5.8 Endocrine disorders

5.8.A Diabetes

**BOX 5.8.A.1 Minimum standards**
- ABC resuscitation skills and equipment.
- Oxygen.
- IV 0.9% saline or Plasma-Lyte 148.
- Insulin.
- Potassium.
- Mannitol or 3% saline.
- ECG monitoring.

**Diabetic ketoacidosis**
Diabetic ketoacidosis (DKA) is the commonest endocrine emergency that may occur in individuals with previously diagnosed diabetes, but should be suspected in any child with:
- dehydration (diarrhoea is not the only cause)
- abdominal pain
- ketone smell on the breath
- acidosis
- acidotic breathing
- unexplained coma.

A child with DKA may die from inhalational pneumonia, hypokalaemia, severe metabolic acidosis or cerebral oedema. Cerebral oedema is unpredictable, occurs more frequently in younger children and those newly diagnosed with diabetes, and has a mortality of around 80%.

These guidelines are intended for the management of children who are more than 3% dehydrated and/or vomiting and/or drowsy and/or clinically acidotic.

Children who are 3% dehydrated or less and not clinically unwell usually tolerate oral rehydration and subcutaneous insulin.

Every unit should have a written policy for the care of children with DKA. The following guidance is adapted from that provided by the British Society for Paediatric Endocrinology and Diabetes (BSPED) (www.bsped.org.uk/clinical/docs/DKAGuideline.pdf).

**Emergency management of children who are over 3% dehydrated and clinically unwell**

**General resuscitation: A, B, C**
- **Airway:** ensure that the airway is patent, and if the child is comatose consider inserting an oropharyngeal airway. If they are comatose or suffering from recurrent vomiting, insert a nasogastric tube, aspirate and leave on open drainage.
- **Breathing:** give 100% oxygen. Give bag-and-mask ventilation if the child is apnoeic or hypoventilating.
- **Circulation:** insert an IV cannula and take blood samples (see below). Only if the child is shocked (tachycardia with poor capillary filling or hypotension) give 10mL/kg 0.9% saline or Plasma-Lyte 148 solution as quickly as possible, and repeat as necessary up to a maximum of 30mL/kg. Note that normal (0.9%) saline causes a hyperchloraemic acidosis because of its excess of the chloride anion. In patients who are acidic because of diabetes, Plasma-Lyte 148 may be preferable, as it does not contain such a high concentration of chloride ions.

**Confirm the diagnosis**
- History: polydipsia, polyuria.
- Clinical signs: acidotic respiration, dehydration, drowsiness, abdominal pain/vomiting.
- Biochemical investigations: high blood glucose levels on finger-prick or venous blood test, presence of ketones or glucose in the urine.

**Investigations**
- **Weigh the child.** If this is not possible because of their clinical condition, use the most recent clinic weight as a guideline, or an estimated weight from centile charts.
- Blood glucose concentration.
- Urea and electrolytes (if plasma bicarbonate is not available, measure arterial blood gas).
- Packed cell volume (PCV) and full blood count.
- Blood culture.
- Urine microscopy, culture and sensitivity.
- Set up a cardiac monitor to observe T waves (hypokalaemia causes flat T waves and may cause cardiac dysrhythmias; hyperkalaemia causes peaked T waves).
- Other investigations (e.g. chest X-ray, CSF, throat swab, etc.) if indicated if the child is febrile, as there may be an underlying infection.

**Assessment**
Assess and record the following in the child's notes, so that comparisons can be made by others later:
- **Degree of dehydration:**
  - < 3%: dehydration is only just clinically detectable.
  - 3–5%: dry mucous membranes, reduced skin turgor.
  - 5–8%: as above with sunken eyes, poor capillary return.
  - > 8%: with shock – severely ill with poor perfusion, tachyarrhythmia, reduced blood pressure.
- **Conscious level:**
  - Assess the AVPU score (Alert, responds to Voice, responds to Pain, Unresponsive).
  - Institute hourly neurological observations. If less than Alert on admission, or there is any subsequent deterioration, record the Glasgow Coma Scale score (see Section 7.3.C) and transfer the child to a...
high-dependency-care unit (if available). Consider instituting cerebral oedema management.

- Full examination, looking in particular for evidence of the following:
  - Cerebral oedema: irritability, slow pulse, high blood pressure and papilloedema. Examine the fundi: papilloedema is a late sign.
  - Infection: look for a focus. DKA can cause a leukocytosis but not a fever.
  - Ileus.

- Observations to be carried out (ensure that full instructions are given to the nursing staff):
  - Strict fluid balance and urine testing of every sample for glucose.
  - Hourly capillary blood glucose measurements.
  - Twice daily weights.
  - Initially hourly or more frequent neurological observations.

- Report immediately to the medical staff (even at night) symptoms of headache or any change in either conscious level or behaviour.

- Report any changes in the ECG trace, especially T-wave changes.

### Management

By this stage, the circulating volume should have been restored if shock was initially present. If not, give a further 10 mL/kg of 0.9% saline or Plasma-Lyte 148 over 30 minutes. Avoid overzealous fluid replacement, as this may be a risk factor for cerebral oedema.

#### Estimating fluid requirements

The amount of fluid that the child needs over a 24-hour period must be calculated. It is the sum of:

\[
\text{estimated fluid deficit} + \text{maintenance requirements} + \text{ongoing losses}
\]

### Deficit

In DKA the deficit must be replaced more slowly than in gastroenteritis, over 48 hours rather than 24 hours. Even in very severe dehydration, use no more than 10% dehydration as the maximum in your calculations. Document the fluid balance carefully.

Determine the degree of dehydration, and never estimate more than 10% dehydration in this situation.

- Weigh the child, or else estimate their weight from their age as follows:

\[
\text{weight (kg)} = 2 \times \text{[age (years) + 4]}
\]

- Use the following formula: percentage dehydration \times weight (kg) \times 10 = deficit (in mL).

For example, a child whose weight is estimated to be 10 kg is 10% dehydrated.

Their estimated fluid loss is 10 \times 10 \times 10 = 1000 mL (40 mL/hour if replaced over 24 hours or 20 mL/hour if replaced over 48 hours, which is safer in DKA).

### Maintenance

#### TABLE 5.8.A.1 Estimated maintenance fluid requirements based on child’s body weight

<table>
<thead>
<tr>
<th>Body weight</th>
<th>Volume of fluid needed per day</th>
<th>Volume of fluid needed per hour</th>
</tr>
</thead>
<tbody>
<tr>
<td>First 10 kg of body weight</td>
<td>100 mL/kg</td>
<td>4 mL/kg</td>
</tr>
<tr>
<td>Second 10 kg of body weight</td>
<td>50 mL/kg</td>
<td>2 mL/kg</td>
</tr>
<tr>
<td>Subsequent kg</td>
<td>20 mL/kg</td>
<td>1 mL/kg</td>
</tr>
</tbody>
</table>

#### Ongoing losses

<table>
<thead>
<tr>
<th>For each diarrhoea stool</th>
<th>&lt; 2 years old: give 50–100 mL</th>
<th>&gt; 2 years old: give 100–200 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>For each vomit</td>
<td>2 mL/kg oral rehydration solution (ORS): give small frequent volumes (e.g. 5 mL/minute in a child) via a spoon, syringe or cup</td>
<td></td>
</tr>
<tr>
<td>For nasogastric tube aspirates</td>
<td>Replace volume for volume with either ORS or 0.9% saline or Plasma-Lyte 148 containing 5% or 10% glucose</td>
<td></td>
</tr>
</tbody>
</table>

#### Type of fluid

Initially use 0.9% saline or Plasma-Lyte 148. Once the blood glucose concentration has fallen to 14 mmol/litre, change the fluid to 0.9% saline or Plasma-Lyte 148 containing, in addition, 5% glucose and 20 mmol KCl per 500-mL bag.

Expect the sodium concentration to rise initially as the glucose level falls and water is removed from the circulation.

Cerebral oedema may be related to a plasma sodium concentration that falls or does not show the expected rise as glucose levels fall.

#### Electrolytes

**Bicarbonate**

Bicarbonate is rarely, if ever, necessary. Continuing acidosis usually indicates insufficient resuscitation. Bicarbonate should only be considered in children who are profoundly acidotic (pH < 7.0) and shocked with circulatory failure. Its only purpose is to improve cardiac contractility in severe shock. The maximum volume of 8.4% sodium bicarbonate for half-correction of acidosis is calculated according to the following formula, and given over 60 minutes:

\[
\text{Volume (mL) of 8.4% sodium bicarbonate} = \frac{1}{3} \times \text{weight (kg)} \times \text{base deficit (mmol/litre)} \div 2
\]

If no blood gas measurement is available, do not give bicarbonate unless the child is in profound shock.

#### Potassium

- Commence potassium immediately unless anuria is suspected, or there are peaked T waves on the ECG, or the serum potassium concentration is higher than 7.0 mmol/litre.

- Potassium is mainly an intracellular ion, and there is always massive depletion of total body potassium, although initial plasma levels may be low, normal or even high. Potassium levels in blood will fall once insulin is commenced.

- Add 20 mmol KCl to every 500 mL unit of IV fluid given.

- Check urea and electrolytes 2 hours after resuscitation.
is commenced and then at least 4-hourly thereafter, and alter potassium replacements accordingly (more potassium is sometimes needed).

- Use a cardiac monitor to observe frequently for T-wave changes, and alert nursing staff to any changes that might be seen, and advise them when to call for medical help.
- If potassium-containing fluids are not available, start insulin (see below) after 1–2 hours of rehydration, and arrange transport to a unit that can provide this (if available).

**Insulin**

Once fluids are running, calculation of the insulin infusion rate may be undertaken at leisure, as the blood glucose levels will already be falling. Continuous low-dose IV infusion is the preferred method.

However, if a syringe pump is not available or not safe to use after at least 1 hour of rehydration treatment give subcutaneous boluses of short-acting insulin 1- to 2-hourly at 0.1 unit/kg/dose. Give half the dose if the blood glucose level is falling too fast.

There is no need for an initial bolus, and some evidence that insulin should not be given during the first hour of IV fluid treatment.

- If an infusion system is available and safe to use, make up a solution of 1 unit/mL of human soluble insulin (e.g. Actrapid) by adding 50 units (0.5 mL) of insulin to 49.5 mL of 0.9% saline in a syringe pump. Attach this using a Y-connector to the IV fluids that are already running. Do not add insulin directly to the fluid bags. The solution should then run at 0.1 unit/kg/hour (0.1 mL/kg/hour).

Once the blood glucose level is down to 14 mmol/litre, change to 5% glucose in 0.9% saline (add 50 mL of 50% glucose to a 500 mL bag of saline) and potassium as above. Do not reduce the insulin infusion until the pH is > 7.3 and the glucose concentration is < 14 mmol/litre, when it may safely be reduced to 0.05 mL/kg/hour.

If the blood glucose level falls below 7 mmol/litre, consider giving more 0.9% saline or Plasma-Lyte 148.

If an infusion system is available and safe to use, make up a solution of 1 unit/mL of human soluble insulin (e.g. Actrapid) by adding 50 units (0.5 mL) of insulin to 49.5 mL of 0.9% saline in a syringe pump. Attach this using a Y-connector to the IV fluids that are already running. Do not add insulin directly to the fluid bags. The solution should then run at 0.1 unit/kg/hour (0.1 mL/kg/hour).

Discontinue the insulin infusion 60 minutes after the first subcutaneous injection in order to avoid rebound hyperglycaemia.

**Care of the newly diagnosed diabetic child**

After treatment of DKA in the newly presenting but well diabetic child, the process of education and treatment should commence. It is not feasible to stabilise the child’s control or to teach all aspects of diabetic care while they are an inpatient, so ideally (if resources permit) this should take place at home, although some authors advocate a prolonged initial admission for this process.

- Exclude hypoglycaemia as a cause of neurological symptoms.
- Give mannitol 500–1000 mg/kg immediately (2.5–5 mL/kg 20% mannitol over 15 minutes). Alternatively, give 3% saline 5 mL/kg over 5–10 minutes. Give this as soon as cerebral oedema is suspected.
- Restrict IV fluids to two-thirds maintenance, and replace the deficit over 72 hours rather than 48 hours.
- Keep Na⁺ levels > 135 mmol/litre. Keep the head in the midline and 30 degrees elevated.
- Avoid fever > 38.0°C.
- Repeated doses of mannitol or strong saline (at the dose stated above, every 2–4 hours) should be used to control intracranial pressure.
Ensure that the parents and the child (if he or she is able to do so) understand or can perform the following:

- insulin administration
- urine testing for ketones
- blood testing
- dietary measures
- other general issues.

**Insulin**

Draw up the specified dose of insulin correctly. As a rough guide, a new patient will need approximately 0.5 unit/kg/day.

The frequency and choice of insulin depends entirely on local resources. This may mean twice daily medium-acting insulin alone (60% in the morning, 40% in the evening), or medium-acting insulin mixed together with short-acting soluble insulin (usually in a 30% short/70% long ratio). If never analogue fast-acting insulins are available, these may be given before every meal in an initial dose of 1 unit for every 20 grams of carbohydrate eaten, with a longer-acting insulin (40% of the total daily dose) given before bedtime.

It is very rarely possible to achieve adequate control with a single daily dose of insulin except in very small children. However, once-daily medium-acting or pre-mixed insulin should be seen as a minimum fallback position if availability of insulin is a problem. Likewise, although it is common practice to use human or genetically modified insulins, pork or beef insulin may be substituted if necessary.

Further modification of the dose will take place as an outpatient, as more insulin will be needed after the initial period and with growth and puberty.

**Urine testing**

Test the urine for sugar using stick tests. Clinitest tablets for reducing substances are too cumbersome for routine use, but may be used as a substitute if they are the only option. Suggest stick testing about twice daily at home. Emphasise the value of testing the first morning urine to estimate overnight control.

Test the urine for ketones using Ketostix or tablets. This only needs to be routinely done if the urine contains 3% glucose or more, and in times of intercurrent illness when the persistence of ketonuria should prompt the seeking of medical attention for incipient DKA.

The importance of accurate recording of the results in a control book, if possible, should be emphasised, to aid decision making at follow-up.

**Blood testing**

If resources allow, all parents should be able to test the blood glucose level, at least in an emergency, and ideally also for routine monitoring of control. The parent or carer (and also the child, if appropriate) should be taught the following:

- how to use a lancet (or automatic finger-pricking device) to draw blood from the side (not the pulp) of the finger
- how to ensure that an adequate sample is placed on the strip
- how to read the strip visually (a meter may be used if resources allow)
- if this method of monitoring control is chosen, the importance of providing test results at staggered times through the day (ideally one or two tests per day) should be explained; the need for accurate recording of the values in a diary should be emphasised (ascertain the parents’ literacy and numeracy levels)
- the instantaneous nature of the result obtained and the detection of hypoglycaemia with blood testing should be highlighted, and compared with urine testing.

**Diet**

The parents or carers and the child should ideally meet a specialist diabetic dietitian and discuss the concept of carbohydrate balance and how the diet is spread through the day. The diet must be adequate for growth and nutrition, and should contain around 50% of energy as complex carbohydrate. It is not advisable to allow “free” fatty foods, as they may accentuate later macrovascular complications.

Explain the importance of fairly close adherence to the advised diet, and that the diet may need to be revised from time to time as the child grows and their pattern of activity changes.

The parents or carers and the child should understand the influence of food intake on blood sugar levels. Diabetic carbohydrate 10-gram ‘portions’ are often used with analogue short-acting insulin boluses before meals (if available), but need considerable expertise to be taught effectively.

Sweet unrefined sugars should ideally only be taken before exercise or as occasional treats, although ideally the insulin dose should be varied to take this into account.

**General care**

- It is essential that the parents or carers and the child (if he or she is old enough) understand how inadequate glycaemic control may predispose to micro- and macrovascular complications in the longer term. These are not uncommon findings in teenagers in Africa, due to their appalling glycaemic control in earlier childhood.
- It is also important that the parents or carers ensure that a supply of insulin is always available, as the commonest cause of DKA is lack of insulin at home in resource-limited environments.
- The parents or carers and child (if appropriate) should understand how exercise, diet and insulin interact to influence blood sugar levels.
- The symptoms of hypoglycaemia should be explained. It is important that the parents or carers understand the possible signs of an attack and what can be done to terminate the “hypo”. They should know how to use rapid-acting sweet sugary gel, non-“diet”/“lite” sugary drinks or tablets during the early stages of the attack. Ideally, a 1-mg glucagon pack (if available) should be given to each family prior to discharge, and the parents should be shown how to prepare and give the pre-packed injection in an emergency to terminate a severe hypoglycaemic attack with unconsciousness or fits. If a “hypo” is treated, a more complex carbohydrate snack should be given to prevent immediate recurrence.
- The family should be given the address of any local support groups for individuals with diabetes and their families (if such groups exist). If possible, give the parents and child a folder containing relevant booklets on diabetes.
- The family should ideally have access to medical advice and treatment 24 hours a day if they are worried about their child’s immediate health, or can be seen at the next outpatient clinic for less urgent problems.
Hypoglycaemia is an important cause of morbidity and mortality that needs to be recognised, as the complications are potentially preventable.

**Definition**
Hypoglycaemia is now widely defined as a blood glucose concentration of less than 2.5 mmol/litre (45 mg/dL) at any age. The measurement should ideally be made in a laboratory with appropriate quality control. Testing with reagent strips is less accurate, particularly within the critical range.

**Introduction**
Hypoglycaemia is an important cause of morbidity and mortality that needs to be recognised, as the complications are potentially preventable.

**Presentation and aetiology**
Hypoglycaemia may present at any age from birth into adulthood. Symptoms are varied and rarely specific, particularly in infants. In neonates, fits and apnoeic attacks may be important clues. In infants and children the most important presentation, because of the risk of complications, is also fits and encephalopathy (see Table 5.8.B.1). The common causes are listed below.

In infants and children in well-resourced countries, ketotic hypoglycaemia, endocrine disorders and metabolic disorders usually predominate. By contrast, in resource-limited countries, malnutrition and infections such as malaria (and its treatment) are more common.

**Treatment**

**Glucose dosage**
There is insufficient scientific data to be definite about the quantity of glucose to give parenterally to a hypoglycaemic child. 5 mL of 10% glucose was the standard dose for a time but there is evidence that this much glucose can raise the plasma glucose to a level high enough to produce an insulin surge which then results in another hypoglycaemic episode. Of course, in a diabetic child who has become hypoglycaemic because of insufficient calories or too much insulin, this will not occur, so in these circumstances 5 mL of 10% glucose is safe.

- state of injection sites
- foot examination and discussion of foot care
- fundoscopy (at diagnosis, for cataracts; after 5 years of diabetes or in teenagers, for retinopathy)
- microalbumin/creatinine ratio in the first morning urine sample for detection of renal complications (after 5 years of diabetes or in teenagers)
- glycosylated haemoglobin for monitoring long-term control (ideal control is a level of < 5.5 mmol/mol).
- thyroid disorders and coeliac disease are both more likely to occur in children with diabetes. Although, ideally, anti-thyroid antibodies and antigliadin antibodies could be checked at the time of diagnosis of diabetes, and every 4 years thereafter, they are expensive tests and in resource-limited environments it is better to undertake a careful clinical assessment for additional thyroid or coeliac disease at annual outpatient appointments.

Transfer to adult services should take place in a planned manner, ideally at a joint handover clinic.

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**Ideal checklist for use at discharge**

- Dextrose gel: 1 box of plastic tubes or 50 grams of dextrose tablets.
- Disposable syringes and needles, ideally 0.3-mL low-volume syringes with as small a needle as can be located (down to 31-gauge are available).
- Insulin.
- Glucagen Novo 1 mg pack.
- Glucose testing blood sticks, finger-pricking device, plus lancets or urine sticks.
- Control book and pen.
- Ketostix.
- Sharps disposal bin.
- Appointment at next diabetic clinic.

Outpatient care

The patient should be reviewed at regular intervals (as frequently as resources allow). Ideally, at least once a year the child should have the following reviewed:

- their knowledge of diabetes and emergency management
- growth
- blood pressure
- state of injection sites
- foot examination and discussion of foot care
- fundoscopy (at diagnosis, for cataracts; after 5 years of diabetes or in teenagers, for retinopathy)
- microalbumin/creatinine ratio in the first morning urine sample for detection of renal complications (after 5 years of diabetes or in teenagers)
- glycosylated haemoglobin for monitoring long-term control (ideal control is a level of < 5.5 mmol/mol).
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Transfer to adult services should take place in a planned manner, ideally at a joint handover clinic.

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**5.8.B The child with hypoglycaemia**

**BOX 5.8.B.1 Minimum standards**
- Oral glucose solutions.
- IV 10% and 50% glucose.
Diagnosis of the cause of hypoglycaemia

If the blood sugar level is less than 2.5 mmol/litre, it is important to establish a cause. Transfer 1 mL of blood into a fluoride tube, if possible also 1 mL heparinised blood, and the first urine after the hypoglycaemic episode to send for metabolic analysis, in particular for ketones.

- Is there ketosis? If so, look for signs of hypopituitarism and/or growth hormone deficiency.
- If feasible, check the cortisol growth hormone level and insulin levels in blood taken at the time of hypoglycaemia.
- If the blood lactate level is raised, consider organic acidemia or a defect of gluconeogenesis.
- If ketosis is absent, consider hyperinsulinism (high birth weight) or disorders of fatty acid oxidation.

Prevention

As the symptoms are non-specific, measure blood glucose levels if possible in any suspected situation. If hypoglycaemia is suspected and blood glucose measurement is not possible, treat with glucose and observe the response.

If the response is clearly related to giving glucose, assume that hypoglycaemia was present.

In the neonate, every effort should be made to avoid those factors that will exacerbate hypoglycaemia, including delayed feeding and hypothermia (see Section 3.4).

### TABLE 5.8.B.1 Common symptoms and signs of hypoglycaemia

<table>
<thead>
<tr>
<th>In childhood</th>
<th>In neonates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Convulsions</td>
<td>Convulsions</td>
</tr>
<tr>
<td>Reduced conscious level</td>
<td>Reduced conscious level</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Jitteriness, tremor</td>
</tr>
<tr>
<td>Sweating, pallor</td>
<td>Cyanotic episodes</td>
</tr>
<tr>
<td>Palpitations</td>
<td>Apnoeic episodes</td>
</tr>
<tr>
<td>Headache</td>
<td></td>
</tr>
<tr>
<td>Behaviour abnormalities</td>
<td></td>
</tr>
<tr>
<td>Visual disturbances</td>
<td></td>
</tr>
<tr>
<td>Slurred speech</td>
<td></td>
</tr>
<tr>
<td>Ataxia</td>
<td></td>
</tr>
<tr>
<td>Hunger</td>
<td></td>
</tr>
</tbody>
</table>

Some causes of hypoglycaemia

**Neonates**

- Birth asphyxia.
- Small for gestational age.
- Preterm birth.
- Sepsis.
- Malnutrition.
- Hypothermia.
- Infant of diabetic mother.
- Liver disease, endocrine and metabolic disorders (see below).

**Infants and children**

Endocrine disorders

- Diabetic on treatment.
- Persistent hyperinsulinaemic hypoglycaemia of infancy (formerly nesidioblastosis) and other congenital and inherited hyperinsulinaemic syndromes.
- Islet-cell tumours.

- Hypopituitarism.
- Growth hormone deficiency.
- Adrenal insufficiency (any cause).

**Metabolic disorders**

- Disorders of glycogen metabolism, gluconeogenesis or fatty acid oxidation, organic acidemias, etc.
- Ketotic hypoglycaemia (‘accelerated starvation’).
- Liver disease: any severe acute liver disease.
- Malnutrition.
- Infections: malaria, especially when treated with quinine.
- Any severe illness.

**Poisoning**

- Alcohol.
- Salicylates.
- Insulin.

**Drugs**

- Oral hypoglycaemic agents.

How to give glucose in suspected hypoglycaemia

If the patient is conscious, give sugary drinks or foods such as jam, candy or honey.

If the patient is unconscious:

1. Insert an IV or IO line and draw blood for emergency laboratory investigations.
2. Check blood glucose levels with a glucose monitoring stick. If low (< 2.5 mmol/litre (45 mg/dL) in a well-nourished child or < 3 mmol/litre (54 mg/dL) in a severely malnourished child) or if blood glucose cannot be measured because no stick test is available, treat as for hypoglycaemia anyway.
3. Give 2–5 mL/kg of 10% glucose solution rapidly by IV or IO injection or 2.5 mL/kg of 10% glucose in the neonate.
4. Recheck the blood glucose level after 20 minutes. If it is still low, repeat 2–5 mL/kg of 10% glucose solution. Continue if necessary with an infusion of a glucose containing fluid such as 5 mL/kg/hour of 10% glucose solution or IV fluids containing 5–10% glucose (dextrose).
5. If venous or intra-osseous access is impossible in an unconscious patient, give sublingual sugar (see below for technique).
6. Feed the child as soon as they are conscious.
7. If it is not possible to feed the child without risk of aspiration, give:
   - milk or sugar solution via a nasogastric tube (to make sugar solution, dissolve 4 level teaspoons of sugar (20 grams) in a 200-mL cup of clean water)
   - IV fluids containing 5–10% glucose (dextrose).

**Note:** 50% glucose solution is the same as 50% dextrose solution or D50.

If only 50% glucose solution is available: dilute 1 part of 50% glucose solution to 4 parts of sterile water, or dilute 1 part of 50% glucose solution to 9 parts of 5% glucose solution. For example, 10 mL of 50% solution with 90 mL of 5% solution gives 100 mL of an approximately 10% solution.

**Note:** For the use of blood glucose stick tests, refer to the instructions on the box. Generally, the strip must be stored in its box, at 2–3°C, avoiding sunlight or high temperatures.
humidity. A drop of blood should be placed on the strip (it is necessary to cover all of the reagent area). After 60 seconds, the blood should be washed off gently with drops of cold water and the colour compared with the key on the bottle or on the blood glucose reader. (The exact procedure will vary with different strips.)

**Sublingual sugar (sucrose) for treatment of hypoglycaemia**

Sublingual sugar may be used as an immediate ‘first-aid’ measure when managing hypoglycaemia in an unconscious child in situations where IV or IO administration of glucose may be impossible or delayed.

1. Give ½ to 1 teaspoonful of sugar, moistened but not dissolved with 1–2 drops of water and insert under the tongue (sublingually) and between the lower jaw and the gums (in the buccal area). Children should be monitored for early swallowing, which leads to delayed absorption, and in this case another dose of sugar should be given. If sublingual sugar is given, repeat the doses at 20-minute intervals. This is a useful technique in the community where facilities for parenteral glucose may not be available. However, note that sublingual and buccal absorption is not as effective as gastrointestinal absorption of sugar.

2. Recheck the blood glucose level after 20 minutes, and if the level is still low (< 2.5mmol/litre or < 45mg/dL), repeat the IV glucose (5mL of 10% glucose/kg) or repeat the sublingual sugar.

3. Prevent further hypoglycaemia by feeding where possible. If IV fluids are being given, prevent hypoglycaemia by adding 10mL or 20mL of 50% glucose to 90mL or 80mL, respectively, of Ringer-lactate solution or 0.9% saline to give a 5% or 10% glucose solution, respectively.

**5.8.C Other endocrine disorders**

**Adrenal crisis**

**BOX 5.8.C.1 Minimum standards**

- ABC resuscitation skills and equipment.
- Hydrocortisone and fludrocortisone.
- IV saline 0.9%.
- IV glucose 10%.

**Diagnosis**

An adrenal crisis is most likely to be encountered in a neonate with congenital adrenal hyperplasia (CAH) or hypopituitarism (look for virilisation in the female with CAH, and microphalanx and cryptorchidism in the male with hypopituitarism). It may occur in older children with adrenal destruction secondary to autoimmune processes or tuberculosi.

Suspect adrenal crisis in a severely ill child with:

- acidosis
- hyponatraemia
- hypotension
- hyperkalaemia
- hypoglycaemia.

**Children receiving long-term steroid therapy**

Replacement steroids given as hydrocortisone up to 10mg/m²/day replicate natural secretion and are free of side effects if adequately monitored.

Therapeutic doses of steroids for asthma, rheumatoid arthritis, etc. will produce adrenal suppression in a manner related to the dose and duration of treatment. Short 5-day courses of prednisolone therapy will produce measurable adrenal suppression that almost never requires action. Longer courses up to 1 month should be tapered off over a 2-week period to allow recovery of the pituitary-adrenal axis.

More prolonged treatment with high-dose steroids may produce profound hypoaldosteronism for months after cessation of treatment. In this case, taper the steroid dose to the equivalent of 5mg/m²/day of prednisolone. Then convert this to an equivalent dose of hydrocortisone given in the morning (1 mg prednisolone is equivalent to approximately 3mg hydrocortisone). Then reduce the hydrocortisone by 2.5mg/week until the child is on approximately 6mg/m²/day, when it is probably safe to stop treatment after 2 weeks. If possible, check the 9 a.m. pre-dose cortisol level and stop treatment if this exceeds 150 nmol/litre at any time. Severe stress, infection or injury will require increased steroid cover during the next 6 months.

Children on physiological replacement treatment or prolonged pharmacological doses of steroids should ideally carry some warning identification for medical staff, advising against the abrupt cessation of steroids, and stating the emergency stress dose of oral (usually three times replacement dose) or parenteral treatment for operative cover or at times of illness associated with vomiting (hydrocortisone, 12.5 mg for infants, 25 mg for children, 50 mg for older children and 100 mg for adults, given as an immediate IV/IM dose and then 4- to 6-hourly IV).

**Management of adrenal crisis**

- Treat airway, breathing, shock and hypoglycaemia (see Section 5.8.B).
- Continue 0.9% saline to correct the deficit and for maintenance (see Section 5.8.A).
- Give hydrocortisone IV 6-hourly as follows: 12.5 mg dose for neonates and infants, 25 mg for children aged 1–5 years, 50 mg for children aged 6–12 years, and 100 mg for adolescents aged 13–18 years.
- If the diagnosis is established, continue maintenance hydrocortisone, 8–12 mg/m²/day in three divided doses (12–15mg/m²/day for CAH) and, if salt loss is demonstrated in the context of CAH or adrenal destruction, fludrocortisone 150–250 micrograms/m²/day in one dose. Infants may also require oral sodium chloride, 1 gram/10kg/day (80 mg = 1 mmol).

**Hypoglycaemia**

For a discussion of neonatal hypoglycaemia, see Section 3.4.
Thyroid disorders

BOX 5.8.C.2 Minimum standards
- Thyroxine
- Carbimazole
- Propranolol
- Iodine supplements

Neonatal thyrotoxicosis
Mothers who have active thyrotoxicosis or who have become hypothyroid as a consequence of treatment of thyrotoxicosis may still pass thyroid-stimulating antibodies to the fetus during the last trimester. The neonate (or fetus) will show the following:
- hydrops in severe cases
- tachycardia with heart failure: this may occur at up to 1 week post delivery, especially if the mother is on anti-thyroid drugs
- thinness/light for dates
- diarrhoea
- hyperkinesis
- possibly craniosynostosis.

Management
- If hyperthyroidism is detected antenatally, treat the mother with low-dose carbimazole, 5–15 mg/day (use the lowest dose possible for control).
- Treat the infant with:
  - propranolol, 1 mg/kg three to four times orally daily
  - carbimazole, initially 250 micrograms/kg 3 times a day
  - aqueous iodine oral solution (5% iodine plus 10% potassium iodide), 130 mg/mL of total iodine, 1 drop 0.05–0.1 mL every 8 hours until thyroid control is achieved.
- Stimulating antibodies will clear by 3 to 6 months of age, and treatment can be stopped.

Congenital hypothyroidism
Between 1 in 2000 and 1 in 10000 babies are born with a maldescended or absent thyroid gland. There are rarer cases of dyschromonogenesis (dominant and recessive – more common as a consequence of consanguineous relationships) associated with neonatal goitre and very rare central isolated thyroid-stimulating hormone (TSH) deficiency.

Untreated early hypothyroidism results in cretinism.

Many countries screen for this condition in the first month of life, looking for elevated TSH (except in TSH deficiency) and/or low thyroxine or free thyroxine levels. Different screening laboratories will produce different assay results.

In general, TSH in high double figures (mU/litre) is unequivocally raised and will be confirmed by a total thyroxine concentration of less than 50 nmol/litre or a free thyroxine in single figures (pmol/litre).

In resource-limited countries, X-ray of the knee or wrist to detect delayed bone age in infants and young children is helpful for diagnosis where TSH or thyroxine assays are unavailable.

An untreated affected child will develop, in the following order:
- jaundice
- constipation
- hoarse cry
- umbilical hernia
- coarse features
- mental retardation
- poor growth.

Therefore clinical awareness is important in order to identify possible cases of hypothyroidism in babies with the common symptoms of jaundice and constipation. Prolonged jaundice should lead to investigations, including those for hypothyroidism (see Section 3.4).

Management
Give thyroxine, 10–15 micrograms/kg once daily, titrated to maintain TSH in the normal range with normal growth and development. The adult dose is around 2–3 micrograms/kg.

Iodine deficiency
This most commonly occurs in inland mountainous areas. The clinical features vary among different ethnic groups, with deafness, mutism, mental impairment and poor growth being common, and goitre being universal. The disorder may be prevented by adding potassium iodide to cooking salt (10 mg/kg salt) or providing it as supplemented sweets and bread. Iodide as an oily suspension can be given intramuscularly every 3 years.

Acquired hypothyroidism
This is usually part of an autoimmune process (which may be familial), and may be associated with diabetes mellitus. It is much more common in older girls, who will usually have the following:
- goitre
- lethargy
- poor growth rate with excess weight gain
- pallor
- constipation
- hair loss/dry skin
- delayed puberty.

The diagnosis is confirmed by raised blood TSH levels and, if possible, demonstration of antithyroid peroxisomal antibodies.

Management
Thyroxine is given to suppress TSH to the normal range and allow normal growth and pubertal development.

Doses of thyroxine
Neonate: initially 10–15 microgram/kg once daily (maximum 50 micrograms daily) then adjusted in steps of 5 micrograms/kg every 2 weeks or as clinically indicated; usual maintenance dose 20–50 micrograms daily.

Child 1 month–2 years: initially 5 microgram/kg once daily (maximum 50 micrograms daily) then adjusted in steps of 10–25 micrograms daily every 2–4 weeks or as clinically indicated; usual maintenance dose 25–75 micrograms daily.

Child 2–12 years: initially 50 micrograms once daily then adjusted in steps of 25 micrograms daily every 2–4 weeks or as clinically indicated; usual maintenance dose 75–100 micrograms daily.

Child 12–18 years: initially 50 micrograms once daily then adjusted in steps of 25 micrograms daily every 3–4
weeks or as clinically indicated; usual maintenance dose 100–200 micrograms daily.

**Thyrotoxicosis**

This is much more common in older girls, often those with a family history of thyroid disease. It should be suspected if the following are present:

- fine tremor
- weight loss
- psychiatric disturbance
- exophthalmos (rare in children)
- tachycardia with a wide pulse pressure
- loose stools
- goitre with bruit.

The diagnosis is confirmed by suppressed TSH (level is undetectable) with raised thyroxine level.

**Management**

Treatment is with low-dose carbimazole. In neonates to children aged 12 years initially 250 micrograms/kg 3 times a day (maximum 30 mg/day) and adjusted as necessary until euthyroid. In children aged 12 to 18 years initially 10 mg 3 times a day adjusted as necessary. Carbimazole should be continued for at least 2 years, after which withdrawal should be attempted. If relapse occurs, the options include further medical therapy, surgery by an experienced thyroid surgeon, or radio-iodine in a specialised centre.

**Thyroid mass**

**Smooth goitre**

An isolated smooth goitre with or without a bruit may occur in:

- iodine deficiency
- acute and subacute thyroiditis (viral, bacterial, lymphocytic or other), which is usually tender
- ingestion of goitrogens (e.g. cabbage, kale or other brassicas)
- familial dyshormonogenesis
- idiopathic pubertal goitre
- thyrotoxicosis (Graves’ disease, thyroiditis, thyroid hormone resistance)
- Hashimoto’s thyroiditis.

If thyroid function is normal, no treatment is necessary; otherwise treat as described above. In iodine-deficient areas where thyroid investigations are not available, treat with oral aqueous iodine as described above. Nodules require investigation by fine-needle aspiration and histology.

**Nodular goitre**

Nodular goitre may occur in:

- Hashimoto’s thyroiditis
- adenoma (hot, cold, euthyroid)
- lymphoma
- non-thyroidal masses (lymph nodes, branchial cleft cyst, thyroglossal cyst)
- isolated simple cyst
- carcinoma
- histiocytosis.

**Disorders of sexual development (DSD)**

Uncertainty regarding a child’s gender is a distressing emergency for the family.

Most of these children are well unless associated with congenital adrenal hyperplasia (CAH) and salt loss (see above) or other major congenital abnormalities.

Avoid the urge to decide the appropriate sex of rearing of the child until the results of diagnostic tests are available.

Support the parents during this difficult time.

- DSD may be the result of excess androgens in females (the commonest situation, usually secondary to CAH of the 21-hydroxylase deficiency variety), lack of androgens (or the receptor) in males, or (rarely) mixed gonadal DSD with the presence of ovarian and testicular tissue. Minimum investigations are chromosome analysis and plasma for 17-hydroxyprogesterone (which is elevated in the commonest form of CAH). If a baby with a DSD becomes unwell with hypotension, hyponatraemia and hyperkalaemia, assume an adrenal crisis and treat as described above.

- Further investigation requires highly specialised tests (i.e. blood, radiology and ultrasound, fibroblasts, laparoscopy or laparotomy). Treatment of non-CAH DSD is also complex, but can often be deferred to allow appropriate transfer of care to a specialist centre. In specialist centres there need to be close working relationships between the different specialists. It is not appropriate for surgeons to operate without involving endocrinologists in working up these patients, and it is essential that the members of the multidisciplinary team work closely together in the management of these cases.

**Congenital adrenal hyperplasia (CAH)**

Congenital adrenal hyperplasia (CAH) is an autosomal-recessive condition, and therefore is more common in consanguineous relationships. Many forms exist, as several enzymes involved in the synthesis of cortisol and aldosterone may be deficient; partial cases also occur within each subtype.

Salt-losing 21-hydroxylase deficiency is by far the commonest type. Most forms result in over-masculinisation of the female (although under-masculinisation of the male can also occur in defects near the start of the biosynthetic pathway). Salt loss occurs in several forms (see above), although the second commonest deficiency (11-beta-hydroxylase) causes salt retention and hypertension.

Females usually present as DSD (see above) and males with salt loss, which usually occurs after the first week of life (see above for acute and long-term management). In non-salt-losing forms there will be incomplete early puberty (see below).

Once the diagnosis is established, treat with mildy suppressive doses of hydrocortisone, 12–15mg/m²/day in three divided doses and, if salt loss is demonstrated, fludrocortisone, 150–250 micrograms/m²/day in one dose. Infants may also require oral sodium chloride, 1 gram/10kg/day (60mg = 1 mmol).
Addison’s disease and Cushing’s syndrome

Addison’s disease (hypoadrenalinism)
Hypoadrenalinism may present as an emergency (see above) or be suspected if there is:
- unexplained lethargy
- failure to thrive
- pigmentation of scars and skin
- vitiligo or other signs of autoimmune disease
- a strong family history of hypoadrenalinism or unexplained sudden death
- hypernatraemia and hyperkalaemia
- syndrome of candidiasis and hypoparathyroidism preceding the hypoadrenalinism (HAM or APECED syndrome).

If confirmed by a low 9 a.m. cortisol level (< 150 nmol/litre), treat as outlined above for adrenal crisis.

Cushing’s syndrome (hyperadrenalinism)
Cushing’s syndrome is usually the result of iatrogenic corticosteroid administration (> 12 mg/m²/day hydrocortisone or the equivalent; see above). Over-secretion of adrenal steroids is rare. Signs of corticosteroid excess include the following:
- poor (zero) growth rate
- red cheeks
- striae
- glucose intolerance
- excess weight gain (central)
- muscle weakness
- hypertension.

Adrenal carcinoma or adenoma may produce Cushing’s syndrome. There is often accompanying virilisation and an abdominal mass. The child is usually young, in contrast to the older child with Cushing’s disease secondary to an ACTH-secreting pituitary adenoma.

The diagnosis is supported by a detectable midnight cortisol level (> 50 nmol/litre) or raised urinary free cortisol excretion. The 9 a.m. cortisol level fails to be reduced to undetectable levels in response to dexamethasone 0.3 mg/m² given as a single dose the previous night.

Treatment usually requires specialist surgery.

Precocious puberty
- In precocious puberty, early sexual maturity (at less than 8 years of age in females, or less than 10 years of age in males) is usually accompanied by a growth spurt and relatively tall stature for age.
- If the hypogonadism is likely to be permanent, continue and gradually increase testosterone to 250 mg/month or oestrogen to 25–50 micrograms/day over a 2½-year period (the latter eventually as a combined oral contraceptive medication to allow withdrawal bleeding).

TABLE 5.8.C.1 Causes of delayed puberty

<table>
<thead>
<tr>
<th>Low LH/FSH + low testosterone/oestrogen</th>
<th>High LH/FSH + low testosterone/oestrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic ill health</td>
<td>Gonadal trauma/infection</td>
</tr>
<tr>
<td>Constitutional/familial</td>
<td>Gonadal dysgenesis or Turner’s syndrome (XO)</td>
</tr>
<tr>
<td>Starvation, low body mass index</td>
<td>Klinefelter’s syndrome (XXY)</td>
</tr>
<tr>
<td>Genetic (e.g. Kallmann’s syndrome, Prader–Willi syndrome)</td>
<td>Some cases of DSD</td>
</tr>
<tr>
<td>Prolactinoma (rare)</td>
<td>Autoimmune ovarian damage</td>
</tr>
<tr>
<td>Hypopituitarism, hypothyroidism</td>
<td>Galactosaemia</td>
</tr>
<tr>
<td>Thalassaemia</td>
<td></td>
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</tbody>
</table>

Hypogonadism and delayed puberty
- Hypogonadism may be secondary to central gonadotrophin deficiency (hypogonadotrophism: LH/FSH low) or peripheral gonadal failure (hypergonadotrophism: LH/FSH high).
- Suspect congenital central hypogonadism in a male neonate with undescended testes and micropenis (shaft length < 2.5 cm). Hypopituitarism may also be present.
- If hypogonadism remains undetected, failure of or incomplete pubertal development will occur.
- Delayed puberty is often familial, but may be induced by emotional or nutritional deprivation.
- There is delayed maturation of gonadotrophin secretion.
- Treat if the delay is severe enough to cause psychological damage.
- Give a brief course of testosterone esters (100 mg by deep IM injection (Sustanon) at 1-month intervals three times in boys) or oral oestrogen (5–10 micrograms/day for 3 months in girls). This allows puberty to be induced and also reduces the risk of later osteoporosis.
- If the hypogonadism is likely to be permanent, continue and gradually increase testosterone to 250 mg/month or oestrogen to 25–50 micrograms/day over a 2½-year period (the latter eventually as a combined oral contraceptive medication to allow withdrawal bleeding).

Growth hormone deficiency and short stature
Growth hormone deficiency (GHD) may be idiopathic, familial, part of hypopituitarism or isolated.

In the neonatal period, isolated GHD or hypopituitarism may cause hypoglycaemia (see Section 3.4). After excluding or treating hypoadrenalinism (see above), growth hormone may be required to maintain normoglycaemia and normal growth but such treatment requires expert input.

Growth hormone is essential for normal growth, and GHD should be suspected in the child who is:
• short in relation to their peers and in comparison with their parents
• growing slowly
• relatively heavy for their height.

Outside the neonatal period, treatment is rarely urgent. Growth hormone is administered as a subcutaneous injection. It is expensive and difficult to store.

The causes of severe short stature include the following:
• secondary to chronic ill health or under-nutrition; these patients are often thin
• secondary to chronic emotional trauma; these patients are often thin
• endocrine (hypothyroid, hypopituitary, GHD, Cushing’s syndrome); these patients are often relatively heavy
• syndromic (e.g. Turner’s syndrome, etc.); these patients are usually dysmorphic, but some may have few external features, so it should be suspected in all short females outside their genetic range
• disproportionate with short limbs (bony dysplasias, rickets)
• metabolic (storage disorders, osteogenesis); these patients have longer limbs than back.

Short stature in the latter three causes is extremely difficult and expensive to treat.

Hypopituitarism
In the neonate there will be hypoadrenalism with or without GHD leading to hypoglycaemia. Suspect hypopituitarism in any male neonate with cryptoorchidism and micropenis. Onset later in life may signal an intracranial lesion such as craniopharyngioma (which may be visible as a calcified mass on plain lateral skull X-ray or CT scan; MRI scans show a cystic cavity at the base of the brain). Symptoms outside the neonatal period include the following:
• poor growth/short stature (secondary to GHD)
• lethargy
• hypotension
• hypothermia
• hypothyroidism (see above)
• hypogonadism (see above)
• visual field defects, headache and/or raised intracranial pressure if secondary to tumour.

Treatment is outlined in the sections on individual hormone deficiencies above.

Diabetes insipidus
Isolated diabetes insipidus is rare, but it can occur as part of hypopituitarism or secondary to infiltration of the posterior pituitary by tumour or destruction by infection. Suspect it in any case of:
• dehydration with dilute (colourless) urine
• polyuria and polydipsia not due to diabetes mellitus
• secondary daytime wetting without an obvious cause
• familial history.

It is important to request a fluid balance diary at home, and for carers to allow access to water alone between meals as the only fluid permitted. This will help to identify the many behavioural causes of polydipsia, and will avoid the need for awkward and unnecessary tests of urinary concentrating capacity.

Diagnosis is confirmed by the simultaneous presence of hyperosmolar serum (> 290 mOsm/litre) and dilute urine (< 300 mOsm/litre or specific gravity < 1005).

Treat by allowing free access to water and, if possible, replacement of antidiuretic hormone with a long-acting analogue, DDAVP, which can be given intramuscularly, by nasal spray or orally. The dose is titrated to keep the specific gravity of the urine in the range 1005–1010 and/or the serum osmolarity normal. Try to allow one period of diuresis before each dose is due, to prevent dangerous hyponatraemia from over-treatment.

5.9 The child or adolescent with a mental health problem

BOX 5.9.1 Minimum standards

Knowledge, skills and tests that exclude organic medical causes.

Effective child protection systems.

Fluoxetine.

Risperidone, chlorpromazine and flupenthixol.

Supportive family therapy.

Introduction

Around 10–20% of all children have one or more mental or behavioural problems (World Health Report 2001). The rates are higher in urban areas and increase in adolescence. One in ten young people suffers from mental illness or symptoms of mental distress severe enough to cause some level of impairment, yet less than one in five receives the treatment that they need.

Prematurity, poor nutritional status, low birth weight, organic brain damage and physical handicap often bring about biological stressors. A disadvantaged socio-economic status of families contributes negatively to the mental health of children. Child development suffers where there is persistent marital discord, parental psychiatric ill health and/or a history of substance abuse. Protective factors include stable care, an adaptable and engaging personality, problem-solving abilities and a supportive network of family and friends.

The aggregate disease burden of these disorders has