Clinical Overview of CRF in Children

CRF is the irreversible deterioration of renal function that gradually progresses to endstage renal disease. ESRD is severe CRF to the point at which homeostasis and patient survival cannot be maintained without renal replacement therapy or transplantation. Symptoms of CRF are usually when GFR is between 10 to 15% of normal. Children

with CRF may suffer from failure to thrive, growth retraction, renal osteodystrophy, acidosis and anemia.

Management of CRF aims at retarding the progression of renal damage, replacement therapy and treatment of complications. Growth retardation is a unique and consistent feature of CRF in children.

CRF can be considered in four stages, depending on GFR, clinical manifestations and complications. GFR in children can be calculated by using serum creatinine, the Schwartz constant and applying the following formula:

[K x Height in cm] / serum creatinine in umol/L].

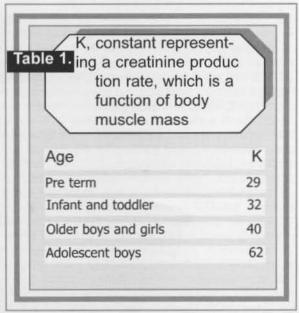
Table 1 gives the K constants for different ages, and Table 2 gives the normal GFR at different ages.

Stages of renal failure

Stage one coincides with GFR 50 to 75%. At this GFR, there is increased incidence of short stature otherwise asymptomatic.

Stage two, or CRI, coincides with GFR at 25 to 50%. The child is still clinically asymptomatic but takes longer to recover from catabolic stress and illnesses, but abnormality can be detected in the blood (urea, creatinine, PTH) and

Normal GFR in Children ble 2.	
Age ml per minute	e per 173 m2
Pre term	12
Full term	15
2 weeks	50
8 weeks	65
1 year	120
Adults	120



urine, poor weight gain and diminished linear growth. At this level of GFR, progressive deterioration of renal damage is likely.

Stage 3, or CRF, coincides with GFR 10 to 25%. At this stage clinical abnormality is present: acidosis, growth failure, renal osteodystrophy, hypertension and anemia.

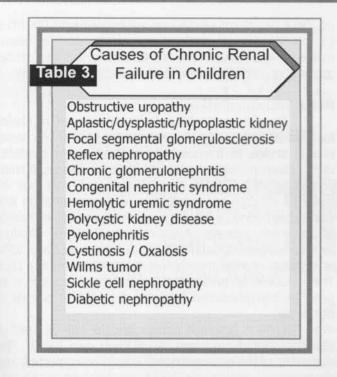
Stage 4, or ESRD, is indicated when GFR is less than 10. Preparation and initiation of dialysis or transplantation should start at this stage as GFR less than 5% is insufficient to sustain life in the absence of renal replacement therapy. **Epidemiology**

The incidence of CRF in children is one to three per million total population, with a prevalence rate of 40 per million population.

Early in life, the most common cause is congenital structural abnormality and reflex nephropathy. Later in life glomerulonephritis is the most common cause.

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Metabolic Changes

Sodium homeostasis is well-maintained throughout the course of CRF, while potassium homeostasis is maintained until GFR is less than 10%, by increasing colonic and distal renal excretion under the influence of Aldosterone.

Metabolic acidosis appears when GFR is less than 50% and phosphorous remains normal until GFR is less than 25%.

In patients with CRF and fixed urinary osmolality, the urine volume is the function of osmolar load. This means the urine output can be decreased by reducing the salt and protein intake.

Anemia occurs when GFR is less than 35%.

Growth and development

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Most children with CRF do not grow to their genetic potential. At starting dialysis it has been noted that between one third to one half of children have a height below the third percentile for their chronological age. The younger the child at the onset of renal failure, the more severely affected the growth. Growth is more rapid at infancy and at pubertal spurts in early life. It is affected more by nutrition and electrolyte disturbances, while growth at childhood and puberty is more under the influence of growth hormone and sex hormones, respectfully.

In CRF, intake is low related to altered taste and anorexia, and when it is less than 80% of the recommended daily allowance (RDA,) growth retardations will occur. Unfortunately, if the intake is not improved early in life, the child may not catch up later to his or her peers' height.

Clinically there is no evidence to suggest that energy intake greater than 100% recommended is desirable, and it may only lead to obesity unless there are other associated conditions known to increase caloric requirement and dietary protein only restricted to recommended daily allowance. Further restriction in children may adversely affect growth and development.

In CRF, therefore, it is important to keep up a good nutritional intake, and the daily administration of rhGH should be considered in children with CRF and short stature.

Renal Osteodystrophy

Renal osteodystrophy is a bone disease, which affects children with moderate or severe chronic renal failure. In chronic renal failure, hypocalcaemia results from the impaired excretion of phosphate and the impaired formation of active metabolites of vitamin D, hypocalcaemia, hyperphosphatemia and the increased resistance to PTH, all of which lead to secondary hyperparathyroidism and renal osteodystrophy.

Manifesting as growth retardation, bone pain myopathy, skeletal deformity and signs of rickets, radiologically it manifests as osteopenia and superiosteal resorption, and biochemically as increased ALP and increased PTH.

Care of Children with CRF disease

Children with CRF require specialized complex care for the rest of their lives, ideally provided by an interdisciplinary team that includes a pediatric nephrologist, dialysis and transplant nurse, nurse practitioner, pharmacist, pediatric urologist, transplant surgeon, social worker and psychologist.

Growth should be monitored by regular measurement of height, weight and head circumference for children lass than 3 years of age, and each visit should be recorded on a growth chart.

Measurements of triceps, skin fold and mid-arm circumference are useful to assess body fat and muscle mass.

Regular measurement of CBC, urea, creatinine, electrolytes, calcium, phosphate, magnesium, alkaline phosphatase, albumin, PTH, iron ant TIBC should be carried out, as well as yearly fasting blood sugar and lipid profile. X-ray evaluation for renal osteodystrophy at 6 monthly intervals and bone age yearly should be done.

Nutrition

Calorie intake should be maintained between 100 and 120% of RDA. Energy supplement with polyunsaturated fat, medium chain triglycerides and complex carbohydrates might also be needed.

Protein intake should be kept at RDA, and blood urea, if possible, should be kept below 25 mmol/L.

In a significant number of children, the oral intake is not adequate to meet energy and fluid requirement. In those children, nasogastric, nasojejunal or gastrostomy tube feeding may be necessary. The use of gastrostomy tube feedins in these children has improved calorie and protein intake and reduced the incidence of malnutrition.

Calcium supplements may be needed to maintain normal serum calcium. Phosphate intake should be limited to RDA, and phosphate binders may be needed. The use of aluminum containing phosphate binders should be avoided in children. Vitamin D supplement in the form of 1,25 dihydroxyvitamin D should be considered when the GFR is below 50% of normal.

Anemia is treated by iron supplement to keep iron saturation above 20% and by administration of erythropoietin aiming for hematocrit around 35%. Erythropoietin can be administered subcutaneiously, intravenously for those on hemodialysis or intraperitoneally for those on PD. The weekly dosages vary between 50 to 600 units/kg.

Drug dosing in children with CRF

Drug elimination by the kidney is directly related to GFR, and, generally, if the GFR is above 50 ml/min/1.73m2, no adjustment is needed. Otherwise, drug toxicity and a side effect may occur if dosages are not adjusted according to the patient's GFR. In general, the loading dose of a drug need not be adjusted; however, the maintenance dose should be adjusted by either reducing the dose or lengthening the interval between dosages. Dose reduction is preferred with the short half-life medication, whereas lengthening the interval between dosages is preferred for medication with a long half-life.

Dialysis

About 15% of adults are treated with PD, where

as about two-thirds of children are treated with PD. PD is technically easier to perform and can be done at home, making it less disruptive to the family life, full time school attendance and minimizing patient dietary restrictions.

Renal Transplantation

Renal transplantation is the treatment of choice for children with ESRD, and dialysis should only be considered a bridge to transplantation. Data shows mortality rates of transplantation are lower than for dialysis. A small percentage of adults are transplanted each year, but virtually all children are candidates for transplantation and were about 75% of adult-transplanted patient recipients of cadaveric kidneys. Approximately 50% of children receive living graft, and NAPRATICS data show about 25% of children receive preemptive transplants, mainly LRD. The outcome of preemptive renal transplantation is as good as transplantation following a period of dialysis, if not better.

Potential donors should not be used if donation should pose any risk to their own health. The autonomy of the potential donor should be respected, and the improved outcome to the recipient should not be permitted to influence the living donor. Most of the pediatric programs do not consider donors less than 18 years of age.

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