

AMA/CME ARTICLE

Diagnosis and Treatment of Chronic Renal Failure in Children

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This activity is designed for primary care and specialist physicians.

GOAL

To provide an overview of the unique features and treatment of chronic renal failure in children.

OBJECTIVES

1. Describe the diagnosis of chronic renal failure in children.
2. Discuss the medical treatment of chronic renal failure in children.
3. Understand the treatment of end-stage renal disease in children.
4. Discuss the financial impact of caring for a child with chronic renal failure.

Chronic renal failure compromises the ability of the kidneys to excrete metabolic waste products and regulate the composition of the extracellular fluid. In chronic renal failure, the glomerular filtration rate (GFR), an index of kidney function, is less than 80 mL/min/1.73 m² (normal GFR is 90 to 120 mL/min/1.73 m²). During the initial stages of

chronic renal failure, affected children appear well, with no signs or symptoms of illness. As kidney function worsens and the GFR declines, the syndrome of chronic renal failure becomes more apparent.¹ Ultimately, chronic renal failure progresses to end-stage renal disease (ESRD), a condition in which the GFR is insufficient to maintain normal homeostasis. At this point, plans for renal replacement therapy, namely dialysis or transplantation, must be considered.² This article reviews the clinical features and medical management of chronic renal failure in children, including the preliminary evaluation for dialysis or transplantation.

Chronic Renal Failure in Childhood

Epidemiology. Chronic renal failure is rare in children, with only 2 to 4 new cases of ESRD occurring per 1,000,000 population per year.³ This figure is comparable to those cited in several large patient registries, such as the North American Pediatric Renal Transplant Cooperative Study (established in 1987) and the European Dialysis and Transplantation Association. Although the causes of renal disease vary in boys and girls and in different ethnic groups, the total incidence is fairly constant in diverse patient populations.³

Etiology. In adult patients, acquired forms of renal disease predominate among the causes of chronic renal failure. Among children, congenital and acquired diseases contribute equally as the underlying cause of chronic renal failure.³ Common congenital causes of chronic renal failure are hypoplastic or dysplastic kidneys; obstructive uropathy, including prune-belly syndrome, posterior urethral valves, and megacystis-megaureter syndrome; and vesicoureteral reflux. In the neonatal period, some infants experience clinical difficulties that cause kidney ischemia or renal vein thrombosis, injuries that can lead to chronic renal failure. Among the hereditary or genetic causes of chronic renal failure are polycystic kidney disease (autosomal dominant or recessive) and Alport syndrome. Polycystic kidney disease is much more likely to cause chronic renal failure in the first decade of life. In contrast, Alport syn-

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drome usually does not significantly compromise kidney function until the middle to end of the second decade of life. Acquired causes of chronic renal failure in children include focal segmental glomerulosclerosis, lupus nephritis, hemolytic uremic syndrome, and Henoch-Schoenlein purpura nephritis.

Clinical Presentation. Initial signs and symptoms of chronic renal failure may be vague and nonspecific. They also vary significantly depending on the age of onset and the underlying disease. Clinicians must have a high index of suspicion for chronic renal failure in children of all ages to avoid overlooking the problem.

In the newborn period, the infant may have an abdominal mass or urosepsis. In the first 2 years of life, urinary tract infections and failure to thrive should prompt consideration of renal disease. In school-age children, abnormalities in the urinalysis, including gross hematuria, as well as hypertension, nephrotic syndrome, short stature, and enuresis may be clues to the presence of chronic renal failure. Impaired linear growth, neurocognitive disabilities, and delayed pubertal development are clinical concerns related to chronic renal failure. The first two problems are especially pronounced in children with congenital abnormalities of the kidney who develop chronic renal failure in the first 3 years of life. Because these complications can be irreversible, recognizing the problem and initiating treatment as early and quickly as possible in very young children is vital. However, in many cases, especially in older children, there are few complaints unequivocally referable to the kidney. Instead, there may be ambiguous problems, such as malaise, anorexia, and generalized weakness, that do not explicitly suggest kidney disease. Thus a diagnosis of chronic renal failure may be unexpected by the patient, parents, and physician alike.

Diagnostic Evaluation. The first critical step in evaluating patients with renal disease is to distinguish between glomerular and non-glomerular illnesses. In glomerular illnesses, hematuria (dysmorphic erythrocytes and red blood cell casts) and proteinuria are invariably present. If urine protein excretion is massive, the child may have edema and nephrotic syndrome. Hypertension also is a sign of glomerular disease. In suspected cases of glomerular illness, the diagnostic evaluation must include tests to measure urinary protein excretion and serologic tests for serum complement levels, antinuclear antibodies, anti-double stranded DNA antibody titers, and other markers of systemic diseases that cause glomerulonephritis.⁴ A renal biopsy may be warranted to establish the diagnosis. However, renal imaging is of marginal value when glomerular illness is suspected except as an indirect measure of disease duration. On ultrasonography, the

kidneys will be small in children with long-standing renal disease.

In cases of suspected non-glomerular disease, the focus is on assessing the anatomic integrity of the genitourinary tract. A range of radiologic tests can be used to determine the cause of chronic renal failure. Renal sonography is the most efficient method of detecting hydronephrosis or renal cysts. Additional tests, including an abdominal computed tomographic scan and magnetic resonance imaging, may be required to confirm a diagnosis of polycystic kidney disease. Renal scintigraphy coupled with a diuretic renogram can be used to measure GFR, assess the clinical significance of an obstructive lesion of the urinary tract, and demonstrate renal scarring. Specific radiopharmaceuticals are required for each of these purposes (eg, DTPA or MAG-3 for renal function, DMSA for renal scarring).⁵ A voiding cystourethrogram, using conventional contrast agents or radioisotopes, is needed to establish the diagnosis in cases of suspected vesicoureteral reflux.

Overview of Medical Treatment

Role of the Nephrologist. The first task in treating children with chronic renal failure is to prescribe medications that compensate for impaired renal excretory function and restore normal biochemical homeostasis.⁶ Although sodium restriction may be needed to decrease hypertension in children with glomerular disease, patients with non-glomerular disorders may have salt wasting and require sodium supplementation. When hypertension is present, antihypertensive agents should be used to maintain normal blood pressure because persistent hypertension accelerates the deterioration in kidney function and damages other target organs, including the heart. Hyperkalemia is almost always a concern, regardless of the underlying disease, and is treated with dietary potassium restriction and oral potassium-binding agents that promote gastrointestinal excretion of potassium. Metabolic acidosis is frequently observed in children with chronic renal failure and contributes to abdominal pain, malaise, and bone disease. This abnormality is easily treated with supplemental bicarbonate.

Renal osteodystrophy, a complex disorder of calcium, phosphorus, parathormone, and vitamin D metabolism that develops in patients with chronic renal failure, is difficult to treat. The cornerstones of therapy are restriction of dietary phosphorus, initiation of oral phosphorus binders (eg, calcium acetate) when the GFR falls below 30 mL/min/1.73 m², and administration of calcitriol or 1,25-(OH)₂-vitamin D₃, the active metabolite of vitamin D.⁷ Metabolic bone disease may be refractory to this medical regimen, and in severe cases, parathyroidectomy may be needed.

Impaired nutrition and short stature are cardinal features of chronic renal failure in children.⁸ Thus a nutritionist skilled in working with children with chronic renal failure must be part of the treatment team. Dietary records should be reviewed to determine whether the child is ingesting a sufficient amount of calories and protein each day to promote growth. Caloric intake usually is low in pediatric patients with chronic renal failure. Moreover, use of calories by the body is impaired. Therefore, these children need nutritional supplements to increase caloric intake to more than 125% of the recommended daily allowance (RDA). This can usually be accomplished with oral supplements, with nasogastric tube feeding being a last resort. Although excessive dietary protein accelerates the deterioration in kidney function, daily protein intake should match the RDA to ensure that growth is not compromised. However, despite optimal nutritional support, patients may still not grow properly. In these cases, recombinant human growth hormone (0.05 mg/kg/day) should be prescribed to foster linear growth.⁹ This hormone has been given to children with chronic renal failure for up to 5 years and results in a doubling of growth velocity and significant "catch-up" growth. Recombinant human growth hormone is well tolerated, has no severe side effects, and significantly improves the quality of life of these patients.

Treating the anemia of chronic renal failure also is vitally important. Many of the signs and symptoms of chronic renal failure are not due to the azotemia per se but result from severe anemia. Although the pathogenesis of anemia is multifactorial, the principal abnormality is insufficient production of erythropoietin.¹⁰ This hormone is produced in the kidney and mediates increased erythropoiesis in the bone marrow. With progressive chronic renal failure, renal production of erythropoietin declines, leading to worsening anemia. Administration of recombinant human erythropoietin (50 to 100 U/kg/dose) reverses this process and safely raises the hematocrit to levels at which the symptoms of chronic renal failure are significantly alleviated.

Role of Other Pediatric Subspecialists. Chronic renal failure is a systemic disease that affects every organ in the body.¹² Optimal care of children with chronic renal failure requires coordination of care with many subspecialists. Neurologists may be needed to manage seizures and other neurologic problems. Developmental pediatricians and clinical psychologists should be consulted regularly to detect developmental delays and learning disabilities in a timely manner and devise strategies to optimize neurocognitive growth and school performance. Child psychiatrists are almost always needed to manage adolescent patients who rebel at the

notion of having a chronic disease and are poorly compliant with medical therapy. Cardiologists may be needed to treat those children who develop cardiomyopathy related to uremia or hypertension, pericardial effusions, or arrhythmias. Orthopedic deformities requiring surgical correction may develop despite all efforts to treat renal osteodystrophy. The pediatric nephrologist must integrate the services of many disciplines to provide optimal care to a child with chronic renal failure. Care of children with chronic renal failure is a complex process that can be daunting to both the patient and the nephrologist.

Planning for End-Stage Renal Disease

Kidney transplantation is the preferred treatment for children with ESRD, since its long-term outcome has steadily improved over the last decade.¹¹ Because of the expected life span of children with kidney failure, dialysis is not a long-term solution. In general, there are no causes of chronic renal failure for which kidney transplantation is contraindicated. However, there are circumstances in which an interval of dialysis support is necessary. For example, a living related kidney donor may not be available, and a child may need to be dialyzed until a matching cadaveric kidney can be found. Parents may not immediately be ready or willing to accept the risks of transplantation for their child. Therefore, dialysis may be required temporarily until all parties are psychologically ready for the procedure. Children who are too small to receive a kidney transplant may need dialysis until they grow sufficiently to make surgery a technically feasible option. Finally, the general health of the child, other complicating medical conditions, or the risk of recurrent disease after transplantation can make this procedure less attractive for certain patients. Both hemodialysis and peritoneal dialysis should be available for any child who needs dialysis support so the choice can be individualized for the patient.

The long-term prognosis for children undergoing kidney transplantation from a living related donor, either a parent or sibling, continues to improve. This type of donation is superior to cadaveric transplantation in adults and children. In adults, outcomes after kidney transplantation from living unrelated kidney donors, such as a spouse, is also superior to cadaveric kidney transplants.¹² However, in children, fully two thirds of kidney transplants are from cadaveric sources. Preference is given to children who are on waiting lists for transplantation, those who have been waiting for longer periods of time, and those with high cytotoxicity profiles.¹³ Outcomes have been improved by increased human leukocyte antigen

matching and shorter cold ischemia times. Improved organ sharing between different parts of the United Network for Organ Sharing also increases the likelihood of successful outcomes. However, in certain circumstances, such as focal segmental glomerulosclerosis, membranoproliferative glomerulonephritis, oxalosis (preferably treated with combined kidney-liver transplant), and cystinosis, families must be counseled about the risk of recurrent disease after transplantation.

Financial Impact of Chronic Renal Failure in Childhood

Chronic renal failure is a complicated illness requiring input from many medical subspecialists and administration of numerous drugs. Some of these medications profoundly improve the quality of life and outcome for children with chronic renal failure, albeit at a high price. The annual cost of recombinant human growth hormone or erythropoietin may exceed \$15,000.

The general practitioner and the pediatric nephrologist must work together closely to identify renal disease as early as possible. Although never rigorously tested, prompt identification and initiation of appropriate medical care may lead to an improved outcome by decreasing the risk of irreversible complications, such as neurocognitive deficits, stunted growth, and target organ damage. Pediatric nephrologists must take the initiative in verifying this claim through careful longitudinal follow-up of children with chronic renal failure. With these data, adequate guidelines can be formulated for children with suspected chronic renal failure that meet the needs of families, general practitioners, and subspecialists.

Communication between generalists and renal subspecialists is critical since all children experience numerous problems as they grow up. Some problems are simple and others complex, and some can be handled by the general pediatrician while others require the expertise of the nephrologist. By working together, generalists and specialists can care for the child in an appropriate, timely, and cost-effective manner.

With regard to cost containment, nephrologists must be prepared to justify their proposed treatments and directly address cost issues. Yet a child with chronic renal failure should not be denied appropriate treatment because health insurance companies refuse to pay. Data are available to support the use of costly, high-technology therapies, and nephrologists can make a case for covering short-term expenses to reap long-term gains.

Conclusion

Chronic renal failure in childhood is a challenge to all parties involved. Families must cope with a

serious progressive disease, numerous medications, diet modifications, and significant lifestyle changes. Although general practitioners have much to offer a child with chronic renal failure, they may be strained to the limit in handling these difficult patients. Nephrologists must coordinate treatment among a myriad of healthcare professionals in planning an effective course of action. All this must be accomplished in an age of cost containment perceived as antagonistic to expensive high-technology treatments. However, a successfully treated child with chronic renal failure is the ultimate justification for these efforts and should provide encouragement that good outcomes can be achieved routinely.

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CME QUESTIONS: TEST #039705

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Instructions

After reading the article, "Diagnosis and Treatment of Chronic Renal Failure in Children," select the best answer to each of the following questions. In order to receive 1 CME credit, at least 7 of the 10 answers must be correct. Estimated time for this activity is 1 hour. CME credits are distributed on a yearly basis.

1. **Acquired renal diseases are the most common cause of chronic renal failure in children.**
a) true
b) false
2. **All the problems that arise in children with chronic renal failure involve the kidneys.**
a) true
b) false
3. **Children with chronic renal failure usually require interdisciplinary medical care.**
a) true
b) false
4. **Early treatment of chronic renal failure can improve neurocognitive development.**
a) true
b) false

5. **Untreated metabolic acidosis in children with chronic renal failure is associated with worsening bone disease.**
a) true
b) false
6. **Dietary protein restriction is recommended for children with chronic renal failure.**
a) true
b) false
7. **Which of the following is a consideration in allocating a cadaveric kidney to a child with end-stage renal disease?**
a) socioeconomic status
b) cytotoxicity profile
c) patient sex
d) underlying disease
8. **Which of the following are not used to treat renal osteodystrophy in children?**
a) sodium polystyrene sulfonate
b) phosphate binders
c) vitamin D
d) low phosphate diet
9. **The annual incidence of end-stage renal disease in children is approximately:**
a) 3 cases per 100,000 population
b) 6 cases per 100,000 population
c) 3 cases per 1,000,000 population
d) similar to the incidence in adult patients
10. **The use of erythropoietin has demonstrated that many symptoms of uremia are related to:**
a) metabolic acidosis
b) renal osteodystrophy
c) anemia
d) neurocognitive deficits

<p>AMA/CME TEST FORM AJMC Test #039705</p> <p>Diagnosis and Treatment of Chronic Renal Failure in Children</p> <p><i>Application for 1 Credit Hour of AMA Category I</i></p> <p>(Test valid through May 15, 1998 No credit will be given after this date.)</p>	<p>Please circle your answers:</p> <p>1. a b 2. a b 3. a b 4. a b 5. a b 6. a b 7. a b c d 8. a b c d 9. a b c d 10. a b c d</p>	<p>(PLEASE PRINT CLEARLY)</p> <p>Name _____</p> <p>Address _____</p> <p>City _____</p> <p>State/Zip _____</p> <p>Phone # _____</p> <p style="text-align: center;">Please enclose a check for \$10, payable to American Medical Publishing, LLC, and mail with this form to:</p> <p style="text-align: center;">The AJMC CME Test American Medical Publishing 1816 Englishtown Road, Suite 101 Old Bridge, NJ 08857</p>
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