Reviewing the full blood count and biochemistry

- Blood tests were taken at the beginning of treatment, but it is useful to check the blood tests again (taking the blood from a vein with no IV in place).
  - Check the haemoglobin level to see whether there is now a need for a blood transfusion (fresh blood would be best). Studies have shown that the haemoglobin concentration should ideally be above 10 grams/dL when treating shock in children.
  - Check the blood glucose level and treat with 2 mL/kg of 10% dextrose in a neonate and 2–5 mL/kg of 10% dextrose in an older infant or child if the level is less than 2.5 mmol/litre. Also add glucose to any infusion fluid.
  - Check the calcium level, and if the concentration of ionised calcium is less than 1 mmol/litre, give 0.3 mg/kg of 10% calcium gluconate IV slowly (over 30 minutes, as calcium can cause cardiac arrest if given too quickly).
- Consider giving 0.5–1 mmol/kg of sodium bicarbonate (0.5–1 mL/kg of 8.4% sodium bicarbonate) over 15 minutes IV for refractory acidosis that is not responding to fluid resuscitation and effective ventilation.

Steroids

- There is some evidence that IV steroids can be helpful in some cases of septic shock. If the suspected organism is meningococcus or the child has previously been on a prolonged course of steroid treatment (e.g. for nephrotic syndrome), IV hydrocortisone can be given at a dose of 1–2 mg/kg/day in divided doses or as a continuous infusion. Occasionally higher doses up to 50 mg/kg/day have been used.

Further treatment

- Many children with septic shock may respond to the above treatments. For those who have not done so, paediatric intensive or high-dependency care is needed. If this is available, contact should be made with the PICU team as soon as it becomes clear that the child has septic shock. Advice on their care can then be given by experts and arrangements made, if possible, for the child to be ‘retrieved’ by the intensive care team coming to stabilise and transfer them.

Box 5.6.A: Minimum standards

- Accurate weight-measuring scales.
- Fluid input and output charts.
- Urine microscopy, culture and sensitivity.
- Antibiotics: trimethoprim, cephalosporins, amoxicillin, nitrofurantoin, gentamicin, penicillin.
- Blood biochemistry: urea, creatinine, sodium, potassium, chloride, bicarbonate.
- Urinary electrolytes.
- Full blood count.
- Ultrasound scan.
- Blood pressure measurement.
- Furosemide and chlorothiazide.
- Nifedipine or amlodipine, hydralazine, propranolol or atenolol, captopril or enalapril.
- Prednisolone, levamisole and cyclophosphamide.
- IV albumin.
- Analgesia: morphine.
- IV Ringer-lactate solution, Hartmann’s solution, phos- phamid and 5% albumin.
- IV glucose 10% and insulin.
- Sodium bicarbonate, calcium gluconate, calcium reso- nium and calcium carbonate.
- Antihypertensive drugs.

Introduction

Common renal investigations: plasma or serum biochemistry

Electrolytes

Sodium (Na⁺) and potassium (K⁺) assays are essential for the logical management of children with kidney dysfunction. Bicarbonate (HCO₃⁻) is also extremely helpful, but more difficult to measure.

Problems with fluid and electrolyte balance are common in ill children. They can occur in a wide variety of clinical situations and with a wide range of underlying diagnoses. A methodical approach to history taking and clinical examination is therefore essential, and interpretation of biochemical results must always be done in the context of the clinical situation.
TABLE 5.6.A.1 Maintenance water, sodium and potassium requirements

<table>
<thead>
<tr>
<th></th>
<th>Age Preterm</th>
<th>Term</th>
<th>1 year</th>
<th>5 years</th>
<th>12 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium (mmol/kg/24 hours)</td>
<td>5</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Potassium (mmol/kg/24 hours)</td>
<td>5</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Water (mL/kg/24 hours)</td>
<td>200</td>
<td>150</td>
<td>100</td>
<td>75</td>
<td>50</td>
</tr>
<tr>
<td>Fluid (mL/kg/hour)</td>
<td>8</td>
<td>6</td>
<td>4</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

Dehydration and hypovolaemia
Fluid within the body is distributed between the intracellular fluid (ICF) and extracellular fluid (ECF) compartments, the ECF being composed of the intravascular and interstitial components. Differential solute composition of the ICF and ECF compartments is maintained by cell membrane pump activity and solute size and electrical charge. Fluid movement is regulated by a balance between osmotically active solutes and hydrostatic pressure.

It is useful when clinically assessing the fluid volume status of a patient to try to consider which compartment has insufficient or excess volume.

The effects of ECF volume depletion are usually shared between the intravascular and interstitial compartments, and are seen as hypovolaemia and dehydration, respectively. However, assessment can be complex. For example, in a condition like nephrotic syndrome, on examination there may be weight gain and oedema. However, since there is hypoalbuminaemia, and albumin is the primary intravascular osmotic component, the intravascular fluid volume may be low but the total ECF volume is high. Conversely, in acute renal failure there can be weight gain and oedema in a situation where both the total ECF and the intravascular volume are high. In heart failure, oedema can be present with high, normal or low intravascular volume, depending on other additional pathologies. In summary, oedema can occur with high, normal or low intravascular fluid volume, which makes the clinical history and a full examination vitally important for understanding the individual patient.

Often, in dehydration, sodium and water have been lost in an approximately normal ratio and therefore the deficit should be replaced as Ringer-lactate or Hartmann’s solution. Normal saline can be used if these two solutions are unavailable, but it is less satisfactory because large volumes cause the patient to develop a hyperchloremic acidosis, due to the larger chloride load in normal saline than there is in plasma.

Practical point
When prescribing rehydration fluids:
A Make an assessment of volume deficit and replace this as Ringer-lactate or Hartmann’s solution.
B Calculate maintenance fluids and insensible losses.
C Initially estimate, and then measure, ongoing losses and replace them appropriately in volume and content.

Fluid prescription should consist of A + B + C.

Aim to treat cardiovascular collapse or ‘shock’ quickly over the first 1–2 hours. Infuse Ringer-lactate or Hartmann’s solution to restore the circulating blood volume, reviewing to assess the response (see Section 5.5.A), and thereafter use a slow replacement rate so that the total deficit is replaced over at least 24 hours.

In hypernatraemic dehydration, after an acceptable cardiovascular state has been restored, aim to reduce plasma sodium levels slowly over 24–48 hours by altering the sodium concentration of the infusion fluid appropriately, and repeatedly monitoring the rate of fall of the plasma sodium and urinary sodium concentration.

Fluid and electrolyte disorders
Good management depends on measurement of input and output, plus repeated:
- clinical examination
- biochemical data on urine and blood
- weight measurements.

Hyponatraemia
Hyponatraemia is defined as a plasma sodium concentration of less than 130 mmol/litre, and it occurs when there is:
- sodium loss in excess of water loss
- or water gain in excess of sodium gain.

The total body sodium level may be high, low or normal, and therefore initial and ongoing clinical assessment of the extracellular fluid volume is essential.

Hypernatraemia
Hypernatraemia is defined as a plasma sodium concentration greater than 150 mmol/litre, and occurs when there is:
- water loss in excess of sodium loss
- or sodium gain in excess of water gain.

Again, the total body sodium level may be high, low or normal.

TABLE 5.6.A.2 Clinical estimation of ECF volume deficit in dehydration

<table>
<thead>
<tr>
<th></th>
<th>Mild</th>
<th></th>
<th>Moderate</th>
<th></th>
<th>Severe</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3–5% weight loss</td>
<td>Thirsty</td>
<td>Increased severity of the above</td>
<td>Increased severity of the above</td>
<td>Drowsiness, confusion or coma</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mucous membranes dry</td>
<td>Depressed fontanelle</td>
<td>Increased severity of the above</td>
<td>‘Shock’</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Decreased skin turgor</td>
<td>Sunken eyes</td>
<td>Cool peripheries</td>
<td>Cool peripheries</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Tachycardia</td>
<td>Prolonged capillary refill time</td>
<td>Prolonged capillary refill time</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Hypotension</td>
<td>Hypotension</td>
<td></td>
</tr>
</tbody>
</table>
Hypernatraemic dehydration: water loss in excess of sodium loss
Because sodium is the principle ECF osmole, the ECF volume is relatively well maintained, and signs of dehydration and hypovolaemia are less apparent.

Creatinine
Plasma creatinine concentration is the best available, most clinically useful and relatively inexpensive guide to glomerular renal function. It is easily, quickly and cheaply measured on a small blood sample. Individual measurements are of use in determining whether renal function is within the normal range. Sequential measurements are useful for following deterioration or improvements in renal function over a short time scale of hours or days, or over a long time scale of months or years. Although formulae can be used, the following guidelines allow the glomerular filtration rate (GFR) to be estimated in most clinical situations.

The plasma creatinine concentration depends on the bulk of the patient’s muscle (where it is produced) and the patient’s height, so on average men have higher values than women, and older children have higher values than babies, except in the first few days of life (see Table 5.6.A.3). For example, a creatinine concentration of 150 mmol/litre in a well-nourished 5-year-old girl would be three times the upper limit of normal, indicating a GFR of one-third normal. The same creatinine concentration in a very undernourished girl with little muscle bulk would imply a GFR considerably lower than one-third.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Plasma creatinine concentration (micromol/litre)</th>
<th>Plasma creatinine concentration (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well-nourished average man</td>
<td>100</td>
<td>1.15</td>
</tr>
<tr>
<td>Well-nourished average woman</td>
<td>75</td>
<td>0.85</td>
</tr>
<tr>
<td>Well-nourished average 10-year-old child</td>
<td>60</td>
<td>0.70</td>
</tr>
<tr>
<td>Well-nourished average 5-year-old child</td>
<td>50</td>
<td>0.65</td>
</tr>
<tr>
<td>Well-nourished average baby or toddler</td>
<td>40</td>
<td>0.45</td>
</tr>
<tr>
<td>Baby aged 3 days to 3 weeks</td>
<td>Variable</td>
<td></td>
</tr>
<tr>
<td>Baby in first 2 days of life</td>
<td>Maternal</td>
<td></td>
</tr>
</tbody>
</table>

Urea
Although useful for managing children with renal failure, urea concentration is an inaccurate way of measuring renal function because it is also highly dependent on hydration, and on carbohydrate and protein intake.

Urine biochemistry
Concept of fractional excretion
Clearance of any substance which is filtered by the glomeruli and then reabsorbed by the tubules can be compared to the clearance of creatinine which is filtered and then excreted largely unmodified by the tubule. The fractional excretion is that fraction of substance \( x \) that has been filtered at the glomerulus that actually reaches the urine.

\[
\text{Fractional excretion (FE)} \times \% = \frac{\text{urine} \times x}{\text{filtered} \times x} \times 100
\]

Fractional excretion of sodium
Normally, most of the filtered sodium (\( \text{Na}^+ \)) is reabsorbed; the majority of this reabsorption occurs in the proximal tubule. When plasma sodium is normal and the patient is not shocked, physiologically fractional excretion of sodium can vary. However, calculating FE Na can give useful clues in pathological states.

The normal renal response to intravascular fluid volume reduction is to excrete urine with a low sodium content. It does this by a number of mechanisms, including reduction of glomerular filtration rate (GFR) and aldosterone-stimulated sodium reabsorption, which requires intact tubules.

Fractional excretion of sodium (FE Na) is calculated from the urine (U) and plasma (P) concentrations (check that P and U creatinine values are expressed in the same units), using the following formula:

\[
\text{FE Na (\%)} = \frac{U}{P} \times \frac{P}{U} \times 100
\]

<table>
<thead>
<tr>
<th>FE Na</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1%</td>
<td>Tubules functioning = pre-renal failure</td>
</tr>
<tr>
<td>&gt; 1%</td>
<td>Acute tubular necrosis (ATN)</td>
</tr>
<tr>
<td>&lt; 1%</td>
<td>Salt loss or water overload (appropriate renal response)</td>
</tr>
<tr>
<td>&gt; 1%</td>
<td>Renal salt wasting (tubular disease)</td>
</tr>
<tr>
<td>&lt; 1%</td>
<td>Renal concentration defect</td>
</tr>
<tr>
<td>&gt; 1%</td>
<td>Salt overload (may be abuse)</td>
</tr>
</tbody>
</table>

Urine collection and examination
Collecting urine from babies can be time consuming, but is important in establishing a diagnosis.

Methods of urine collection
- Clean catch into a sterile pot.
- Sterile collecting pads are cheaper and easier to use than an adhesive bag.
- For toddlers it is fine to use a potty or equivalent which has been thoroughly washed in hot water and detergent (using antiseptics or bleach, or scalding with boiling water, are unreliable).
- Suprapubic or catheter urine sampling is useful in ill children when antibiotics need to be started without delay.
**Stick testing of urine and protein measurement**

- Dipstick testing for blood, protein and glucose is useful and reliable.
- Stick testing for nitrite to identify urinary tract infections (UTIs) is useful when positive to rule in UTIs, but unreliable when negative because it remains negative in 50% of cases.
- Stick testing for white cells to diagnose UTIs is unreliable because they may occur without white cells, and because white cell numbers also increase in the urine of febrile children without UTIs.

**Laboratory measurement of protein in urine**

Urine protein should be < 20 mg protein/mmol creatinine in an early-morning sample of urine.

In nephrotic syndrome there is typically > 500 mg protein/mmol creatinine.

**Microscopy of urine**

Microscopy of unspun fresh urine can provide a cheap and reliable way of rapidly diagnosing UTIs (by identifying bacteria directly, rather than by counting white cells), and of diagnosing schistosomiasis.

Red blood cells can be identified as being due to glomerulonephritis (when they are small, fragmented and of varied and distorted shapes), or due to other causes, such as trauma, stones or bladder inflammation (when they are all similar, and typically biconcave).

A standard light microscope with a magnification of × 400 is sufficient. Using a counting chamber (or a microscope slide with a scratched surface) and cover slip ensures that the microscope is focused at the correct plane, otherwise it is not possible to tell when microscoping a normal urine. A counting chamber with a mirrored surface is not essential, but makes identification of bacteria easier. Phase contrast makes identification even easier. A highly reliable, almost pocket-sized microscope (McArthur) is available with phase contrast.

**Urinary tract imaging techniques**

All renal imaging techniques are relatively expensive, and many will have limited availability.

**Ultrasound scanning**

Useful information can only be obtained from ultrasound scanning by a skilled operator using an adequate machine. It demonstrates anatomy, but not function. It is ionising radiation free, and, when available, is the first choice for initial imaging of most renal conditions in children. It is excellent at demonstrating cysts, stones and dilatation, and has a similar sensitivity to the intravenous urogram (IVU) for demonstrating long-standing or extensive scarring. Nephritis causes echo brightness of the kidneys. Tumours and cysts are easily seen, usually before they are visible by other modalities. Stones can be easily identified, but may be misinterpreted by the inexperienced because the whole stone is not seen; a bright line identifies where the ultrasound hits the front edge of the stone, and an acoustic shadow is thrown behind it. Nephrocalcinosis can be detected easily as white renal pyramids long before it can be seen on X-rays.

Ultrasound scanning during the acute phase of the UTI will often show dilatation of the ureters. It is therefore suggested that this investigation should be undertaken 2–3 weeks after the infection. Any dilation of the ureters should then be regarded as significant.

**Micturating cystogram (MCUG)**

This is still the most reliable way to assess vesico-ureteric reflux (VUR), but unfortunately depends on invasive urethral catheterisation, and depending on the equipment used it may require a relatively high dose of radiation. It should be reserved for use when the result will affect management.

(Reflex is less commonly found in Afro-Caribbean children.)

This investigation is very important to confirm posterior urethral valves, one of the commonest obstructive uropathies seen in Afro-Caribbean children. The age of presentation is variable. When it presents in the neonatal period there is usually severe renal involvement.

**Plain abdominal X-ray**

This demonstrates radio-opaque stones, but these and nephrocalcinosis are usually easier to see on an ultrasound scan.

**Urinary tract infections (UTIs)**

**Background**

UTIs are very common. The risk of UTI is increased in babies with anatomical nephro-urological abnormalities, those with obstruction, those with VUR, and in girls. Management of VUR is controversial (see Section 5.6.B). Recent studies have shown that about 10% of girls and 3% of boys will have had a UTI diagnosed by the age of 16 years in the UK. Most children with UTIs have no underlying renal tract problem and suffer no serious consequences. However, UTI may be the first indicator of underlying renal tract abnormality, and may be associated with acquired renal scarring. Distinguishing the small group of children with important findings in this common condition remains a challenge, and the question of how intensively to investigate children after UTI remains controversial.

Large scars may cause renal failure, but even small ones can cause hypertension, often in later childhood or in adulthood. To prevent serious sequelae of hypertension, children with scars should have lifelong blood pressure monitoring, as symptoms do not occur until serious irreparable disease is present.

Infants are the most vulnerable to scarring, and most children who will acquire scarring will have started to do so by the age of 4 or 5 years. Animal studies and case series suggest that a UTI in a vulnerable individual may cause permanent scarring rapidly, in a matter of a very few days.

**Diagnosis**

**Symptoms**

Older children may present with typical ‘cystitis’ symptoms, typically due to bladder and urethral irritation, such as frequency and dysuria. Loin pain suggests likely upper renal tract involvement, but some children have few or no symptoms. Younger children (under 2 years of age) often only have non-specific symptoms such as anorexia, failure to thrive, unexplained fever or prolonged jaundice. Therefore all young children with an unexplained illness, particularly with a fever, should have a UTI excluded.
**Urine testing**

A diagnosis is usually made by culture of a pure growth of one species of bacteria (most commonly *E. coli*) at a concentration of more than 10^5/mL. Any concentration of bacteria in a suprapubic urine sample suggests infection. White blood cells (> 50/microlitre) are usually considered helpful in making the diagnosis, but UTIs can occur without any white cells (sometimes because they lyse in minutes), and urinary white blood cells can be found in children with fever who have some other cause and do not have a UTI.

As stated above, the organism most commonly involved is *E. coli*. If unusual organisms such as *Pseudomonas* are cultured at the first episode of UTI, it is mandatory to rule out an underlying urinary tract abnormality.

**Microscopy**

Microscopy of freshly voided unspun urine is a quick, reliable and cheap way to diagnose UTIs if a × 400 microscope is available, and it enables an immediate diagnosis to be made. This allows the best-guess antibiotic to be started at once. Infected urines need to be cultured to obtain antibiotic sensitivities. Infected urine will contain many bacteria, up to thousands per high-power field, depending slightly on the depth of urine under the cover slip. The bacteria will all look the same, and are typically rods of identical length. Occasionally, UTIs are caused by streptococci, which are seen as long chains of dots. Separate small dots that appear to be swimming are not streptococci, but are phosphate crystals (the shimmering movement is due to Brownian motion). Most but not all children with UTIs will also have > 50 white blood cells/microlitre, or at least 1 per 10 high-power fields.

If no bacteria are seen in about 5 high-power fields, the urine is not infected; the samples therefore need no further testing and can be discarded. Urine samples containing less than 1 bacterium per high-power field, or mixtures of rods and cocci, are likely to have been contaminated. Because this can be identified quickly, further samples can and should be collected until a clearly uninfected or infected one is obtained.

**Imaging**

Imaging after the first UTI is controversial. Young children and infants warrant more intensive investigation, as do those with a family history of renal disease.

**Ultrasound scanning**

This should be undertaken for all children after their first recognised UTI in order to identify structural abnormalities, and to try to identify scars. The likelihood of detecting a scar is much greater if it is large, involving multiple renal segments, or several years old, so that it will have had time to shrink and distort. Negative scans in young children (under 4 years) therefore need to be interpreted with caution.

Ultrasound scanning during the acute phase of the UTI will often show dilation of the ureters. It is therefore suggested that this investigation be undertaken 2–3 weeks after the infection. Any dilation of the ureters should then be regarded as significant.

**Micturating cystogram (MCUG)**

It is probably ideal to perform an MCUG on very young children who have had a definite UTI. It is recommended that an MCUG be performed on all those under 1 year of age, because about a third will have an anatomical abnormality detected, usually vesico-ureteric reflux (VUR). However, there is not universal agreement about this, as there is a high percentage of normal results.

Posterior urethral valves may present with a UTI, especially in parts of the world where there is little or inadequate antenatal scanning. Thus in baby boys who have had a UTI, a good view of the urethra is essential.

Children with VUR are at risk of developing scars with UTI. Therefore finding VUR should make you suspect that the child may have a scar that was not identified by ultrasound.

Management of VUR is controversial (see Section 5.6.B). Prophylactic antibiotics may reduce the recurrence of infection; awareness and rapid treatment of infection is important. Most VUR is self-resolving and the aim of medical treatment is to keep free of UTI while allowing natural resolution (over a period of years). The possibility of VUR should be considered and, if possible, tested for if scarring is identified on ultrasound scanning.

Most VUR resolves with time; the lower the grade, the more likely it is that resolution will occur (80–90% resolution of grade 1–2 over 5 years).

**Treatment of UTIs**

Encourage a high fluid intake to produce dilute urine and reduce the symptoms of dysuria.

- Treat the child for 7 days initially with:
  - oral trimethoprim (4 mg/kg twice daily)
  - or cephalaxin (10 mg/kg three times daily)
  - or amoxicillin (1 month to 1 year 62.5 mg: 1–5 years 125 mg: 5–18 years 250 mg, all three times daily)
  - or nitrofurantoin (3 months to 5 years: 750 micrograms/kg 4 times daily, 12–18 years: 50 mg 4 times daily).

Intravenous antibiotics may be necessary for very unwell children (particularly under 2 years of age) for as long as they are unable to tolerate oral medication. This may include gentamicin 7.5 mg/kg as a loading dose and then 7.5 mg/kg once daily only after confirmation that the plasma creatinine concentration is normal. If there is renal failure, no more should be given after the single dose, unless blood levels are available to guide the dosage. If necessary, change the antibiotic according to the laboratory sensitivity testing, when and if it is available.

Use of prophylactic antibiotics is controversial. Use may reduce recurrence of UTI and should be considered when there is VUR. A night-time dose of trimethoprim (2 mg/kg) or cephalaxin (12.5 mg/kg maximum 125 mg) or nitrofurantoin

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**FIGURE 5.6.A.1** Rods seen in 10 high-powered fields.
(1 mg/kg) may be used. Do not use amoxicillin for prophylaxis, because resistant organisms are likely to emerge.

In many resource-limited countries where there may be inadequate procedures for ensuring that antibiotics are used appropriately and where disposal of body fluids containing antibiotics may contaminate drinking water supplies, UTIs are resistant to trimethoprim but remain sensitive to cephalosporins and amoxicillin. Ideally, where available, cultures for antibiotic sensitivity should be undertaken.

**Hypertension**

**Background**

There is a steady increase in blood pressure with age, and definitions of hypertension are arbitrary. However, in most children with hypertension the blood pressure becomes very much higher than normal (unlike the majority of adult hypertension patients, whose blood pressure is only moderately elevated, causing a skewed frequency distribution curve). Primary hypertension is rare in children, and in more than 80% of them hypertension is secondary, and in at least 75% it is renal in origin. Diagnosis of the underlying cause is therefore very important in management. Children are relatively intolerant of hypertension, so they are at major risk of sequelae, especially encephalopathy, blindness and death.

**Measurement**

Blood pressure is best measured with a simple sphygmomanometer, as automatic blood pressure machines may be unreliable. It is more reliable to use the largest cuff that will fit on to the upper arm, rather than using ‘formulae’ that relate the cuff size to the child’s size. A cuff that is too large will not significantly underestimate the blood pressure, but one that is too small will overestimate it. In children, it is best to use systolic blood pressure; it is just as important as diastolic pressure for diagnosis and treatment, and is easier and more reliable to measure. In most children, palpating the reappearance of the pulse at the wrist is as accurate as using a stethoscope at the antecubital fossa, or a Doppler (if available) may be used at the wrist to detect the reappearance of the pulse. High values should be confirmed with the child relaxed to reduce the effects of anxiety. Measurements should be repeated several times if they are abnormal. Table 5.6.A.5 shows the upper limit of normal blood pressure ranges according to age.

<table>
<thead>
<tr>
<th>Value</th>
<th>1 month</th>
<th>1 year</th>
<th>5 years</th>
<th>10 years</th>
<th>15 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (mmHg)</td>
<td>75</td>
<td>85</td>
<td>95</td>
<td>105</td>
<td>115</td>
</tr>
<tr>
<td>Upper limit of normal (mmHg)</td>
<td>80</td>
<td>90</td>
<td>100</td>
<td>110</td>
<td>125</td>
</tr>
<tr>
<td>Needing urgent treatment (mmHg)</td>
<td>100*</td>
<td>120</td>
<td>130</td>
<td>140</td>
<td>150</td>
</tr>
</tbody>
</table>

*In infants, the likeliest cause of hypertension is coarctation of the aorta.

**Causes and diagnosis**

It is important to find the underlying cause of the hypertension to guide management. Sometimes the cause is clear from the history, examination or urine testing, and sometimes it requires diagnostic imaging. Ultrasound is the most useful screening technique, but is quite operator dependent. Hypertension can be caused by renal scarring that is difficult to detect with ultrasound.

**Treatment**

If the hypertension is known to be of recent onset, as in acute glomerulonephritis, it is safe to reduce the blood pressure quickly. Usually salt and water overload is a major factor; if so, restrict sodium and give furosemide 1–2 mg/kg (the oral route is as effective as the intravenous one). In other cases, treat the blood pressure slowly because cerebral arterial vasoconstriction may have occurred to protect the brain parenchyma from the impact of the hypertension, and made the cerebral blood flow dependent on a high blood pressure being sustained.

A rapid fall in blood pressure may cause cerebral infarction and blindness. Reduction over 2 days or more allows the vascular tone to return to normal. Slow control may be achieved by introducing oral hypotensive drugs slowly at well below the maximum dose.

**Glomerular disease**

Glomerular disease is characterised by proteinuria with or without haematuria. It may be caused by a primary glomerular disease or be secondary to a systemic illness, and it can cause a wide spectrum of clinical pictures, including the following:

- nephrotic syndrome
- acute glomerulonephritis
- chronic glomerulonephritis
- asymptomatic proteinuria or haematuria.
Nephrotic syndrome

**Background and clinical features**

The clinical picture is of proteinuria, hypoalbuminaemia and oedema.

It must be differentiated from other causes of hypoalbuminaemia, such as protein malnutrition (see Section 5.10.B) and protein-losing enteropathy (see Section 5.12.D).

It is traditionally classified as early-onset (congenital, diagnosed at under 6 months of age) and later-onset types.

**Early onset**

Children with congenital nephrotic syndrome frequently do not survive, many of them dying early of protein malnutrition, infection or thrombosis unless they are aggressively treated.

Those with severe proteinuria, including the recessively inherited Finnish type, tend to fare worse. Diffuse mesangial sclerosis is a similar condition, but is usually less acute. Congenital syphilis can cause neonatal nephrotic syndrome which may respond to penicillin treatment. Some early nephrotic syndromes are self-resolving, but this is uncommon.

Treatment is often difficult. Early-onset nephrotic syndrome is generally not responsive to steroids. Treatment may be supportive, including frequent albumin infusions, and in the most severe cases may require early unilateral or even bilateral nephrectomy, leading to dialysis and transplantation. Reduction of proteinuria by the use of ACE inhibitors or indomethacin may be attempted, but very careful monitoring is required.

**Later onset**

Most children with nephrotic syndrome presenting in childhood (after the age of 1 year and before the teenage years) are steroid responsive, losing their proteinuria within 1 to 2 months of treatment. They share clinical characteristics (see Table 5.6.A.8). Children with steroid-resistant nephrotic syndrome may have a range of diagnoses, including focal segmental glomerulosclerosis, Henoch–Schönlein purpura, lupus and mesangiocapillary glomerulonephritis. There is a strong association with infections, especially malaria and hepatitis B, as well as hepatitis C and HIV.

**Acute management**

It is reasonable to attempt to induce a remission with steroids, unless the clinical picture virtually excludes the possibility of steroid sensitivity.

- Use prednisolone 60 mg/m² daily (see Section 9 to convert from body weight to surface area) for up to 6 weeks (about 95% of children who are going to respond do so within 1 month). Monitor carefully for the development of hypertension on steroids.
- Limit fluid retention by imposing a tight dietary sodium restriction.
- Prevent secondary pneumococcal infection with prophylactic penicillin V (125 mg twice daily up to 5 years of age, and 250 mg twice daily thereafter).
- Avoid the sequelae of hypovolaemia (thrombosis).
- Intravascular hypovolaemia is a high risk and should be monitored clinically by the appearance of cold peripheries and sometimes abdominal pain. There may be initial paradoxical hypertension, and hypotension may not occur until late. The best laboratory test is a urinary sodium concentration of less than 15 mmol/litre, especially if combined with a urine osmolality of over 800 mosmol/kg. Blood tests are seldom helpful.
- Treatment of hypovolaemia should be with 1 gram/kg

### Table 5.6.A.7 Renal and arterial causes of hypertension in childhood

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Notes</th>
<th>Renal ultrasound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reflux nephropathy</td>
<td>Also called pyelonephritis (see UTI)</td>
<td>Focal scars or shrunken kidney</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-infective</td>
<td>Typically have proteinuria and glomerular haematuria. Typically after a streptococcal infection, sore throat/skin infection. Give a 10-day course of penicillin</td>
<td>Echo bright</td>
</tr>
<tr>
<td>Other causes</td>
<td>May have evidence of Henoch–Schönlein purpura or lupus; if not, renal biopsy is needed</td>
<td></td>
</tr>
<tr>
<td>Inherited polycystic disease</td>
<td>Kidneys large at birth, typically severe hypertension, renal failure in early life</td>
<td>Huge, homogeneous, echo bright</td>
</tr>
<tr>
<td>Infantile type (recessive)</td>
<td>Seldom causes renal failure in childhood, but may cause hypertension. Screen blood pressure of children of affected parents</td>
<td>Discrete cysts develop through childhood</td>
</tr>
<tr>
<td>Adult type (dominant)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Narrowed arterial supply</td>
<td>Check femoral pulses; may need surgical treatment or balloon angioplasty</td>
<td>May be small, and difficult to diagnose without expensive imaging</td>
</tr>
<tr>
<td>Coarctation of the aorta</td>
<td>Requires long-term medical treatment. May occur with neurofibromatosis; screen for this</td>
<td></td>
</tr>
</tbody>
</table>
of IV 20% albumin over 4 hours, preferably with 2 mg/kg of IV furosemide given halfway through. If shocked, give 10 mL/kg of 4.5% albumin.

- Avoid the use of furosemide in the acute situation without adequate volume replacement.

**Subsequent management if steroid-sensitive**

This is ideally based on daily home monitoring of the morning urine protein level by stick testing. A common definition of a relapse is ++ proteinuria for 7 consecutive days, or +++ for 3 days, and it should be responded to by reintroducing salt restriction, penicillin V and prednisolone.

Protocols for doses and duration of use of prednisolone and steroid-sparing agents vary. The following is a proposed example:

**First presentation:** give prednisolone 60 mg/m² daily (see Section 9), and if the patient responds (by loss of proteinuria), complete 6 weeks of 60 mg/m² daily, followed by 40 mg/m² on alternate days for a further 6 weeks.

**Subsequent relapse:** restart 60 mg/m² daily until there is no proteinuria for 3 days, then give 40 mg/m² on alternate days for a further 4 weeks.

**Frequent relapses:** give prophylactic low-dose (e.g. 200 micrograms/kg) alternate-day prednisolone. Titrate the dose up until either relapses are prevented, or steroid side effects develop.

If steroid prophylaxis causes unacceptable side effects, add prophylactic levamisole 2.5 mg/kg on alternate days (approximately 50% of cases will benefit), which can be used relatively long term.

If levamisole is ineffective, consider giving cyclophosphamide 2.5–3 mg/kg daily for 12 weeks, monitoring weekly with white blood cell count, and reducing the dose if the absolute neutrophil count falls below 1 x 10⁹/litre, or stopping if it falls below 0.5 x 10⁹/litre. Or give 6 x monthly cyclophosphamide infusion (600 mg/m²). Note that this is potentially dangerous in resource-limited circumstances where infections are frequent.

**Subsequent management if steroid resistant**

Persistent haematuria and hypertension at the first presentation may be early warning signs of steroid resistance. Steroids should be used with caution, as the hypertension may be aggravated.

There is a wide range of conditions that may induce steroid-resistant nephrotic syndrome. These include infective agents, autoimmune diseases, some drugs and poisons, and unknown causes. The cause may be apparent from the history and examination and other tests, but in most cases the diagnosis relies on the accurate interpretation of a kidney biopsy.

The infective causes include hepatitis B, HIV, Schistosoma mansoni, leprosy, tuberculosis and malaria. These conditions should be sought in those parts of the world where they are likely to be found, and treated appropriately. Hepatitis B typically causes a membranous nephropathy which tends to improve spontaneously. Post-streptococcal glomerulonephritis may cause nephrotic syndrome, but it is seldom the presenting feature. Although it is not the only cause of this clinical picture, it is sensible to treat any child who develops nephrotic syndrome after an acute nephrotic illness with 10 days of oral penicillin V, 1–6 years 125 mg, 6–12 years 250 mg, 12–18 years 500 mg per dose 6-hourly.

The autoimmune causes of nephrotic syndrome include Henoch–Schönlein purpura and IgA nephritis, lupus, mesangiocapillary glomerulonephritis, and some cases of membranous nephropathy. The commonest cause of steroid-resistant nephrotic syndrome in many parts of the world is focal segmental glomerulosclerosis (FSGS), the pathophysiological mechanism of which is unknown. In some of these conditions (including lupus, mesangiocapillary glomerulonephritis and FSGS), some children do respond to steroids. However, many children with steroid-resistant nephrotic syndrome do not respond to any treatment at all. Most of those who do only respond to more powerful immunosuppressants, such as cyclophosphamide or cyclosporine. Some conditions have been treated with plasmapheresis, but in most conditions the evidence for this is purely anecdotal. These treatments are difficult to use because they are expensive, and they require close monitoring for side effects. Even under ideal medical conditions with considerable resources, many cases still progress to end-stage renal failure.

**Protein in the diet**

Children with nephrotic syndrome may lose huge quantities of protein in their urine. If they are on a low-protein diet they will quickly lose muscle mass as the body proteins are utilised to synthesise plasma albumin. A relatively high-protein diet will be muscle sparing, but will make no significant difference to the plasma albumin concentration.

**Glomerulonephritis**

Glomerulonephritis (GN) strictly refers to inflammation of the glomeruli with cellular proliferation, although it is often used to include other glomerulopathies such as FSGS and membranous nephropathy, both of which typically cause steroid-resistant nephrotic syndrome.

The commonest cause of childhood glomerulonephritis varies widely across the world. In resource-limited countries, acute post-streptococcal glomerulonephritis is the commonest type. In wealthier countries this is now becoming more unusual, and IgA nephropathy predominates.

**Post-streptococcal glomerulonephritis**

This is caused by antibodies produced in response to specific strains of streptococci. These bacteria typically cause throat and skin infections. The antibodies then form complexes and are deposited within the glomeruli along with C3. Because it takes time for antibody production to occur, the signs and symptoms of nephritis do not usually begin to appear until 10–20 days after the start of the infection.

The inflamed glomeruli leak blood and protein, so the first symptom is usually the child passing smoky or frankly bloody urine. The glomerular filtration rate usually falls slightly, so the plasma creatinine concentration is typically slightly elevated. Also the tubules reabsorb sodium and water excessively, which causes water retention out of proportion to the fall in glomerular filtration rate. This leads to swelling, which is most easily noticed around the eyes and face, and in the legs, but which does not pit as easily as oedema does in the nephrotic syndrome. The water retention also leads to hypertension. Most children with acute post-streptococcal glomerulonephritis do not lose enough protein into the urine to cause nephrotic syndrome as well, although some do, producing a mixed nephrotic–nephritic picture.
A presumptive diagnosis is made by examination of the urine for the presence of protein (using stick tests) and granular red cells and casts (by microscopy; see Section 8.5), in a child with a history of a recent sore throat or skin infection. Culture of a specific strain of Streptococcus from a throat or skin swab may confirm the diagnosis. It is not reliable to make a diagnosis from a single titre of an anti-streptococcal antibody such as the ASOT or the anti-DNase B, because many children have an elevated level from previous exposure to other strains of streptococci. Confirmation requires a significant rise between two titres taken at least 10 days apart.

If plasma complement levels (C3 and C4) can be measured, they may give a clue to the underlying diagnosis but are not confirmatory. In post-streptococcal glomerulonephritis the plasma C3 concentration is reduced, and often stays subnormal for up to 6 weeks before rising back to normal. The plasma C3 level is usually low in mesangiocapillary glomerulonephritis, and the C3 and C4 levels are often both low in lupus, and these conditions may present clinically identical to post-streptococcal glomerulonephritis.

**Treatment**

If post-streptococcal glomerulonephritis is suspected, immediately start penicillin V, 1–6 years 125 mg, 6–12 years 250 mg, 12–18 years 500 mg per dose four times daily for 10 days, to eradicate the organism. There is always a delay in obtaining bacteriological confirmation, either from culture or from paired titres, so it is best to start the penicillin at once, and use these tests as retrospective confirmatory evidence.

It is essential to measure the child’s fluid intake and losses accurately as well as daily weighing, and restrict the amounts of sodium and water allowed. This should be to balance the losses, or to cause net fluid reduction if the child is significantly fluid-overloaded. The insensible loss is about 300 mL/m² daily, but will be higher in a hot dry climate. (Estimate the surface area from Table 9.16 in Section 9.) Salt restriction is far more important than water restriction, and is sometimes all that is required for a child to maintain fluid balance. This is because the tubules retain sodium avidly, so any salt that is eaten will be retained in the body and cause hyponatraemia. This drives an intense thirst, and it then becomes almost impossible to stop the child drinking. By contrast, a tight salt restriction will minimise the thirst, which aids management.

If the plasma albumin concentration is normal or only slightly reduced, it is safe to give an oral dose of furosemide, 1–2 mg/kg. This will increase the urinary excretion of sodium and water, and thus improve fluid overload and hypertension. It will also increase potassium loss, which is helpful if the fall in glomerular filtration has led to hyperkalaemia. It may be repeated as needed. However, if the child has a very low plasma albumin concentration from a mixed nephrotic–nephritic picture, giving furosemide may precipitate hypovolaemia. Because of this, either give intravenous albumin combined with furosemide (see section on acute management of nephrotic syndrome), or give furosemide under close observation and be prepared to give albumin if hypovolaemia occurs. Cold peripheries and abdominal pain (from splanchnic vasoconstriction) are important signs of this. The raised blood pressure is frequently fully controlled by salt and water restriction and furosemide, but in some cases hypotensive agents are also needed (see Table 5.6.A.5). Under such acute conditions it is safe to reduce the blood pressure rapidly.

In children with post-streptococcal glomerulonephritis, the kidneys usually make a full recovery, and progression to renal failure is rare. Therefore most of these children will have no sequelae, provided that their fluid and electrolyte balance and blood pressure are carefully managed.

**IgA nephropathy (Berger’s disease)**

The typical presentation is of a child aged 5–15 years who develops an acute upper respiratory tract illness, and simultaneously has heavy haematuria that lasts for several days. Urine microscopy reveals distorted ‘glomerular’ red cells (see above). Usually the urine then clears completely, but the haematuria may return with subsequent illnesses. Some children with IgA disease have a more insidious illness with little or no macroscopic haematuria.

The diagnosis is suggested in children who present with recurrent heavy glomerular haematuria. There may be a family history. The plasma IgA concentration may be elevated in affected children, but this test is a poor discriminator. In children with a less obvious clinical picture the diagnosis can only be made on a kidney biopsy. Antibody staining will show granular deposits of IgA in glomeruli that have mesangial proliferation. Histologically, IgA disease is identical to Henoch–Schönlein nephritis.

The best prognostic indicator in IgA nephropathy is the amount of proteinuria that persists between the acute episodes of haematuria. Most children have heavy haematuria but little or no proteinuria between attacks, and virtually all of these grow out of the condition, usually without any sequelae. Often the ones with the most dramatic haematuria recover particularly well. The children with a more insidious onset are more likely to have persistent proteinuria, and to continue with the condition into adulthood, eventually developing end-stage renal failure by middle age. There is no good evidence for treatments to prevent this happening. However, adequate blood pressure control is important in slowing the progression of renal disease.

Rarely, IgA disease first presents as a severe rapidly progressing glomerulonephritis. The picture is one of an acute nephritis in which the creatinine level rises rapidly and inexorably. It is therefore clinically indistinguishable from any other rapidly progressive glomerulonephritis, other than by renal biopsy. Treatment options include various immunosuppressive drugs and plasmapheresis. These have not been subjected to controlled trials, are expensive and may lead to serious complications.

**Haematuria**

- Urine test sticks are highly sensitive and detect the smallest traces of blood.
- For most conditions that can cause haematuria, the clinical significance is best predicted by the quantity of protein present, so always test for that, too.
- The most important test for determining the cause of haematuria is to check the shape of the red cells, ideally under phase-contrast microscopy (see above).

**Macroscopic glomerular haematuria**

The presence of distorted red cells may be due to any...
form of glomerulonephritis, as listed above. The history of a simultaneous infection may suggest IgA nephropathy, while a recent infection points to post-streptococcal glomerulonephritis. The presence of a rash, or joint involvement, or abdominal pain might suggest Henoch–Schönlein or lupus nephritis as causes, but most other types can only be diagnosed on renal biopsy.

Macroscopic non-glomerular haematuria
The presence of red cells with a normal bicconcave appearance indicates bleeding into the urine, and excludes glomerulonephritis as a cause. This may be due to trauma, but this would have to be major, because the renal tract is physically well protected. Minor trauma will only cause bleeding if the kidney is enlarged with cysts, as in adult-type (dominantly inherited) polycystic kidney disease, or if it is vulnerable due to being ectopically positioned. Urinary tract stones can also cause bleeding. The cystitis caused by a urinary tract infection or by Schistosoma mansoni may cause frank haematuria. These can be distinguished on phase-contrast microscopy of a fresh sample, when either bacteria or ova are easily visible. Although bleeding into the urine can be due to a malignancy, this is rare in childhood, and is then usually from a Wilms’ tumour. Frank haematuria in a newborn suggests a renal vein thrombosis, which may be unilateral or bilateral, and the affected kidney is usually easily palpated.

Trauma, stones, an ectopic kidney, adult polycystic disease, a Wilms’ tumour and renal vein thrombosis can each be identified by their characteristic appearance on ultrasound scanning. In cases for which no cause has been found, cystoscopy should be considered.

Microscopic glomerular haematuria
Blood may be detected in urine that looks completely clear. Rarely, the red cells appear normal on microscopy; these children should be investigated as for frank non-glomerular haematuria. Most children with microscopic haematuria have distorted ‘glomerular’ red cells. In this group, management depends on how much proteinuria they have. Those with massive nephrotic-level proteinuria should be assessed for the blood disappearing, follow-up may be discontinued. If the blood disappears, follow-up may be discontinued. If it persists without proteinuria or hypertension developing, continue the annual reviews. If proteinuria or hypertension appears, the child needs to be investigated accordingly.

Haemolytic uraemic syndrome (HUS)
HUS is a common cause of established (parenchymal) acute renal failure (see above). Children with HUS fall broadly into two groups, according to their pathophysiological mechanisms. It is important to divide them clinically into diarrhoea-associated HUS (D + HUS) and diarrhoea-negative HUS (D – HUS).

D + HUS
This is the common type, and it occurs in otherwise normal children, often in outbreaks or clusters of cases. It is triggered by a toxin that is produced by some colonic bacteria, including Shigella and some strains of enteropathic E. coli. Infection is from ingestion of contaminated food or fluids. Public health measures to identify a source of the organism are important in preventing and limiting outbreaks. Typically the child has several days of bloody diarrhoea, and then becomes pale and mildly jaundiced (from haemolytic anaemia), may bruise and have petechiae (from thrombocytopenia), and develops oligo-anuria. A blood film shows fragmented red blood cells and a low platelet count. Antibiotics are not of benefit, and may worsen the condition by causing the acute release of more bacterial toxin. Blood transfusion may be needed (usually when the haemoglobin level falls below 6 grams/dl). Platelet transfusion may exacerbate the condition, and should only be used in the face of uncontrolled bleeding. There is no evidence that any specific medication is of benefit. Management is as for other children with acute renal failure (see above). Mortality from this condition has decreased with active management of fluid and electrolyte imbalance and dialysis.

In a minority of cases, D + HUS can affect other organs, sometimes severely. Effects can include bowel perforations, pancreatitis with diabetes mellitus, and cerebral involvement, with fits, coma and death.

The long-term outcome for children who survive the acute episode of D + HUS is relatively good. Most appear to fully recover renal function, although up to 25% have persistent hypertension or proteinuria. Few develop end-stage renal failure.

D – HUS
This variant is very rare, and is often associated with a functional or actual deficiency of factor H, so a minor trigger (such as a minor viral illness) can precipitate the typical clinical and haematological HUS picture, but without a diarrhoeal prodrome. Typically, D – HUS patients fare much worse long term than D + HUS patients.

Confusing findings
Blood may be present on stick testing without any red cells visible on microscopy. This indicates acute haemolysis such as may occur in glucose-6-phosphate dehydrogenase (G6PD) deficiency or malaria.

Large quantities of urate make the urine brick red. Although families may think the colour resembles blood, it is easily distinguished visually. Porphyrin is a very rare cause of confusion. Ingestion of red vegetables, especially beetroot, causes red urine. Rarely, but this possibility must not be forgotten, a parent may place their own blood in a child’s urine, leading to unnecessary investigations. This condition is called fabricated or induced illness (FII).

Urinary tract stones
Background
There is wide geographical variation in the frequency of stone disease, and there have been major changes in prevalence with time within populations. The incidence appears to be influenced by a wide range of factors, such as climate, race, diet, dehydration, infections and socioeconomic status.
### Causes

There are three broad causes of urinary tract stones (which may coexist in individual children).

**Proteus urinary tract infections**

The mechanism is twofold. The infection results in turbid urine containing cells and debris, and secondly Proteus splits urea to form ammonia, which raises the urinary pH. Because calcium ammonium phosphate is relatively insoluble in alkaline urine, it will co-precipitate readily on to the urinary debris under these conditions to form thick sludge initially, and subsequently a stone. This explains why these stones take up the shape of the tract they form in (‘staghorns’ in the pelvi-calyceal system, ‘date stones’ in the lower ureter, and round stones in the bladder). Preschool boys are affected much more than any other groups.

**Relative dehydration and possibly dietary factors**

The mechanisms of stone formation are probably similar to those for infection stones, with chemicals normally found in the urine reaching relatively high concentrations due to low urine volumes, and high dietary intake and consequent excretion rates of relatively insoluble chemicals.

**Rare inherited metabolic conditions**

These result in excessive urinary excretion of poorly soluble chemicals. Calcium stones are most commonly caused by isolated hypercalciuria (without hypercalcaemia), and more rarely by hypercalciuria combined with hypercalcaemia in hyperparathyroidism. Cystine stones are seen due to an inherited (dominantly or recessively) failure of the proximal tubules to reabsorb this amino acid. Oxalate stones may be due to excessive gut absorption of oxalate when the calcium is unavailable to precipitate it, such as with steatorrhoea. Rarely it is also produced and excreted in excess due to a recessive liver enzyme deficiency.

**Presentation and diagnosis**

Children may pass a stone or present with severe colicky abdominal pain (typically in one loin), often with frank haematuria. Ultrasound scanning is a sensitive imaging tool, showing the front edge as a bright line, with an acoustic shadow thrown behind it, rather than showing the whole stone. Nephrocalcinosis associated with hypercalciuria is seen as white (echo-bright) renal pyramids.

A plain abdominal X-ray will show radio-opaque stones, and is thus useful for distinguishing the type. Similarly, the appearance of a passed stone or fragment may aid identification. Infection and dehydration stones are usually grey, and only moderately X-ray dense, and take up the shape of the collecting system. Calcium (white) and cystine (yellow) stones are very X-ray dense, may grow up to 2 cm or more in diameter, and are typically smooth, and round or oval wherever they form. Oxalate stones are yellowish-buff coloured and typically grow to 5 mm, with irregular spiky edges. A high oxalate load will result in many small stones rather than large individual ones.

If the type of stone is not clear from the history, chemical measurements can be made and compared with urinary creatinine measurements on an untimed ‘spot’ urine sample collected during the morning (but not the overnight sample).

The **upper normal limits** of the ratio of the chemical x to creatinine concentrations, both in mmol/litre, are as follows:

- Calcium:creatinine ratio of < 0.8
- Cystine:creatinine ratio of < 25
- Oxalate:creatinine ratio of < 0.15.

These ratios will be normal in children with infection stones, or those secondary to dehydration.

**Preventing recurrences**

Infection stones should not recur in the absence of infection. Stones due to metabolic causes and those related to dehydration are all helped by a consistently high fluid intake, but it is probably even more important to avoid episodes of acute dehydration (e.g. with vomiting or diarrhoea) than increasing daily fluid intake.

Chlorothiazide up to 10 mg/kg twice daily reduces urinary calcium excretion; its dose can be titrated in hypercalciuria to keep the urinary calcium:creatinine ratio in the normal range. Furosemide should be avoided because it increases urinary calcium excretion.

Children with hyperparathyroidism may require parathyroidectomy.

In cystinuria, it is essential to maintain a lifelong high fluid intake. Alkalising the urine increases the solubility of cystine. Give oral sodium bicarbonate supplements (start with 1 mmol/kg daily) until the urine pH is usually ≥ 7 on home testing with strip test paper.

With oxalate stones due to malabsorption, treat the underlying bowel problem. Inherited hyperoxaluria typically leads to renal failure and widespread calcification of soft tissue.
5.6.B The child with vesico-ureteric reflux

Introduction
Vesico-ureteric reflux (VUR), which is the abnormal flow of urine from the bladder into the upper urinary tract, occurs in about 1 in 100 members of the general population and is more common in girls. Reflux nephropathy is a cause of hypertension and chronic renal failure in children and young adults.

Renal scarring is an acquired phenomenon that usually occurs during the first few years of life, and rarely after the age of 5 years.

Grades of VUR (International Reflux Study Group classification)
These are as follows:
- Grade I: partial filling of an undilated ureter.
- Grade II: total filling of an undilated upper urinary tract.
- Grade III: dilated calyces but sharp fornices.
- Grade IV: blunted fornices and degree of dilatation greater than in lower stages.
- Grade V: massive hydronephrosis and tortuosity of the ureters.

Figure 5.6.B.1 illustrates the different grades of VUR.

Clinical presentation
- VUR almost always occurs in conjunction with an associated UTI.
- It is rarely a cause of flank pain.
- Fever is the single most important symptom for differentiating children with upper tract infections (pyelonephritis) from those with lower tract infections (cystitis).

Investigations
The minimal acceptable standards of investigation would include the following:
- Ultrasonography (useful for detection of dilatation, but not for demonstrating scars or reflux)
- Micturating cystourethrogram

BOX 5.6.B.1 Minimum standards
- Ultrasound scanning.
- Micturating cystogram.
- Antibiotics: trimethoprim, nitrofurantoin, nalidixic acid.
- Paediatric surgery.

Medical management
- Spontaneous resolution occurs most often in the first 2–3 years after diagnosis and then at the rate of 10–15% per year.
- The main goal is the prevention of ascending UTI and renal scarring.

The following measures should be used to prevent UTI:
- Proper wiping techniques (girls should be taught to wipe their bottoms backwards, and to avoid using soap on the vulva if possible; they should be discouraged from wearing nylon knickers).
- Frequent voiding.
- Avoidance of constipation.
- Low-pressure voiding.
- Continuous antibiotic prophylaxis, usually maintained for 2 years. Trimethoprim, 2 mg/kg/day, is the usual prophylactic agent. If breakthrough infections that are resistant to this occur, a suitable alternative prophylactic such as nitrofurantoin (1 mg/kg/day) or nalidixic acid (7.5 mg/kg twice daily) may be used.

In children of all ages the preferred initial treatment is medical, but they need regular follow-up. The need for surgery is becoming increasingly uncommon, but re-implantation of the ureters is occasionally necessary if the VUR is not resolving, is bilateral, in late presentations and in children, or with higher grades of VUR and with antenatally detected hydronephrosis.
5.6.C Acute renal failure

**Types of acute renal failure**

Acute renal failure (ARF) may be caused by a wide variety of insults to the renal tubule cells. Each type of ARF has a different management. It is therefore important to distinguish them clearly.

**Pre-renal failure**

This is caused by poor perfusion and hypovolaemia secondary to gastroenteritis, septic shock, haemorrhage, burns, nephrotic syndrome or cardiac failure.

**Established (intra-) renal failure**

Established renal failure most commonly results from more extreme or more prolonged versions of the same insults that cause pre-renal failure, leading to acute damage to the kidney cells. Other causes include haemolytic–uraemic syndrome and drug toxicity and acute rapidly progressive glomerulonephritis. The prognosis for recovery depends on the underlying cause, whether only the tubule cells are damaged, and whether the glomeruli are also involved.

**Post-renal failure**

Acute complete obstructions of the renal tract causing failure of urine production are rare, but include posterior urethral valves, obstruction of a single kidney, bilateral stones and trauma.

**Diagnosis and initial management of ARF**

**Pre-renal ARF**

Pre-renal failure is essentially a reversible renal dysfunction due to the kidneys being under-perfused, but where the perfusion is still sufficient to prevent necrosis of the renal tissue.

The clinical diagnosis is made by recognising the signs of shock, the commonest of which are a delayed capillary refill time, cool peripheries, a weak pulse, and usually a low blood pressure. However, the blood pressure may also be unexpectedly high because of the powerful renin drive in response to hypovolaemia. An important feature is that the child may complain of abdominal pain (induced by splanchnic ischaemia as blood flow is diverted from the gut to more vital organs).

Laboratory support of the clinical diagnosis is made by measuring the fractional excretion of sodium (FE Na; see Section 5.6.A). This requires measurement of the sodium and creatinine concentrations in a sample of blood and urine. If the FE Na is less than 1% this indicates that the renal tubule cells are still alive, and able to respond to shock by reabsorbing sodium avidly. This therefore confirms a diagnosis of pre-renal failure. No other tests, including measurements of osmolality, urinary sodium concentration alone, or urine microscopy, can reliably differentiate pre-renal from established renal failure. Ultrasound scanning is useful to exclude obstruction, but cannot differentiate pre-renal from established renal failure.

**Treatment**

This consists of urgent volume expansion followed by furosemide. Percentage dehydration should be estimated, and rehydration should be with Hartmann’s or Ringer-lactate solution, plasma, 4.5% albumin or other similar isotonic fluid or plasma substitute. Give 10–20 mL/kg as rapidly as possible initially, and repeat if necessary. If urine output does not commence after adequate volume replacement and furosemide, consider whether this is actually established renal failure, and do not continue repeating fluid boluses. Thereafter give Hartmann’s or Ringer-lactate solution to fully correct the fluid deficit within 2–4 hours. The deficit can be estimated by multiplying the child’s weight by the estimated percentage dehydration. For example, a 6 kg infant estimated to be 10% dehydrated is deficient of approximately 600 mL. According to the above guidelines he would receive 60–240 mL of plasma or plasma substitute very rapidly, and the rest of the 600 mL as Hartmann’s or Ringer-lactate solution over a few hours.

Once rehydration has started, give furosemide 2 mg/kg orally or IV. If there is a urine output response to furosemide this will usually indicate that the renal failure can recover. If the blood pressure remains markedly depressed after rehydration, it may be due to cardiogenic shock, so consider administering inotropes (see Section 5.5.C).

**Established ARF**

Established failure is due to acute parenchymal damage to the kidneys. In most cases the causes are exactly the same as for pre-renal failure, but an increased severity or duration of the insult has led to death of some of the renal cells. Therefore the pertinent history and clinical signs are usually the same as for pre-renal failure. Other cases are due to directly toxic effects of drugs such as gentamicin, or poisons to the tubular cells. Some forms of glomerulonephritis may lead to ARF (see Section 5.5.A), as may the arteriolar disease, haemolytic–uraemic syndrome.

The laboratory diagnosis of established renal failure due to under-perfusion or an ischaemic insult can be made reliably by calculating the FE Na from a measurement of the sodium and creatinine concentrations in a plasma sample and a spot urine sample. The FE Na is typically greater than 2% because the damaged tubules are usually unable to reabsorb sodium avidly. Again, attempts to use other laboratory criteria are unreliable. The history, clinical examination and laboratory confirmation of glomerulonephritis and haemolytic–uraemic syndrome are described in Section 5.6.A.

The most vulnerable region of the kidney is the highly metabolically active mass of proximal tubule cells. If these cells alone die from the insult, this causes acute tubular necrosis (ATN), which will fully recover in 2–4 weeks if the child is maintained in good health during that period of renal failure (likely to require dialysis). More severe insults
may result in damage to some or all of the glomeruli as well, which are in the renal cortex. Glomerular damage is irreversible, and acute cortical necrosis may therefore result in chronic or end-stage renal failure.

Fluid repletion and furosemide administration will not result in recovery of renal function. If an FE Na is not available to distinguish between pre-renal and established ARF, it is sensible to give a trial of fluid bolus and furosemide. Management consists of correcting the dehydration, as for pre-renal failure, and thereafter careful maintenance of fluids (usually restriction) and electrolyte balance and nutrition (restricting potassium intake) while it is hoped that some recovery of tubule cells will lead to recovery of kidney function.  **This is likely to require dialysis.** If recovery is going to happen it is likely to have begun by 4 weeks, but can occur up to 2 or even 3 months later. There are no reliable imaging techniques for determining whether the child has recoverable ATN or irrecoverable cortical necrosis, but renal biopsy if available may distinguish between these.

**Post-renal ARF**

Post-renal causes are due to obstruction to all of the urinary flow, and are uncommon. This will not occur if the flow from just one kidney is blocked (unless a single kidney is present). Causes in a child with two kidneys include congenital urethral valves, or a bladder stone obstructing the urethra. Causes in a child with a single kidney include a ureteric stone, or a pelvi-ureteric junction narrowing (which is congenital, but often blocks intermittently and presents later).

All of these pathologies cause severe acute colicky abdominal pain. This is well localised in older children to either unilateral pain with ureteric obstruction, or lower abdominal pain with bladder neck obstruction. An ultrasound scan will reveal stones and dilatation of the urinary tract proximal to the site of the obstruction.

**Treatment**

The treatment of post-renal ARF is to remove or bypass the obstruction. For a bladder neck stone obstruction, catheterise the child. Giving pain relief with an opiate analgesic may allow time for an obstructing urethral stone to pass, or for the intermittent blockage from a pelvi-ureteric junction narrowing to clear. If not, the stone may need to be removed cystoscopically or by ureterolithotomy, or the pelvi-ureteric junction narrowing to clear. If not, the stone may need to be removed cystoscopically or by ureterolithotomy, or the pelvi-ureteric junction narrowing to clear.

**Ongoing management of persistent ARF**

**General management**

The management of ARF consists of the provision of good general care for an acutely ill child, plus the specific management of fluid and electrolyte balance, blood pressure, and the adjustment of some drug dosages. In many instances the limitations that need to be imposed to keep in metabolic balance compromise the care that can be given in other areas.

**The safe management of these children requires the maintenance of meticulous fluid balance. To achieve this it is necessary to accurately measure all intake and losses.** For babies, stool and urine losses are best estimated by weighing their clean and dirty nappies. Insensible water losses need to be estimated. This is done most reliably by assuming it to be 300 mL/m² in temperate conditions, and higher in hotter climates and at low humidity (for estimation of body surface area, see Table 9.16, Section 9). The best guide to the overall changes in fluid balance is to weigh the child twice daily.

**Nutrition, fluid and electrolyte balance**

Adequate nutrition is important for recovery, but may be difficult to provide. If a child is old enough and well enough to eat solid food they are relatively easy to manage because they can obtain their requirements with little water. Aim to provide their normal calorie intake from carbohydrates and fats, and limit their protein intake to about 1 gram/kg/day to minimise ureaemia. It is necessary to limit the salt intake to prevent sodium retention and hypernatraemia, which leads to insatiable thirst and hence fluid overload. It may be necessary to provide some of the sodium as bicarbonate to prevent acidosis, typically at a starting dose of 1 mmol/kg/day (note that 1 mL of an 8.4% sodium bicarbonate solution contains 1 mmol, and 1 gram of powder contains 12 mmol).

Dietary potassium must be restricted (avoid in particular bananas, tomatoes, coconut, citrus fruits or juices, and chocolate) to decrease the risk of hyperkalaemia. Dietary phosphate must be restricted (restrict milk and dairy products but not breastfeeding) to reduce the risk of hyperphosphataemia. Giving calcium carbonate with the food (e.g. 0.5–2 grams with each meal) will bind the intestinal phosphate and reduce hyperphosphataemia as well as reducing the tendency to hypocalcaemia.

Young infants who normally take milk, and children who are too ill to eat solid food, or who have gastrointestinal involvement, will need either nasogastric tube feeding or intravenous nutrition. The enteral route should always be used if possible. However, adequate nutrition has to be delivered in a relatively large fluid volume. If the child has polyuric renal failure, or has high non-renal water losses (e.g. from diarrhoea or drain fluids), this can be achieved. However, if the child is oligo-anuric it is very difficult (and often impossible) to give sufficient nutrition without causing fluid overload, which can lead to hypertension and pulmonary oedema. Concentrated fat-based oral feeds can be made up from ingredients such as double cream. Specialist parenteral nutrition solutions will be required if they are to be used for a child in renal failure.

**The need for dialysis**

Although severe fluid and electrolyte restriction is possible for short periods of time while awaiting spontaneous recovery of renal function, it is not possible to both provide adequate nutrition and maintain stable water and chemical balance over a prolonged period in a child with oligo-anuria. If such a child does not start to regain renal function, they will die unless they are dialysed.

The main indications for starting dialysis (where available) are as follows:

- **Hyperkalaemia:** this is discussed below.
- **Fluid overload causing pulmonary oedema and/or hypertension.**
- **Severe metabolic acidosis:** this is another important reason for dialysis (if available). Treatment with sodium bicarbonate is limited because this may lead to massive fluid retention.
sodium overload, and thus to dangerous levels of hypernatraemia, and to greater fluid retention. Fluid overload is worsened if hypoglycaemia occurs (this needs to be treated with IV glucose solutions) and if other fluids are required (e.g. platelets).

- Uraemia: clinical symptoms are apparent at concentrations above 40 mmol/litre, but uraemia is not as acutely life-threatening as hyperkalaemia or pulmonary oedema. It needs to be reduced by providing more non-protein calories.

Hyperkalaemia

Hyperkalaemia causes life-threatening arrhythmias, especially in acute renal failure, where other metabolic changes may exacerbate the risk (e.g. hypocalcaemia). Aim to keep the plasma potassium concentration below 6.5 mmol/litre in older children and below 7.0 mmol/litre in neonates (who appear to tolerate hyperkalaemia better).

There are three pharmacological approaches to managing children with hyperkalaemia.

1. Reduce the risk of it causing arrhythmias. Reduce the effect of hyperkalaemia by increasing the plasma calcium concentration. Give 0.5 mL/kg (0.1 mmol/kg) of calcium gluconate 10% IV.

2. Remove potassium from the body. Give calcium resonium 1 gram/kg orally or rectally, and repeat with 0.5 grams/kg 12-hourly. This ion-exchange resin exchanges potassium for calcium. It is not well tolerated. If volume status and urine flow permit, furosemide will increase urinary potassium excretion.

3. Push potassium into the cells. This last option only results in a temporary improvement, because as soon as the treatment stops the potassium moves back out of the cells. Essentially this approach is only a holding treatment while a more effective therapy such as dialysis is prepared:
   - Give a beta-2-adrenergic agonist, such as salbutamol. Nebulise 2.5 mg for children under 25 kg, and 5 mg for larger children, or give 4 micrograms/kg IV. This works rapidly, but the potassium will move back out of the cells within a few hours.
   - Alternatively, infuse a high concentration of glucose. Monitor the plasma glucose concentration and be prepared to infuse insulin beginning at a dose of 0.05 units/kg/hour if it exceeds 12 mmol/litre. It is unsafe to mix the glucose and insulin and infuse them together in children, as this may cause hypoglycaemia. This necessitates close monitoring, an inevitable fluid load, and only lasts while it is continued.
   - Bicarbonate infusions push potassium into the cells. A dose of 2.5 mmol/kg may be infused over 15 minutes. If a solution of 8.4% is used, containing 1 mmol/mL, it will increase the plasma sodium concentration by approximately 5 mmol/litre very quickly, which may be hazardous. It is better to use a solution of 1.26% which is isonatraemic, but this requires that a volume of 17 mL/kg be infused, adding to fluid overload.

Acute peritoneal dialysis

Indications

Children with acute renal failure can be considered for peritoneal dialysis if their biochemical control is not safe despite careful treatment (see section on management of acute renal failure above). Although the specific indications for initiating peritoneal dialysis vary from case to case, the commonest reason is a high and rising plasma potassium concentration (e.g. above 6.5 mmol/litre in an older child, or above 7 mmol/litre in a neonate). Others indications include a urea concentration above 40 mmol/litre, a phosphate concentration above 3.5 mmol/litre, or acidosis with a bicarbonate concentration below 12 mmol/litre, as well as hypertension or pulmonary oedema due to fluid overload.

The primary underlying reason for needing to proceed to dialysis is usually anuria or severe oliguria. This is because even a moderate urine flow will prevent fluid overload if the intake is restricted, and because it ‘makes space’ for biochemically appropriate replacement fluid. Even poor-quality urine contains potassium, so replacement with potassium-free fluid allows a net loss. Also, urinary sodium losses can be replaced with IV sodium bicarbonate to counter acidosis, and a high infused glucose concentration will reduce catabolism and so minimise urea, potassium and phosphate production. Take advantage of all fluid losses; diarrhoeal losses will ‘make space’ just as effectively as urine losses.

Practical techniques

PD Catheter

Ideally, a catheter with side holes should be inserted so that its tip lies in or near one of the iliac fossae. The ideal catheter is auffed silastic Tenckhoff which has a series of side holes and an end which is cut off straight, but these are expensive and need to be inserted through a peel-away sheath (usually in the midline below the umbilicus). It is possible to dialyse adequately using other more readily available catheters that have side holes, such as chest drains. These are usually inserted over a metal trocar, and have a tapered tip with an end hole that is considerably smaller than the diameter of the tube lumen, which can lead to difficulties with blockage with omentum (see below).

Insertion of catheter

- This must be a strictly aseptic technique performed either under general anaesthetic, or under sedation/systemic analgesia (see Section 1.15) and local anaesthetic. The catheter may be placed directly percutaneously or with a subcutaneous tunnel or with full surgical procedure.
- If the catheter is not tunnelled, to prevent fluid leakage it is essential that it is inserted through the skin with a very tight fit; using a larger skin hole and stitching it closed will inevitably result in leakage in time. Cut a skin slit that is obviously smaller than the tube, and stretch it with a surgical clip or stitch holder.
- Before introducing the catheter, insert an IV cannula through the skin cut and fill the abdomen with about 40 mL/kg of Ringer-lactate solution or 0.9% saline until the abdominal wall is fairly tense.
- To insert the catheter through a tight hole requires some force, and this is best done by pushing the catheter and trocar tip into the dilated skin slit as far as possible, and then suddenly advancing it with a sharp force through the tense abdominal wall. Grip the catheter and trocar tightly about 3 cm from its tip to act as a stop as it pops into the abdomen (the risk of causing damage is greatly reduced by the presence of sufficient instilled fluid).
- To further minimise the risk of trauma, it is better to
enter the upper quadrant lateral to the rectus sheath, and aim towards the opposite iliac fossa, than to use an infra-umbilical approach. Be aware of the possibility of an enlarged spleen or liver.

- Once sited, test to check that fluid flows rapidly in and out, before securing with a skin stitch and sterile dressing.

Problems with omentum

It is common for omentum to wrap around the end of the catheter, and for some to enter the end hole. This slows or stops drainage because the omentum is sucked further into the lumen, but has little effect on filling because the omentum is washed back towards the catheter tip, and the fluid exits through the side holes. Deal with it as follows:

- The omentum can often be forced out by rapidly injecting up to 50 mL of dialysis fluid, Ringer-lactate solution or 0.9% saline into the catheter under pressure.
- If it fails, withdraw the catheter from the abdomen using full aseptic technique. If the omentum has become detached, simply reinsert the catheter, and resume dialysis.
- If (as usually happens) the catheter comes out with the omentum attached, detach it, and gently pull more omentum out, tie round it with an absorbable suture near to the skin surface, cut off the excess, and return the omentum into the abdomen, using the stitch to obtain easy purchase, and replace the catheter.

Fluid and cycles

- Run the dialysis fluid in through a giving set with a burette, and with the bag held about 1 metre above the patient, and leave it to dwell for 30 minutes. Allow it to drain by gravity through a Y-connector into a sealed bag for about 10–15 minutes; by then, it should have drained about as much as was instilled, and the flow should have stopped.
- The osmolality of the dialysis fluid determines the amount of water that is drawn off (ultra-filtered) during each peritoneal dialysis cycle, and this is adjusted by varying the glucose concentration. Typical glucose concentrations available are 1.36% (standard) and 3.86% (high-osmolality) bags. Start with 1.36% glucose.
- Add heparin, 1000 units/litre, to the fluid initially to prevent any blood from the insertion clotting the catheter. Discontinue it once the effluent fluid looks clear.
- Start with 10 mL/kg cycles of dialysis fluid for the first 2 days. Using this small volume minimises the risk of a peritoneal leak of dialysate.
- The first cycle balances are unreliable because there is always a sump of fluid left, but after that the ultra-filtrate required is the volume of fluid that needs to be removed to correct any overload, plus an amount equivalent to the urine that would normally be passed (so just a little less than the normal fluid intake).
- If there is too little ultra-filtrate, increase the glucose concentration of the dialysate by giving some cycles of 1.36% glucose and some of 3.86% glucose. Continue to review the fluid balance, and vary the proportion of cycles of each strength as necessary.
- Increase the cycle volume by 10 mL/kg every 2 days until tolerance occurs, or a maximum of 40 mL/kg. As the cycle volume increases, it is not necessary to dialyse so intensively. Either continue with 30-minute dwells, but just for part of the day (e.g. 8 hours overnight), or lengthen the dwells, eventually moving to chronic ambulatory peritoneal dialysis (CAPD), in which the fluid is left in the peritoneum all the time, and exchanged four to six times per day.

Biochemical control

The sodium, calcium and magnesium content of the dialysis fluid is similar to that of plasma, and the fluid contains lactate, which is converted to base, so is equivalent to bicarbonate. Cycling therefore tends to keep the plasma concentrations stable. Peritoneal dialysis fluid contains no potassium, urea or creatinine, so these are removed.

- Urea equilibrates rapidly, so is cleared well, allowing the child to have a normal protein intake.
- Creatinine is removed slowly, so peritoneal dialysis never restores the plasma levels to normal. This is useful because creatinine is not toxic, and its plasma concentration continues to provide a measure of intrinsic renal function and renal recovery.
- Sometimes the dialysis required to control fluid or urea excretion is sufficient to cause hypokalaemia. If so, reduce the potassium dialysis clearance by adding up to 3 mmol/litre potassium chloride to the dialysate bags (do not use more than this; if the potassium concentration is still too low, give extra orally or intravenously).

Peritonitis

Infection is the major hazard of peritoneal dialysis, and produces a cloudy dialysis effluent in the drainage bag due to white blood cells. Prevention is crucial, by scrupulous hand washing and avoiding touching the open tubing ends while changing peritoneal dialysis bags, and by changing connections as infrequently as possible.

- Monitor constantly by inspecting the clarity of the effluent fluid.
- Undertake daily microscopy for white blood cells (there should be < 50 white blood cells/mL; see Section 8.5).
- If the effluent fluid is cloudy, and microscopy confirms the presence of large numbers of white blood cells (over 100, but typically several hundred), culture a sample of fluid, and start treatment at once by adding heparin (to stop blockage of the tube holes with fibrin) and antibiotics to peritoneal dialysis bags and revert to continuous cycling if not still doing that. Start with vancomycin and cefazidime, and adjust according to the culture and sensitivity results. Concentrations of antibiotics that may be added to peritoneal dialysis fluid are as follows:
  - vancomycin, 25 mg/litre
  - cefazidime, 125 mg/litre
  - ampicillin, 125 mg/litre
  - flucloxacillin, 250 mg/litre
  - gentamicin, 8 mg/litre.
- Continue continuous cycling until a count of < 50 white blood cells/mL is obtained for two samples taken 12 hours apart. Then return to previous dialysis cycles, adding peritoneal dialysis antibiotics for 14 days.
- If accidental contamination occurs, such as touching the open dialysis catheter during a bag exchange, or a fluid leak from a connection or punctured bag, add vancomycin and either cefazidime or gentamicin to the dialysis fluid for the next 12 hours.
- Fungal peritonitis is difficult to clear. It is best to remove
the catheter and treat systemically until the peritonitis resolves.

The urine output must be measured throughout the procedure.

Analgesia for the procedure and throughout the dialysis is likely to be required.

**Chronic renal failure**

**Background**

Chronic renal failure (CRF) is more frequent in boys than in girls. Its commonest cause is congenital renal abnormalities such as dysplasia associated with severe antenatal vesico-ureteric reflux, and often also with posterior urethral valves. It can also follow almost any form of acute renal failure.

It is relatively easy to improve the quality of life of children with milder forms of CRF by simple treatments, especially in the case of older children. In its more severe forms, CRF is very difficult to treat effectively, requiring expensive drugs and intensive laboratory monitoring.

Very young children with CRF are particularly difficult to manage, as they usually have marked anorexia and failure to thrive. Successful treatment requires a massive family and medical input, highly expensive drugs, and a complex medical infrastructure of a kind that has only limited availability worldwide at present. Each country should have a specialised centre that can provide care for such children.

**Progression of CRF**

CRF tends to worsen progressively through childhood. This is mainly because dysplastic or damaged kidneys may not grow in parallel with body growth, and renal function becomes outstripped by demand. Deterioration is likely to be quicker if the child has hypertension, or has recurrent urinary infections with continuing reflux, both of which require active treatment.

**Management**

**Water, sodium and potassium**

Children with dysplastic kidneys usually have polyuric renal failure in which they lose water and salt, and often potassium, in an uncontrolled way. Consequently, they have a persistent thirst, and can become dehydrated extremely rapidly if they vomit persistently. They need IV fluids early, particularly if there is an episode of gastroenteritis.

Hyperkalaemia due to severe CRF occurs relatively late in children with polyuria.

Supplementing with sodium bicarbonate or salt, as needed, can improve well-being and growth. For each of these, start by adding about 1 mmol/kg per day. For bicarbonate, increase daily until the plasma concentration is in the normal range. The total extra sodium needed is best judged by measuring lying and standing blood pressures to detect postural hypotension; a fall in plasma sodium concentration is a very late event. Note that:

- For bicarbonate, 1 mmol is equivalent to 84 mg, so 1 gram contains about 12 mmol bicarbonate. For intravenous use, 8.4% bicarbonate solution contains 1 mmol/mL.
- For sodium chloride (salt), 1 mmol is equivalent to 57 mg, so 1 gram contains about 18 mmoll sodium. For intravenous use, each litre of 0.9% saline contains 5 mmol sodium/mL.

(see Table 5.5.A.2 in Section 5.5.A on ‘shock’ for details of electrolyte concentrations in other more physiological infusion crystalloids, such as Ringer-lactate and Hartmann’s solution), and strong sterile sodium chloride solutions can be used to increase the sodium concentrations of standard IV fluids (e.g. a 30% solution contains 5 mmol sodium/mL).

Children with oliguric renal failure are more difficult to manage because they require salt and water restriction to prevent hypertension, and potassium restriction to prevent hyperkalaemia.

When dialysis is available, indications to begin this treatment are often multiple, and include an intolerable diet or fluid restriction, and symptoms such as poor growth and lethargy as important factors, rather than just specific biochemical parameters.

**Calcium and phosphate**

CRF can lead to abnormalities of the plasma calcium and phosphate concentrations, and these can cause rickets and hyperparathyroidism (renal osteodystrophy), which can result in bone pain, limb deformities, and fractures (especially slipped femoral capital epiphyses). The primary problem is phosphate retention due to a reduced glomerular filtration rate. This causes a high plasma phosphate concentration, which in turn leads to a low plasma calcium level by mass action, and by suppressing the enzyme 1-alpha-hydroxylase, thus lowering the concentration of circulating activated 1-alpha-hydroxyvitamin D. A primary lack of 1-alpha-hydroxylase enzyme from destruction of kidney tissue is rare except in very severe CRF.

Treatment is therefore aimed at reducing the phosphate intake, either directly by dietary restriction (reducing the intake of meat and dairy products), or by giving calcium carbonate with meals. This binds with the phosphate in the gut, and prevents its absorption. The dose needed is very variable. Start at about 50–100 mg/kg, divided among the day’s meals, and titrate the dose (if biochemical monitoring is available) to keep plasma phosphate levels at the lower end of the normal range. This commonly also results in a rise in plasma calcium levels into the normal range. Because of this, it is seldom necessary to treat mild CRF with 1-alpha-hydroxyvitamin D3. If it is needed, in more severe CRF, start with about 20 nanograms/kg once daily, and titrate the dose up until the plasma calcium concentration is normalised. It is extremely potent, and using it without regular monitoring can easily lead to severe hypercalcaemia, which can result in permanent calcification of tissues, including the renal medullae.

**Anaemia**

Severe CRF leads to anaemia because the kidneys fail to produce enough erythropoietin. Treatment by repeated transfusions is unsatisfactory because blood is often scarce, carries infective risks, is always expensive, and eventually leads to iron overload. Recombinant erythropoietin (if available) should be used, after adequate iron levels have been achieved (folate and vitamin B12 supplementation is seldom required, but levels should be checked if possible).

**Growth**

Many factors lead to growth failure in children with CRF.

In older children, attention to fluid and electrolyte intake,
prevention of acidosis with bicarbonate supplements, and control of the bone biochemistry help considerably. Control of uraemia by encouraging a diet containing about 1 gram of protein/kg daily and a high carbohydrate intake will also contribute to good growth.

In young children, the problems are much greater. They are often extremely anorexic; most babies with severe CRF virtually do not feed, and only survive if tube fed for months or even years. Many also vomit excessively. Even when supplemented with tube feeds, very young children with CRF often remain small.

**Transplantation**

Renal transplantation (if it is available) from a living or deceased donor gives the best quality of life for children with end-stage renal failure.

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### 5.7 Liver disorders

#### 5.7.A Acute liver failure

**BOX 5.7.A.1 Minimum standards**

- Vitamin K.
- IV glucose 10%.
- Oxygen.
- Lactulose.
- Blood transfusions and clotting factors.
- Ranitidine/antacids.
- Antibiotics and antifungal treatment.
- High-carbohydrate diet.
- N-acetylcysteine.
- Measurements of prolonged blood clotting times.

**Introduction**

In contradistinction to fulminant liver failure in adults, acute liver failure (ALF) in children may not be accompanied by encephalopathy, which tends to be a late feature, or if it occurs early in the course suggests a metabolic cause.

Prolonged prothrombin time (PT) or international normalised ratio (INR) indicates coagulopathy due to the absence of liver-synthesised coagulation factors, and is the basis of the definition of ALF. However, coagulopathy in the presence of liver dysfunction can also result from vitamin K deficiency (usually due to prolonged cholestasis) and consumption of coagulation factors due to disseminated intravascular coagulation (DIC).

**Definition**

Based on the above, ALF is present in children when coagulopathy accompanies liver disease but is not due to DIC or a lack of vitamin K (see Table 5.7.A.1). Administration of IV or IM vitamin K (300 micrograms/kg for children aged 1 month to 12 years: 10 mg for those over 12 years of age) ensures that remaining coagulopathy is due to failed production (liver failure) or excess consumption (DIC). Markers that suggest DIC, rather than ALF, include a low platelet count, compatible blood film (fragmented cells, schistocytes) and a serum bilirubin that is predominantly unconjugated.

**Diagnosis of ALF**

- The history may establish a recent episode of shock including severe dehydration, sepsis or heatstroke, evidence of ingestion of toxic mushrooms or drugs (including those bought over the counter or obtained from any non-conventional source), or exposure to infection such as *Salmonella typhimurium* (see Table 5.7.A.2).
- The possibility of bloodborne or other parenteral infection with hepatitis B up to 6 months previously should be explored.
- Examination may show features of acute portal hypertension with liver tenderness suggesting Budd–Chiari syndrome or a veno-occlusive disease, or lymphadenopathy suggesting malignancy.
- Urine should be tested for bilirubin, urobilinogen and reducing substances.
- Stools should be examined for colour.
- **Tests to establish many of the causes of ALF require sophisticated laboratory facilities which may not be available.**
  - The cause may be diagnosed from local epidemiology.
  - A blood film and an INR or prothrombin ratio should be measured.
  - A full septic screen, excluding lumbar puncture because of coagulopathy, should be performed (including fungal cultures and chest X-ray).

**TABLE 5.7.A.1 Clinical features of ALF**

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<tbody>
<tr>
<td>1.</td>
<td>Nausea and vomiting is a frequent early feature.</td>
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<tr>
<td>2.</td>
<td>Bruising, petechiae and bleeding secondary to deranged clotting (INR &gt; 4 is associated with 90% mortality).</td>
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<td>3.</td>
<td>Jaundice with tender hepatomegaly or a liver that is enlarged but reducing in size in days.</td>
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<td>4.</td>
<td>Encephalopathy latterly complicated by features of raised intracranial pressure.</td>
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<td>5.</td>
<td>Metabolic alkalosis from failure of the urea cycle associated with a low serum potassium concentration.</td>
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<tr>
<td>6.</td>
<td>Failure to maintain normoglycaemia.</td>
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