, decreases excessive serum phosphatase levels and PTH levels, and decreases bone resorption.

This agent should be used in patients with renal failure who are unable to convert the inactive prohormone forms to the active metabolite. It is also used to suppress parathyroid production and secretion in secondary hyperparathyroidism and for treatment of hypocalcemia in chronic renal failure by increasing intestinal calcium absorption. Paricalcitol is available in oral and parenteral formulations.

Doxercalciferol (Hectorol)

Doxercalciferol is a vitamin D analogue (1-alpha-hydroxyergocalciferol) that does not require activation by the kidneys but does require hydroxylation in the liver to be converted to an active vitamin D metabolite. This agent controls intestinal absorption of dietary calcium, tubular reabsorption of calcium by the kidneys, and in conjunction with parathyroid hormone, the mobilization of calcium from skeleton. Doxercalciferol is indicated for the treatment of secondary hyperparathyroidism in end-stage renal disease (ESRD).

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Growth hormones

Class Summary

These agents are used pharmacologically as a growth-promoting agent to help optimize growth in developing children with chronic kidney disease (CKD).

Growth hormone (Nutropin, Saizen, Genotropin)

Growth hormone is a human growth hormone (hGH) produced by recombinant DNA technology and whose use results in stimulation of linear growth. This agent stimulates erythropoietin, which increases red blood cell mass.

Growth hormone is currently widely available in subcutaneous (SC) injection form. Adjust the dose gradually based on clinical and biochemical responses assessed at monthly intervals, including body weight, waist circumference, serum insulinlike growth factor-1 (IGF-1), insulinlike growth factor binding protein-3 (IGFBP-3), serum glucose, lipids, thyroid function, and whole body dual-energy x-ray absorptiometry (DEXA). In children, assess treatment response based on height and growth velocity. Continue treatment until the child's final height or epiphysial closure or both have been recorded.

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Calcimimetic Agent

Class Summary

Calcimimetic agents reduce parathyroid hormone (PTH) levels. A small clinical trial with cinacalcet by Muscheites et al in children with secondary hyperparathyroidism showed an 80% decrease in serum PTH levels.

Cinacalcet (Sensipar)

Cinacalcet directly lowers intact parathyroid hormone (iPTH) levels by increasing the sensitivity of the calcium-sensing receptor on chief cell of the parathyroid gland to extracellular calcium. This process also results in concomitant serum calcium decrease. Cinacalcet is indicated for secondary hyperparathyroidism in patients with chronic kidney disease on dialysis.

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Questions & Answers

Overview

What is the progression of chronic kidney disease (CKD) in children?

What are the signs and symptoms of chronic kidney disease (CKD) in children?

How is chronic kidney disease (CKD) diagnosed in children?

How is chronic kidney disease (CKD) in children treated?

What is chronic kidney disease (CKD) in children?

How is chronic kidney disease (CKD) in children defined?

What causes chronic kidney disease (CKD) in children?

What is the US prevalence of chronic kidney disease (CKD) in children?

What is the global prevalence of chronic kidney disease (CKD) in children?

What are the sexual predilections of chronic kidney disease (CKD) in children?

What is the prevalence of chronic kidney disease (CKD) in children based on age?

What are the racial predilections of chronic kidney disease (CKD) in children?

What is the role of genetics in the etiology of chronic kidney disease (CKD) in children?

What is the prognosis for of chronic kidney disease (CKD) in children?

What is included in patient education about of chronic kidney disease (CKD) in children?

Presentation

Which clinical history findings are characteristic of chronic kidney disease (CKD) in children?

Which physical exam findings are characteristic of chronic kidney disease (CKD) in children?

How is chronic kidney disease (CKD) in children staged?

DDX

Which symptoms may be early indications of chronic kidney disease (CKD) in children?

What are the differential diagnoses for Chronic Kidney Disease in Children?

Workup

Which tests are performed in the diagnostic evaluation for chronic kidney disease (CKD) in children?

What is the role of CBC count and serum chemistry in the workup for chronic kidney disease (CKD) in children?

What is the role of urine studies in the workup for chronic kidney disease (CKD) in children?

What is the initial urine testing for chronic kidney disease (CKD) in children?

How is proteinuria calculated in the workup for chronic kidney disease (CKD) in children?

What is the role of biomarkers in the diagnosis of chronic kidney disease (CKD) in children?

How is the glomerular filtration rate (GFR) calculated in the workup for chronic kidney disease (CKD) in children?

What is the role of plasma cystatin C concentration in the workup for chronic kidney disease (CKD) in children?

What is the role of ultrasonography in the workup for chronic kidney disease (CKD) in children?

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