CHAPTER 6

NEPHROLOGICAL/UROLOGICAL DISORDERS

6.1. POST-STREPTOCOCCAL GLOMERULONEPHRITIS

N00.9

DESCRIPTION

Acute post-streptococcal glomerulonephritis (APSGN) is a disorder of the kidneys caused by an immunological response of the kidney to nephritogenic strains of streptococci. It develops one to three weeks after a streptococcal throat or skin infection. Immune complexes are deposited in the glomerular basement membrane and/or mesangium of the glomeruli.

DIAGNOSTIC CRITERIA

Clinical

- » Occurs predominantly in children 3–12 years old.
- » Presents approximately 1 week after streptococcal pharyngitis OR approximately 3 weeks after skin infection (impetigo).
- » Characteristic features include:
  - > facial or generalised oedema,
  - > painless macroscopic haematuria (smoky or tea-coloured urine),
  - > oliguria, and
  - > hypertension.

Special investigations to confirm APSGN

Urine analysis	
Macroscopic appearance	smoky, brown, bloody
Urine test strips	1+ to 3+ haematuria; ~ trace to 2+ proteinuria
Microscopic examination	dysmorphic red blood cells; red blood cell and granular casts
Blood investigations	
Streptococcus serology ASO or Anti-DNAse B titre	positive in the absence of prior antibiotic treatment (ASO often negative in preceding skin infections)
Complement study C_3 C_4	 decreased normal

Serum biochemistry	
Serum electrolytes	dilutional hyponatraemia, hyperchloraemic hyperkalaemic metabolic acidosis is common
Serum Urea & Creatinine	mildly elevated in the acute phase
Full blood count	dilutional anaemia; thrombocyte count is normal

GENERAL AND SUPPORTIVE MEASURES

» Bed rest is necessary in children with severe hypertension or pulmonary oedema.
» Monitor fluid balance and prescribe fluid on a daily basis:
  > Weigh daily and record fluid intake and output strictly.
  > Allowed fluid intake should be calculated based on previous day's urine output and insensible losses.
  > In small children, fluid balance is best monitored with regular weighing.
  > Never use a potassium-containing solution in an anuric patient.
  > Do not use parenteral fluids if oral intake is possible.
» Ensure daily fluid calculations are performed using insensible losses and previous day's output. Fluid management according to fluid status:
  > **Pulmonary oedema plus oliguria/anuria**: Do not give fluid.
  > **Hydrated anuric patient without extra-renal fluid losses**: Oral fluid to replace insensible water losses only.
  > **Normally hydrated plus oliguria**: Oral fluid intake to replace insensible water loss and urine output of previous 24 hours.
  > **Normally hydrated plus normal urine output**: Give normal fluid intake.

IMPORTANT
Insensible water loss is calculated as:
- Older children: 25 mL/kg/day (400 mL/m^2/day)

» Dietary measures:
  > Restrict sodium intake in all patients.
  > Restrict potassium intake until result of serum electrolytes is available.
  > Restrict protein intake to 0.5 g/kg/day.

MEDICINE TREATMENT

Eradication of streptococci

- Phenoxymethylpenicillin, oral, 50 mg/kg/24 hours in 4 divided doses (6 hourly) for 10 days.

OR

If unable to take oral medication:

- Benzathine benzylpenicillin (depot formulation), IM, 30 000 units/kg/dose, 2 doses given 5 days apart.
  - Maximum dose: 1.2 million units.

For severe penicillin allergy:

- Refer to Chapter 24: Drug Allergy, section 24.4.1: Allergies to penicillins.

Hypertension

Hypertension usually develops acutely due to fluid overload and presents as hypertension emergency (crisis), hypertension urgency or persistent significant hypertension. See Chapter 4: Cardiovascular System, Section 4.11: Hypertension in children.

If **hypertensive emergency/crisis**: Patient with signs of hypertensive encephalopathy, i.e. convulsions, retinal haemorrhages, visual loss and end-organ disease, e.g. left heart failure.

Management for acute hypertensive emergency/crisis due to post-streptococcal glomerulonephritis:

- Furosemide, IV, 1–2 mg/kg/dose.

If oliguric:

- Furosemide, IV, 5 mg/kg/dose.
  - Administer IV bolus slowly over 5 minutes due to risk of ototoxicity.

AND

- Labetalol, IV, 0.2–1.0 mg/kg/dose as a bolus.
  - Maximum bolus dose: 40 mg.
  - Continue infusion: 0.25–3.0 mg/kg/hour.
  - Monitor blood pressure frequently (every 30 minutes).
  - Taper infusion rate up or down according to response.

If **hypertensive urgency:** Symptomatic patients with significant elevation of blood pressure with complaints of headache, blurred vision and nausea but lack the above clinical manifestations or persistent significant hypertension:

- Propranolol, oral, 1–2 mg/kg/dose, 6 hourly.
  - Maximum dose: 8 mg/kg/24 hours.

If blood pressure is not adequately controlled:

ADD

- Amlodipine, oral, 0.2 mg/kg/dose.
  - May be repeated 6 hours later, thereafter, once every 24 hours.
  - Maximum dose: 5 mg.
  - Crush 5 mg tablet and disperse in 5 mL water: amlodipine 1 mg/mL.

Once blood pressure has normalised, taper and stop antihypertensive treatment. Monitor blood pressure over the next 48 hours to exclude rebound hypertension.

If volume overloaded:
See fluid management in general and supportive measures.

- Furosemide, slow IV, 2 mg/kg/dose.
  - Maximum dose: 5 mg/kg/dose.
  - Maximum cumulative daily dose: 8 mg/kg/24 hours.

If pulmonary oedema:
See fluid management in general and supportive measures.

- Morphine, IV, repeat after 4 hours if required.
  - < 6 months of age: 0.025–0.1 mg/kg/dose.
  - ≥ 6 months of age: 0.05–0.2 mg/kg/dose.

LoE III[1]

- Oxygen, 100%, 2–3 L/minute by nasal cannula.

REFERRAL

Urgent (as soon as possible)

» Anuric patient with acute volume overload and unresponsive to furosemide.
» Uncontrolled hypertension.
» Oliguric and progressive renal failure.
» Cardiac failure or pulmonary oedema not responding to treatment.

For specialist advice

» Macroscopic haematuria persisting for more than 4 weeks or persistent proteinuria.
» Family history of renal disease.
» Streptococcal aetiology unproven (ASOT and anti-DNAse B negative, normal C_3 levels, decreased C_4 levels).
» Decreased complement levels which persist for more than 6 weeks.
» Persistent renal failure after initial recovery.
» Persistent hypertension.

6.2 URINARY TRACT INFECTION (UTI)

N39.0

DESCRIPTION

Bacterial infection of the urinary tract.

Uncomplicated urinary tract infection (UTI) is an infection, which is limited to the lower urinary tract, and there are no associated urological anomalies. It is seen most commonly in girls over two years of age.

Complicated urinary tract infection (UTI) is an infection of the urinary tract involving the renal parenchyma (acute pyelonephritis) or which is associated with underlying congenital anomalies of the kidneys and urinary tract. It may result in significant short-term morbidity, including septicaemic shock and acute renal failure, especially in infants. Permanent renal damage may occur in children who have recurring episodes of pyelonephritis.

DIAGNOSTIC CRITERIA

Clinical

» Signs and symptoms are related to the age of the child and are often non-specific.
Uncomplicated urinary tract infections present with localising symptoms of dysuria, frequency, urgency, cloudy urine and lower abdominal discomfort. Urine test strip shows positive leucocyte esterase, nitrites and haematuria.

» Complicated infections may present with fever and other systemic features described below:

» Neonates may present with:
- > fever,
- > hypothermia,
- > poor feeding,
- > sepsis,
- > vomiting,
- > prolonged jaundice,
- > failure to thrive,
- > renal failure.

» Infants and children may present with:
- > failure to thrive,
- > persisting fever,
- > abdominal pain,
- > frequency,
- > dysuria,
- > enuresis or urgency.

A urinary tract infection must be excluded in any child with fever of unknown origin.

Special investigations

» Urine bag specimens are used for screening purposes only.
- > When a urine strip test of a bag specimen reveals presence of leucocytes, nitrites, or haematuria, collect urine aseptically for urine MCS.
- > Urine specimen is collected aseptically:
  - by in-out catheter or suprapubic aspiration in acutely ill children < 2 years of age or in smaller children who are unable to co-operate **or**
  - by mid-stream clean-catch method in older children.

» Criteria for the diagnosis of UTI:
- > any culture from a suprapubic urine sample,

- > a culture of > 10^4 col/mL urine of a single organism from a catheter specimen,
- > a pure culture of > 10^5 col/mL in a mid-stream clean-catch sample or consistent culture of a pure growth even with counts as low as 10^4 col/mL.

» Ultrasound:
- > Do a renal ultrasound in **all** children with a first UTI as soon as possible, unless a normal ultrasound was previously seen.
- > Posterior urethral valve (PUV) disorder should be investigated in males.

» MCUG:
- > In children who have abnormalities of the kidneys, ureter or bladder demonstrated by ultrasound.

GENERAL AND SUPPORTIVE MEASURES

» Ensure adequate nutrition and hydration. Maintain hydration with oral and/or IV fluids if necessary.

» For recurring infections:
- > avoid irritant soaps and bubble baths,
- > treat constipation, if present,
- > treat pinworm,
- > attend to perineal hygiene,
- > regular complete emptying of the bladder and/or double voiding, i.e. making an additional attempt at voiding after the initial flow of urine has ceased.

Note: Consider the possibility of sexual abuse in children presenting with a UTI with genital, perineal and/or anal bruising, abrasions or laceration, secondary incontinence or a marked fear of examination.

MEDICINE TREATMENT

Uncomplicated UTI

See the Standard Treatment Guidelines and Essential Medicines List for Primary Health Care Level.

Note: Antibiotic therapy for 3 days only.

LoE I[2]

Complicated UTI

Antibiotic therapy

Total duration of antibiotic therapy: 7 days.

IMPORTANT
Increase duration to 10–14 days in infants who have acute pyelonephritis or septicaemia.

LoE I[3]

The empiric choice of antibiotics depends on the expected

sensitivity of the suspected organism. Review antibiotic choice once culture and sensitivity results become available.

Oral treatment:
Children > 3 months old who are unwell but not acutely ill and who are not vomiting:
Children with uncomplicated UTI:

- Amoxicillin/clavulanic acid, oral, 25 mg/kg/dose of amoxicillin component 8 hourly.

Parenteral treatment:
All neonates and acutely ill infants should preferably be treated parenterally for the first few days until temperature has normalised and they are able to tolerate feeds.

- Amoxicillin/clavulanic acid, IV, 25 mg/kg/dose 8 hourly.

OR

- Cefotaxime, IV, 50 mg/kg/dose 8 hourly.

If there is no improvement after 24 hours of IV amoxicillin/clavulanic acid treatment, a resistant organism may be the cause and treatment should be according to culture. Consult a specialist.

If there is evidence of good clinical response to amoxicillin/clavulanic acid alone, change to:

- Amoxicillin/clavulanic acid, oral, 25 mg/kg/dose of amoxicillin component 8 hourly.

Penicillin allergy:
See Chapter 24: Drug allergies, section 24.4.1: Allergies to penicillin.

For pain:

- Paracetamol, oral, 15 mg/kg/dose, 6 hourly as required.

For children with a structural or functional abnormality of the urinary tract:
Investigate for recurrent UTIs if the patient has a temperature > 38.5˚C or symptoms of a urinary tract infection by performing a urine strip test.

If positive for leucocytes and/or nitrites are present in fresh urine, collect urine aseptically for MCS and treat empirically as above for a urinary tract infection.

Prophylactic antibiotic therapy
Prophylaxis may be indicated in specific risk groups, i.e. for children < 2 years of age and who have a structural or functional abnormality of the urinary tract associated with increased risk of recurrent infections, i.e.

grade III or more vesico-ureteric reflux. In this setting, consult nephrologist and microbiologist.

Asymptomatic bacteriuria does not require treatment.
Use of long-term prophylactic antibiotic therapy for UTIs is not recommended.

REFERRAL

» Poor response to adequate therapy, i.e. persistent positive urine culture and/or fever.
» If complicated urinary tract infection, i.e. obstruction is suspected or renal failure present.
» If recurrent urinary tract infections or repeated positive pure culture of any micro-organism.

6.3 NEPHROTIC SYNDROME (NS)

N04

DESCRIPTION

Nephrotic syndrome (NS) is a clinical syndrome associated with massive proteinuria due to increased permeability of the glomerular basement membrane. Most children have primary (idiopathic) nephrotic syndrome associated with minimal change nephrotic syndrome (MCNS) or focal segmental glomerulosclerosis (FSGS). In an undefined proportion of patients, the disease is caused by genetic mutations in podocyte specific genes. Main causes of secondary nephrotic syndrome include infections (HIV, Hepatitis C), Systemic lupus erythematosus (SLE) and reflux nephropathy.

Main complications:

» Increased risk of infections with encapsulated organisms, *S. pneumoniae, E. coli.* Chicken pox and measles are the main major viral infections.
» Hypercoagulable state: increased risk of arterial and venous thrombosis. Aggressive investigation and treatment may be necessary to prevent fatal pulmonary embolism.

DIAGNOSTIC CRITERIA

Clinical

» Massive proteinuria.
» Hypo-albuminaemia.
» Oedema.
» Hyperlipidaemia (hypercholesterolaemia).
» Usually normal blood pressure.

» Transient microscopic haematuria and/or hypertension in 25% of children.
» Usually normal renal function.

Investigations

» Urine test strip: ≥ 3+ proteinuria; may have trace to 1+ haematuria.
» Spot random urine sample protein:creatinine ratio: > 0.2 g/mmol.
» Urine microscopy: hyaline and lipid casts. May have occasional red and white blood cells.
» Serum albumin: < 25 g/L.
» Serum urea and creatinine and electrolytes usually normal.
» Serum cholesterol: increased.
» Investigations to exclude secondary causes of nephrotic syndrome, including: ASO and anti-DNAse B titre, Hepatitis B s-antigen, Hepatitis C antibody, RPR, HIV and CMV antibodies.
» C_3 and C_4
» Antinuclear factor antibody and anti-dsDNA.

A presumptive diagnosis of MCNS can be made in children who are 2–6 years old and who have:

» normal blood pressure,
» normal renal function,
» only a trace/1+ haematuria, but no red cell casts,
» normal complement levels, and
» in whom secondary causes have been excluded.

GENERAL AND SUPPORTIVE MEASURES

» Monitor fluid balance.
» Monitor urine output strictly and weigh daily (1 kg = 1 L of fluid).
» Assess hydration status.
  > Suspect:
    - Hypovolaemia: in the presence of hypotension, small pulse volume and cold extremities.
    - Normovolaemia: with normal moist mucosa and normal blood pressure with well perfused limbs.
  > Replace ongoing extra-renal losses as for a dehydrated child, e.g. oral rehydration for gut losses, etc.

Continued weight gain or anuria is an indication for referral.

» Dietary measures:
  > Do not restrict oral fluid intake.
  > Restrict salt intake in all patients. No salt should be added during preparation of food and there should be no salt on the table during meals. Restrict all salt-preserved foods.
  > Limit intake of saturated fat.
  > Normal energy intake.

> Normal protein diet for all with normal renal function.

MEDICINE TREATMENT

Specific treatment of causative conditions where possible, e.g.

» HIV infection.
» Syphilis infection.
» SLE.
» Streptococcal infection.

For hypovolaemia (hypovolaemic shock):

- Sodium chloride 0.9%, IV, 10ml/kg bolus, immediately over 20–30 minutes.

LoE III

Replace ongoing extra-renal losses as for a dehydrated child, e.g. oral rehydration solution for gut losses, etc.

Note: Beware of intravascular volume depletion which can be induced by over aggressive diuresis. In patients with oedema, exclude hypovolaemia prior to the administration of furosemide.

For patients with oedema and hypervolaemia:

- Furosemide, oral, 1 mg/kg/dose, 12 hourly.

LoE III [4]

AND

- Potassium chloride (100 mg/ml), oral, 75–225 mg/kg/day (1–3 mmol/kg/day or 0.75–2.25 ml/kg/day) in divided doses.
  - Monitor serum potassium.

For patients with intractable oedema who fail to improve with furosemide treatment only:
ADD

- Hydrochlorothiazide, oral, 1 mg/kg, once daily.
  - Do not exceed 12.5 mg daily.

For severe ascites:
Add

- Spironolactone, oral 1.5–2.5 mg/kg/dose, 12 hourly.

For short-term treatment of congenital nephrotic syndrome and for patients with oedema (anasarca), volume contraction and oliguria:

- Albumin, human 20% (salt-poor solution), IV, 1 g/kg (i.e. 5 mL/kg) administered over 5 hours on 2 consecutive days.

AND

- Furosemide, IV, 2 mg/kg, slow IV infusion over 5 hours, i.e. 0.4 mg/kg/hour.

For all children with non-remitting nephrotic syndrome:

- Multivitamin, oral, 5 mL daily.
  (Formulation to include pyridoxine, other B vitamins, vitamin C 30 mg and vitamin D 400 IU.)
- Folic acid, oral, 5 mg daily.
- Calcium (elemental), oral, 10–15 mg/kg/dose, 12 hourly.
  - Maximum dose: 1000 mg (1 g) daily.
  - Calcium carbonate 420 mg = 168 mg elemental calcium.

Give all children with non-remitting nephrotic syndrome renoprotective treatment as for patients with chronic renal failure.

IMPORTANT
Renoprotective strategies are not indicated in children with steroid responsive nephrotic syndrome.

- **ACE inhibitor**

An ACE inhibitor is given to decrease proteinuria, irrespective of presence or absence of systemic hypertension. Begin with low dosage and titrate against response and blood pressure.

  - Enalapril, oral, 0.1 mg/kg once daily.
    - Increase dose to 0.5 mg/kg/day, as a single dose or two divided doses.
    - Monitor for adverse effects: hyperkalaemia (increased risk when potassium-sparing diuretic is used simultaneously) and acute renal failure (increased risk in children with impaired renal function or volume depletion).
    - Do not use if estimated CrCl < 30 mL/minute.

Cholesterol lowering drugs

For children > 8 years who have non-remitting nephrotic-range proteinuria and persistent cholesterol levels > 7 mmol/L:

- HMGCoA reductase inhibitors (statin), e.g.:
  - Simvastatin, oral, 10 mg at night.

Immunisation

Do not give live vaccines to patients receiving steroid and other immunosuppressive treatment.

Once in remission

Provide all other EPI vaccines according to the schedule.

In children > 2 years who received conjugate pneumococcal vaccine 13:

- Pneumococcal vaccine (polysaccharide), IM, 0.5 mL as a single dose.

Give:

- Varicella-zoster vaccine, 0.5 mL, SC, 2 doses 6 weeks apart.

Check Hepatitis B immunity. In the absence of any immunity:

- Hepatitis B vaccine, IM, 1 mL, 3 doses one month apart.
  - If the antibody level is considered non-protective or insufficient, give 2 booster doses one month apart.

Prophylactic antibiotics

For patients with anasarca who have an increased risk for spontaneous pneumococcal peritonitis, there is no evidence that prophylactic antibiotics are beneficial.

Spontaneous bacterial peritonitis

- Ceftriaxone, IV, 50 mg/kg/dose 12 hourly for 5 days.

LoE II[5]

Corticosteroids

Initiate corticosteroid treatment only in consultation with a specialist.

In the absence of a histological diagnosis, empiric steroid treatment should only be given to children with presumed minimal change disease where a rapid response is expected.

In patients with initial macroscopic haematuria, persistent hypertension, persistently low C_3 and renal function impairment, a diagnosis other than MCNS is suggested. These cases should be referred for kidney biopsy before steroid treatment is given.

Initial treatment (first course of steroid treatment)

- Prednisone, oral, 2 mg/kg/dose as a single dose in the morning for 4 weeks.
  - Maximum dose: 60 mg daily. If in remission:
  - Taper dose over next 16 weeks as follows:
    - 2 mg/kg/dose as a single dose on alternate mornings for 4 weeks.
    - 1.5 mg/kg/dose as a single dose on alternate mornings for 4 weeks.
    - 1 mg/kg/dose as a single dose on alternate mornings for 4 weeks.
    - 0.5 mg/kg/dose as a single dose on alternate mornings for 4 weeks.

A shorter initial treatment course, i.e. 8 weeks vs. 20 weeks, is associated with more frequent relapses.

If the patient fails to achieve remission after 4 weeks of treatment, continue with the high dose (2mg/kg to a max of 60mg/kg) for another 4 weeks (maximum of 8 weeks). Patients who go into remission must then use the tapering regimen above. Patients who fail to go into remission after 8 weeks

of steroid treatment are considered steroid-resistant and should be referred for kidney biopsy.

IMPORTANT

Long-term corticosteroid treatment suppresses adrenal function. Therefore, additional steroids or steroid supplementation is necessary during periods of acute stress, e.g. surgery or septic shock.

Assessment of treatment response

For practical reasons, a urine strip test is usually performed on a spontaneously voided urine sample instead of a 24-hour urine sample.

» Test urine every morning during corticosteroid treatment.
» Urine strip tests should be negative for a minimum of 3 consecutive mornings before decreasing the dose.
» If proteinuria recurs, go back one step in the suggested dose for a few more days before again attempting to decrease the dose.

Classifying treatment responses

» **Remission**: No/trace protein on urine test strips for 3 consecutive days (spot sample urine protein:creatinine ratio < 0.02 g/mmol).
» **Steroid-sensitive NS**: No/trace protein on urine test strips for 3 consecutive days within 4 weeks after start of high dose oral prednisone therapy.
» **Steroid-dependent NS**: Relapse develops during tapering of steroid treatment or within 2 weeks after stopping treatment.
» **Steroid-resistant NS**: Failure to achieve remission in spite of maximum 8 weeks of treatment with prednisone 2 mg/kg/day. (Spot sample urine protein:creatinine ratio > 0.02 g/mmol).
» **Relapse of NS**: 3+ proteinuria on urine test strips or urine protein:creatinine ratio > 0.2 g/mmol for 3 consecutive days.
» **Frequently-relapsing NS**: Two or more relapses per 6 months or ≥ 4 per 12-month period.

Schedule for relapse: similar to the initial course, but for a shorter period:

- Prednisone, oral, 2 mg/kg/dose as a single daily dose for minimum of one week. Urine test strips should be negative for minimum of 3 consecutive mornings before the dose is decreased.
- Then taper dose as follows:
  - 2 mg/kg/dose as a single dose on alternate mornings for 2 weeks.
  - 1.5 mg/kg/dose as a single dose on alternate mornings for 2 weeks.
  - 1 mg/kg/dose as a single dose on alternate mornings for 2 weeks.
  - 0.5 mg/kg/dose as a single dose on alternate mornings for 2 weeks.

- If proteinuria recurs, go back one step in the suggested dose for a few more days before again attempting to decrease the dose.

Second-line immunosuppressive treatment

» Second-line immunosuppressive treatment is indicated in children with steroid-sensitive nephrotic syndrome with frequently-relapsing NS, steroid-dependent NS and in those with steroid toxicity.

» It should only be prescribed after consultation with a paediatric nephrologist. It remains the prescriber's responsibility to monitor the patient at regular intervals for side-effects of treatment.
  > Full blood count, urea, creatinine, electrolytes and albumin needs to be done every 10–14 days throughout the course of treatment.

» Second-line immunosuppressive treatment for steroid-sensitive nephrotic syndrome should only be started when the urine strip test is negative.

» It is always given in combination with steroid treatment.

» Kidney biopsy is preferably done before second-line immunosuppressive treatment is started due to the risks associated with this treatment.

» Immunosuppressive therapy – nephrologist initiated:
  - Cyclophosphamide, oral, 2 mg/kg/dose once daily for 12 weeks.
  - Ensure adequate fluid intake to avoid haemorrhagic cystitis.

IMPORTANT
Children with steroid-resistant nephrotic syndrome do not benefit from treatment with cyclophosphamide and should be referred to a paediatric nephrologist.

REFERRAL

» All with congenital nephrotic syndrome.

» All with clinical features and/or laboratory results, which suggest a diagnosis other than MCNS, e.g. initial macroscopic haematuria, persistent hypertension, persistently low C_3 and renal function impairment.

» Patients with steroid-resistant nephrotic syndrome.

» All patients before second-line immunosuppressive treatment is prescribed.

6.4 ACUTE KIDNEY INJURY (RENAL FAILURE, ACUTE)

N17.9

DESCRIPTION

Acute kidney injury (AKI) is a syndrome characterised by a rapid decline in glomerular filtration rate and retention of fluid and nitrogenous waste products. It often presents as a continuum of volume responsiveness 'pre-

renal AKI' up to a point of volume unresponsiveness. AKI is classified as pre-renal, renal and post-renal failure.

Levels of AKI are defined by pRIFLE criteria (mnemonic p=paediatric, Risk, Injury, Failure, Loss and End Stage Renal Failure).

Paediatric modified RIFLE (pRIFLE) criteria

Level	Estimated creatinine clearance (eCrCl)*	Urine output
1	↓ eCrCl by 25%	< 0.5 mL/kg/hour for 8 hours
2	↓ eCrCl by 50%	< 0.5 mL/kg/hour for > 16 hours
3	↓ eCrCl by 75%	< 0.5 mL/kg/hour for > 24 hours or anuria for 12 hours

The previous method of measuring creatinine clearance using a 24-hour urine sample is not recommended due to the difficulty in obtaining an accurate 24-hour urine collection in children. A calculated glomerular filtration rate can be ascertained using the height of the child (in cm), the serum creatinine (in µmol/L) and a factor 'K'. (**Modified Schwartz formula**).

$$*\text{eCrCl (mL/min/1.73 m}^2\text{)} = \frac{[\text{K x height (cm)}]}{\text{S-creatinine (µmol/L)}}$$

Value of K	
Low birth weight (< 2.5 kg) infant	30
Infant 0–8 months	40
Girls 2–16 years	49
Boys 2–12 years	49
Boys 13–16 years	60

LoE III[6]

Normal values for GFR in children:

Age	Mean GFR (ml/min/1.73 m^2)	Range
Birth	20	
7 days	40	25–60
1 month	50	30–70
6 months	75	40–100
12 months	115	65–160
2–12 years	125	90–165

DIAGNOSTIC CRITERIA

Clinical

» In neonates, exclude a congenital abnormality of the urinary tract.

» Oliguria is the most common manifestation, i.e.:
  Neonates: output < 1 mL/kg/hour.
  Older children: output ≤ 0.3 mL/kg/hour.
» Pre-renal: shock and dehydration.
» Post-renal: exclude obstruction, e.g. a palpable bladder.
» Intrinsic kidney disease: oedema, volume overload, hypertension.
» Signs of underlying infection/septicaemia, e.g. fever, skin rash, etc.

Investigations
» Urine macroscopic appearance: brownish with acute tubular necrosis.
» Urine test strip: haematuria, proteinuria indicative of glomerular disease; leucocytes and nitrites in favour of pyelonephritis.
» Urine microscopy: red blood cell casts, leukocyte, hyaline and granular casts.
» Urine culture to exclude pyelonephritis.
» Urine biochemistry:

	Pre-renal failure	Intrinsic renal failure
U-Osmolality (mOsmol/L)	↑ > 320	Equal to serum osmolality
FeNa (%)*	< 1	≥ 3

$$\text{Fractional excretion of sodium (\%)} = \frac{\text{Urinary sodium}}{\text{Urinary creatinine}} \times \frac{\text{Serum creatinine}}{\text{Serum sodium}} \times 100$$

*FeNa becomes an invalid test for pre-renal failure if the child has received furosemide.

Note: Serum creatinine is measured in micromol/L (µmol/L) and urine creatinine in millimol/L (mmol/L). To convert micromol/L to millimol/L ÷ by 1000.

» Ultrasound of kidneys and bladder.
» Serum urea, urate, creatinine, electrolytes and osmolarity, glucose, calcium, phosphate and albumin.
» Typical biochemistry: hyperkalaemic metabolic acidosis, hyponatraemia, hypocalcaemia, hyperphosphataemia.
» Full blood count, differential and platelet count.
» Clotting profile.
» Cultures and DIC workup as indicated.
» ECG to exclude life-threatening hyperkalaemia.
» Chest X-ray to evaluate cardiomegaly, pleural effusions and pulmonary oedema.

GENERAL AND SUPPORTIVE MEASURES
» Treat the underlying cause.
» Monitor fluid intake and output, blood pressure.
» Weigh daily.
» Nutritional support:

> High-energy diet. Give supplementary nasogastric feeds, if required. Infants should preferably be given breast feeds or an infant milk formula.
> Daily requirements:
- Protein: 1 g/kg maximum
- Carbohydrate: 2–3 g/kg
- Fat: 2 g/kg

» Restrict NaCl, potassium and phosphate intake.
» Restrict protein intake when serum urea > 25 mmol/L.

Avoid nephrotoxic or renally excreted medicines, e.g.

NSAIDs, aminoglycosides, vancomycin, cough and cold mixtures, radiocontrast drugs.

» Fluid management:
> Depends on volume status, urine output and extra-renal losses.
> Never use a potassium-containing solution in an anuric patient.
> Only use parenteral fluids if oral intake is not possible.

IMPORTANT

Fluid balance is critical. Assess at a minimum, every 12 hours to make appropriate changes to the fluid prescription.

» Fluid management according to fluid status:

IMPORTANT

Insensible water loss is calculated as:
- Neonates and young babies: 30–40 mL/kg/day
- Older children: 25 mL/kg/day (400 mL/m^2/day)

> **Pulmonary oedema plus oliguria/anuria**: Do not give fluid.
> **Hydrated anuric patient without extra-renal fluid losses**: Oral fluid to replace insensible water losses only.
> **Normally hydrated plus oliguria**: Oral fluid intake to replace insensible water loss plus urine output of previous 24 hours.
> **Dehydrated, oliguric and ongoing extra-renal fluid losses**: Replace fluid losses with an appropriate solution which mirrors losses, e.g.:
- for diarrhoea: ½ Darrows/dextrose 5%, IV or oral rehydration solution;
- for vomiting/gastric fluid losses: sodium chloride 0.9% /dextrose 5%.

> **Normally hydrated plus normal urine output:** Give normal fluid intake.

> **Shock**: See Chapter 1: Emergencies and Trauma, section 1.1.7: Shock.
> **Polyuria** (urine output > 4 mL/kg/hour): which usually occurs during the recovery (diuretic) phase of acute tubular necrosis: Replace fluid and electrolyte losses with ½ Darrows/dextrose 5%, IV. Volume to replace is equal to urine output of preceding 12 hours.

MEDICINE TREATMENT

Hyperkalaemia

Monitor ECG for signs of hyperkalaemia.
Discontinue all sources of intake of potassium.
Treat when serum potassium > 6.5 mmol/L.
Monitor response to treatment and adjust accordingly.

- Calcium gluconate 10%, IV, 0.5 mL/kg/dose slowly over 3–5 minutes.
- Salbutamol, solution, 2.5–5 mg/dose, nebulised over 20 minutes.
  (0.5–1 mL salbutamol in 2–4 mL sodium chloride 0.9%.)
  OR
  Salbutamol, IV, 4 µg/kg in 5 mL water administered over 30 minutes.

- Sodium bicarbonate 4.2%, IV, 4 mL/kg administered over 4 hours.
  - Do not mix calcium and sodium bicarbonate-containing solutions.

Check potassium level, and if there is still no improvement:

- Dextrose 10%, IV, 5 mL/kg over 20 minutes **with/without** insulin, soluble, 0.1 units/kg depending on the blood glucose level.
  - If insulin is used, monitor for hypoglycaemia hourly.
- Sodium polystyrene sulphonate, oral/rectal, 1 g/kg in dextrose water.

If hyperkalaemia persists despite above treatment, refer the patient urgently for dialysis.

OTHER COMPLICATIONS

Metabolic acidosis: serum pH ≤ 7.1

- Sodium bicarbonate 4.2%, IV, 4 mL/kg administered over 2–4 hours.
  - Do not mix calcium and sodium bicarbonate containing solutions.

Hypertension

See Chapter 4: Cardiovascular System, section 4.11: Hypertension in children.

Infection

Avoid nephrotoxic antibiotics.

Uraemic convulsions

See Chapter 13: The Nervous System, section 13.1: Seizures.

» Exclude specific causes of convulsions, e.g. hypoglycaemia, hyper- or hyponatraemia, hypocalcaemia or hypertension and treat accordingly.
» Ensure urea levels are appropriately high.
» Refer for urgent dialysis.

Anaemia

For acute blood loss/active haemolysis and Hb < 7 g/dL:

- Packed red blood cells, IV, 10 mL/kg administered over 6 hours.

Pulmonary oedema, volume overload and hypertension

Do not give fluid to anuric patients with pulmonary oedema.
Intubate and initiate positive pressure ventilation as necessary.

- Furosemide, IV, 2–5 mg/kg administered over 5 minutes.
  - Maximum daily dose: 8 mg/kg/24 hours.

- Morphine, IV, 0.1 mg/kg.
  - Repeat after 4 hours, if required.

- Oxygen, 100%, 2–3 L/minute by nasal cannula.

Pulmonary oedema is an indication for dialysis in non-responsive cases.

REFERRAL

Urgent for dialysis when:

» Fluid overload is causing pulmonary oedema.
» Anuria > 24 hours.
» Central nervous system signs, e.g. convulsions or coma.
» Uraemic bleeding diathesis.
» Uraemic pericarditis.
» Hyperkalaemia or hyponatraemia not responding to conservative treatment.
» Persistent metabolic acidosis, pH < 7.1 or serum bicarbonate < 10 mmol/L.
» Uncontrollable hypertension.
» Severe hyperphosphataemia and/or hypocalcaemia.

6.5 CHRONIC KIDNEY DISEASE (RENAL FAILURE, CHRONIC)

N18.9

DESCRIPTION

Chronic kidney disease (CKD) is defined 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/1.73 m^2".

It is characterised by a progressive decline in renal function to end-stage renal failure due to progressive loss of functioning glomeruli and is accompanied by the onset or worsening of proteinuria.

A calculated glomerular filtration rate can be ascertained using the height of the child (in cm), the serum creatinine (in µmol/L) and a factor 'K'. (**Modified Schwartz formula**).

$$\text{eCrCl (mL/min/1.73 m}^2\text{)} = \frac{\text{[K x height (cm)]}}{\text{S-creatinine (µmol/L)}}$$

Value of K	
Low birth weight (< 2.5 kg) infant	30
Infant 0–18 months	40
Girls 2–16 years	49
Boys 2–12 years	49
Boys 13–16 years	60

Staging of chronic kidney disease (KDQOI definition)

Stage	*eGFR (mL/min/1.73 m^2)	Features
0	≥ 90	Screening of 'at-risk for CKD' patients.
1	≥ 90	Renal parenchymal disease presents with normal eGFR – monitor annually.
2	60–89	Usually asymptomatic – biochemical abnormalities present – monitor annually.
3	30–59	Biochemical abnormalities and poor growth, poor appetite – monitor 3–6 monthly.
4	15–29	Severe disease – consider renal replacement therapy.
5	< 15 (ESRF)	End-stage renal failure – consider renal replacement therapy.

*eGFR: estimated glomerular filtration rate

DIAGNOSTIC CRITERIA

Renal function may deteriorate without clinical symptoms.

» Children are likely to present with acute-on-chronic renal failure during episodes of acute intercurrent illness.
» Poor weight gain and stunting.
» Poor appetite, chronic constipation, polydipsia and polyuria.
» Children with renal tubular disorders or bilateral renal dysplasia have obligatory salt wasting and are often unable to concentrate urine. This

may result in severe dehydration and metabolic acidosis if they do not have free access to water.
» May present with tachypnoea mimicking acute 'respiratory distress' to compensate for metabolic acidosis.
» Chronic anaemia.
» Renal osteodystrophy, i.e. bone pain and skeletal deformities.
» Volume overload: oedema, hypertension, heart failure, pulmonary oedema.
» Uraemic symptoms and signs: nausea, vomiting, pruritus, brownish skin pigmentation, uraemic frost.
» Bleeding tendency (mucosal).
» Convulsions due to hyponatraemia, hypernatraemia, hypocalcaemia, uraemia or hypertension.

Investigations

» Urine:
  > Protein:creatinine ratio is usually increased (normal < 0.02 g/mmol).
  > Iso-osmolar, i.e. urine osmolality ~ 300–350 mOsmol/L (normal maximal urine concentration > 1000 mOsmol/L).
» Urine volume may be:
  > normal, or
  > increased (polyuria): > 4 mL/kg/hour, or
  > decreased (oliguria): < 1.0 mL/kg/hour.
» Urine test strip:
  > May be normal or reveal proteinuria, haematuria, glycosuria.
  > Nitrites and leucocytes may indicate UTI. Do urine MCS.
» Urine microscopy:
  > May be normal or reveal casts.
  > Pus cells, leucocyte casts and bacteria may indicate UTI. Do urine MCS.
» Serum urea:
  > Increased, depending on hydration, nutritional state and protein intake.
» Serum creatinine is a better indicator of renal function than serum urea but:
  > It is influenced by age of the child and muscle bulk.
  > It may be only mildly increased in a malnourished child with little muscle bulk despite advanced renal failure (serum creatinine only starts increasing once renal function has fallen to less than half normal).
» Serum electrolytes:
  > Hyperkalaemia.
  > Hyperchloraemia and decreased bicarbonate.
» Calcium, phosphate and ALP:
  > Decreased calcium.
  > Increased phosphate.
  > Increased ALP.

» Plasma parathyroid hormone:
  > Increased.
» Renal ultrasound:
  > To exclude obstruction.
  > Small shrunken kidneys are indicative of chronic renal failure.

There is no place for renal biopsy in patients with end-stage renal failure.

GENERAL AND SUPPORTIVE MEASURES

» Determine and treat the underlying cause of chronic renal failure.
» Monitor fluid intake and output, and blood pressure.
» Weigh daily.
» If in respiratory distress due to volume overload:
  > Place in sitting position.
  > Give oxygen, 100%, 2–3 L/minute by nasal prongs.
» Dietary management:
  > Monitor potassium closely.
  > Limit potassium intake if serum potassium > 5.5 mmol/L.
  > Restrict fruit juices, dried fruit, all citrus fruits, bananas, guavas and tomatoes.
  > All vegetables should either be soaked for 24 hours before cooking or water should be decanted twice during cooking.
  > Restrict phosphate once serum phosphate reaches or exceeds the upper limit of normal for age, usually > 1.8 mmol/L and when GFR < 70 mL/min/1.73 m^2.
  > Limit dairy products and other foods with high phosphate content like grains and cereals, carbonated cool drinks, etc.
  > Do not limit protein intake.
  > Restrict salt intake. No salt should be added during preparation of food, no salt on the table during meals and restrict all salt-preserved foods. Generally, salt is restricted for hypertensive, oedematous patients, but not for patients with salt-losing nephropathies who are polyuric, unless they are hypertensive.
  > High-energy diet with supplementary nasogastric feeds or nocturnal fluids for children with poor appetite, polyuria/nocturia and with inadequate intake to maintain growth.
» Fluid management:
  > Depends on underlying kidney disease.
  > Use body weight to guide fluid prescription.
  > Only use parenteral fluids if oral intake is not possible.
  > Children with tubular abnormalities may be unable to concentrate their urine and, therefore, require free access to water.
  > **Anuric**: Fluid to replace insensible water losses only.
    Use an electrolyte-free solution, i.e. dextrose 5% or 10%, IV.
    Insensible water loss is calculated as:
    - Neonate and young baby: 30–40 mL/kg/day.
    - Older children: 25 mL/kg/day (400 mL/m^2/day).

> **Oliguric with oedema and hypertension**

> **Total volume of fluid allowed is calculated as**:

INSENSIBLE WATER LOSS:
- Neonate and young baby: 30–40 mL/kg/day.
- Older children: 25 mL/kg/day (400 mL/m^2/day).

Use an electrolyte-free solution, i.e. dextrose 5% or 10%, IV.

PLUS
50% of urine output.

PLUS
Extra-renal losses (volume for volume).
Use a potassium-free solution, e.g. sodium chloride 0.9%.
Once euvolaemic, give same fluids as above to replace 100% of urine output.

> **Dehydrated and hypotensive**: Give sodium chloride 0.9%, IV bolus immediately and re-assess.
Repeat bolus, if necessary.
Strictly monitor urine output and fluid losses.

MEDICINE TREATMENT

Avoid nephrotoxic agents and appropriately adjust renally excreted medicines, e.g. NSAIDs, aminoglycosides, vancomycin, amphotericin B, radiocontrast drugs.

Vitamins and minerals
- Multivitamin, oral, 5 mL daily.
  (Formulation to include pyridoxine, other B vitamins, vitamin C 30 mg and vitamin D 400 IU.)

AND
- Folic acid, oral, 5 mg daily.

For management of hyperphosphataemia/osteodystrophy and hyperparathyroidism:
In combination with restricted dietary intake of phosphate:
- Calcium carbonate, oral, 1–4 tablets chewed 8 hourly with meals.
  - 1 tablet is equivalent to 0.168 g elemental calcium.
- Alfacalcidol, oral, 0.25 µg daily. Specialist initiated.

- If serum phosphate is > 2.5 mmol/L, treat the hyperphosphataemia first with:

- Dietary modification.
- Calcium (elemental), oral, 10–15 mg/kg/dose, 12 hourly.
  - Maximum dose: 1000 mg (1 g) daily.
  - Calcium carbonate 420 mg = 168 mg elemental calcium.

To decrease to below 1.8 mmol/L before beginning the alfacalcidol (to avoid metastatic calcification).

In patients with serum calcium < 2.2 mmol/L start alfacalcidol early:

- Alfacalcidol, oral, 0.25 µg, initially twice weekly. Specialist initiated.
  - Increase dose as necessary to maintain serum calcium in upper-normal range.

Chronic metabolic acidosis

If serum bicarbonate < 18 mmol/L:

- Sodium bicarbonate, oral, 1 mmol/kg/dose, 2–3 doses per day after meals.
  - Adjust according to response.

  Note: The intravenous formulation can be given orally.

Hyperkalaemia

Discontinue all medicines that may cause hyperkalaemia, e.g. potassium sparing diuretics, spironolactone, ACE inhibitors.
Exclude volume depletion as an underlying cause for hyperkalaemia.

If serum potassium remains > 5.5 mmol/L:

- Sodium polystyrene sulphonate, oral/rectal, 1 g/kg/dose in dextrose water, once or twice daily.
  - Treat accompanying metabolic acidosis.

Anaemia

Ensure adequate intake of haematinics.
Ensure adequate iron stores. Measure ferritin, transferrin, transferrin saturation and total iron binding capacity.
Avoid transfusions if possible due to the risk of developing antibodies in a patient who may be a potential candidate for renal transplantation.

If a patient has symptomatic anaemia, haemoglobin usually < 7 g/dL:

- Packed red blood cells, IV, 10 mL/kg administered over 6 hours.

If the patient has a persisting haemoglobin level < 8 g/dL despite correction of possible deficiencies of iron, folic acid or vitamin B_{12}, start recombinant human erythropoietin (rHuEPO) in consultation with a paediatric nephrologist.

Note:
Blood pressure must be controlled before starting rHuEPO treatment.
Dose of erythropoietin is gradually increased according to increase in haemoglobin. Target haemoglobin is 10–12 g/dL.

- Erythropoietin, SC, 75 units/kg/week in divided doses 2–3 times a week.
  - Monitor Hb levels every 4 weeks.
  - Adjust dose until target haemoglobin level of 12 g/dL is reached. Continue with this dose.
  - If the Hb level is increasing, do not change dose.
  - If the Hb level remains unchanged, increase by 25% at 4-week intervals until a maximum dose of 300 units/kg/week is reached.
  - If Hb level increases > 12 g/dL, stop treatment for one week. Thereafter, continue with 25% less than the previous dose per week.

For persistent anaemia:
Refer to tertiary centre for nephrologist assessment.

Hypertension
See Chapter 4: Cardiovascular System, section 4.11: Hypertension in children.

Dyslipidaemia
Dyslipidaemia may contribute to the progression of chronic kidney disease, particularly in children with nephrotic syndrome. Hypertriglyceridaemia and abnormal apolipoprotein metabolism is a feature of CRF. Dietary intervention is necessary, including limiting saturated fat and cholesterol intake.

For children > 8 years with persistent total cholesterol levels > 7 mmol/L:
- HMGCoA reductase inhibitors (statins), e.g.:
  - Simvastatin, oral, 10 mg at night.
    - Maximum dose: 20 mg at night.

Refer for advice on management.

Renoprotective treatment
All children with persistent nephrotic-range proteinuria and GFR > 30 mL/minute:
- ACE inhibitor (with nephrologist supervision).
  - Enalapril, oral, 0.1 mg/kg/dose, once daily.
    - Increase dose to 0.5 mg/kg/day, as a single dose or two divided doses.
    - Monitor for adverse effects: hyperkalaemia (increased risk when potassium-sparing diuretic is used simultaneously) and acute renal failure (increased risk in children with impaired renal function or volume depletion).
    - May cause hyperkalaemia, worsening metabolic acidosis and declining renal function while reducing proteinuria.
    - Monitor serum urea and electrolytes, i.e. serum potassium and bicarbonate, and renal function within 7 days.
    - If serum creatinine has doubled, check hydration status, stop diuretics and halve the dose of ACE inhibitors.

- If renal function does not improve, or hyperkalaemia > 5.5 mmol/L persists, stop ACE inhibitor treatment.

Immunisation
Give all EPI vaccines according to the schedule.
Provide all routine vaccinations or missing vaccinations in older children.
Check immunity against chicken pox and Hepatitis B.

In children > 2 years of age:
- Pneumococcal vaccine (polysaccharide), IM, 0.5 mL as a single dose.

In the absence of any immunity against chickenpox, give:
- Varicella-zoster vaccine, SC, 0.5mL, 2 doses 6 weeks apart.

In the absence of immunity against Hepatitis B, vaccinate as for any non-immune individual.
- Hepatitis B vaccine, IM, 1 mL, 3 doses one month apart.
  - If the antibody level is considered non-protective or insufficient, give 2 booster doses one month apart.

REFERRAL
» All children with chronic kidney disease.
» Patients with dyslipidaemia or hypercholesterolaemia.

6.6 ENURESIS
R32

See Chapter 14: Child and Adolescent Psychiatry, section 14.2.1: Enuresis.

6.7 DYSFUNCTIONAL BLADDER
N31

DESCRIPTION
Abnormalities of filling or emptying of the bladder, i.e. underactive or overactive bladder. Aetiology may be neurogenic, anatomical or functional.

DIAGNOSTIC CRITERIA
Clinical features include:
» Daytime frequency
» Incontinence
» Urgency
» Nocturia
» Hesitancy
» Straining
» Weak stream
» Dysuria
» Holding manoeuvres
» Post-micturition dribbling

Conditions include:

- Overactive bladder (OAB)
- Voiding postponement
- Underactive bladder
- Dysfunctional voiding
- Obstruction
- Stress incontinence
- Vaginal reflux
- Giggle incontinence

Common in co-morbid neurological and behavioural problems.

GENERAL AND SUPPORTIVE MEASURES

- Screen for UTI. See section 6.2: Urinary tract infections.
- May have concomitant constipation – bowel management is essential in management. See Chapter 2: Alimentary Tract, section 2.2.2: Constipation/Faecal loading.
- Intermittent catheterisation is necessary with large post-void residual volumes. Check post-void volume by catheterisation after voiding.
- Symptomatic school-going children may develop anxiety. See Chapter 14: Child and Adolescent Psychiatry, section 14.5: Anxiety disorders.

REFERRAL

All for assessment.

References

[1] Morphine Dose: South African Medicines Formulary (SAMF), 12th Edition. Division of Pharmacology, Faculty of Health Sciences, University of Cape Town. 2016.
[2] Michael M, Hodson EM, Craig JC, Martin S, Moyer VA. Short compared with standard duration of antibiotic treatment for urinary tract infection: A Systematic Review of Randomised Controlled Trials. Arch Dis Child. 2002; 87: 118-123.
[3] Stohmeier Y, Hodson EM, Willis N, Webster AC, Craig. Antibiotics for acute pyelonephritis in children. The Cochrane Library. 2014, issue 7.
[4] Furosemide Dose: Shann F. Drug Doses. 15th Edition, 2010. Royal Children's Hospital, Australia.
[5] Dever JB, Sheikh MY. Review article: spontaneous bacterial peritonitis bacteriology, diagnosis, treatment, risk factors, prevention. Alimentary Pharmacology and Therapeutics. 2015, 41: 1116-1131.
[6] Schwartz Formula: Schwartz GJ, Work DF. Measurement and Estimation of GRF in Children and Adolescents. Clin J Am Soc Nephrol. 2009; 4: 1832-1843.