CHAPTER 7

ENDOCRINE SYSTEM

7.1 DISORDERS OF SEX DEVELOPMENT (DSD)

Q52.9/ Q55.9

DESCRIPTION

The current terminology for neonates or children presenting with incomplete differentiation of the external genitalia is “disorder of sex development”.

DIAGNOSTIC CRITERIA

Clinical

» DSDs present with one or more of the following:
  > varying degrees of hypospadias,
  > maldescent of one or both gonads,
  > atypical size of the phallus,
  > scrotalisation of the labia, and
  > a urogenital sinus.
» Isolated hypospadias is not a DSD.

Suspect congenital adrenal hyperplasia in an infant with non-palpable gonads and DSD.

Investigations

» Urgent urea/electrolytes, venous blood gas and blood glucose to identify possible adrenal insufficiency.
» Elevated 17-hydroxyprogesterone level to confirm a diagnosis of adrenal hyperplasia (to be done after day 3 of life for an accurate interpretation of the result).
» Further investigations (in discussion with referral centre):
  > Genitourinary imaging (e.g. ultrasound).
  > Genetic evaluation.

GENERAL AND SUPPORTIVE MEASURES

» Gender assignment in these infants should only be undertaken after extensive counselling and evaluation by a multidisciplinary team.
» Stabilise all neonates suspected of having congenital adrenal hyperplasia with a salt-losing crisis prior to urgent referral, as a crisis may be life threatening.

MEDICINE TREATMENT

Congenital adrenal hyperplasia can present with an adrenal crisis. See section 7.3: Adrenal insufficiency, acute.

REFERRAL

» All cases for confirmation of the diagnosis, counselling and possible initiation of treatment if necessary.
» Urgent: All cases of congenital adrenal hyperplasia.

7.2 ADRENAL HYPERPLASIA, CONGENITAL

E25.0

DESCRIPTION

Autosomal recessive enzymatic defects of the cortisol biosynthetic pathways in the adrenal gland. The presentation depends on the severity and type of the enzyme defect.

DIAGNOSTIC CRITERIA

Clinical

» Neonates with disorder of sex development (ambiguous genitalia).
» Adrenal insufficiency. See section 7.3: Adrenal insufficiency, acute.
» Accelerated growth velocity or precocious pseudopuberty.

Investigations

See section 7.3: Adrenal insufficiency, acute.
» Elevated 17-hydroxyprogesterone in the serum.
» Elevated serum renin.

GENERAL AND SUPPORTIVE MEASURES

» Psychological support for child and family.
See section 7.3: Adrenal insufficiency, acute – for stress management.

MEDICINE TREATMENT

Glucocorticoid and mineralocorticoid replacement. To be initiated in consultation with a subspecialist.

- Hydrocortisone, oral, 0.5 mg/kg/day in three divided doses. Specialist initiated.
  - The morning dose should be given as early as possible.
  - ½ dose on waking up, ¼ dose at midday, ¼ dose at 16h00.

- Fludrocortisone acetate, oral, 5 mcg/kg/day as a single daily dose.
  - Range: 50–200 mcg daily.

For salt losing patients:

- Sodium chloride, oral, 1–2 g daily, divided and given with feeds.

» Glucocorticoids are administered for life. Once growth is complete, prednisone may be given once daily. Long-acting glucocorticoids are generally avoided in children because of potential growth suppression.
» The dose is individualised by monitoring growth, bone-age and hormonal levels.

LoE II[1]

REFERRAL

» All cases for confirmation of the diagnosis, counselling and initiation, and monitoring of treatment.

7.3 ADRENAL INSUFFICIENCY, ACUTE

E27.4

DESCRIPTION

Acute failure of adrenal function, suspected when a patient presents with hypotension, hypoglycaemia, hyponatraemia, hyperkalaemia and metabolic acidosis.

Patients on chronic steroid therapy are at risk for adrenal insufficiency if treatment is abruptly stopped.

Increase steroid dose during times of stress (fever, trauma and surgery) to prevent adrenal crisis (see below).

DIAGNOSTIC CRITERIA

Clinical

» Acute circulatory collapse. The features include:
  - tachycardia,
  - pallor,
  - cool clammy skin,
  - coma,
  - metabolic acidosis,
  - hypotension,
  - poor peripheral perfusion,
  - dehydration,
  - decreased level of consciousness.

» A history of weakness, anorexia, vomiting, weight loss, salt craving, hyperpigmentation (primary adrenal insufficiency).
» Auto-immune endocrinopathies, steroid-dependence and ambiguous genitalia may be present.
» Hyperkalaemia
» Hypoglycaemia
» Hyponatraemia
» Hypercalcaemia (uncommon).

Investigations

Take blood for estimation of:

» Serum electrolytes and blood glucose.

» In all suspected cases, take a sample of clotted blood for estimation of plasma cortisol prior to treating the patient. Send this sample with the patient to the central hospital if laboratory facilities are not locally available.

MEDICINE TREATMENT

Stabilisation

For shock

- Sodium chloride 0.9%, IV, 20 mL/kg bolus as needed.

For hypoglycaemia

- Dextrose 10%, IV, 2–5 mL/kg bolus as needed.
- Hydrocortisone, IV, 2 mg/kg immediately as a single dose.
  - Follow with 0.5 mg/kg/dose every 6 hours.

Manage hyperkalaemia. See Chapter 6: Nephrological/Urological Conditions, section 6.4: Acute kidney injury (renal failure, acute).

Prevention

Patients on chronic steroid therapy are at risk of adrenal insufficiency during stressful situations, e.g. sepsis, trauma, elective or emergency surgery. Increase the dose of steroids for the duration of the stressful period.

For major stress, e.g. > 39 °C:

- Treble hydrocortisone replacement until recovery (usually 3 days).

For minor stress, e.g. URTI, > 38 °C:

- Double hydrocortisone replacement until recovery (usually 3 days).

Adrenal insufficiency is a life threatening emergency.

REFERRAL

» All cases immediately after stabilisation.

7.4 DIABETES INSIPIDUS

E23.2/N25.1

DESCRIPTION

Suspect diabetes insipidus in any child with polydipsia and polyuria. Infants may present with failure to thrive.

Central diabetes insipidus is due to deficiency of antidiuretic hormone.
Nephrogenic diabetes insipidus occurs if the kidney is unable to respond to antidiuretic hormone.

DIAGNOSTIC CRITERIA

» Pathological polyuria, defined as excretion of > 1.5 L/m^2 of urine. In infants, the corresponding value is > 2.5 L/m^2.
» Serum osmolality > 300 mOsm/kg, with urine osmolality < 300 mOsm/kg is suggestive of diabetes insipidus.
» A positive water deprivation test. (Only conduct under specialist supervision.)

MEDICINE TREATMENT

Central diabetes insipidus (Specialist initiated)

Older children:

- Desmopressin, oral, 50–300 mcg/day given 8 hourly.
  - Start at the lowest dose and titrate up according to response. Use the lowest dose at which an antidiuretic effect is obtained.
  - Maximum dose: 1200 mcg daily.

Younger children:

- Desmopressin, nasal spray, 10 mcg/day (0.1 mL), starting dose.
  - Titrate according to response. Use the lowest dose at which an antidiuretic effect is obtained.
  - Maximum daily dose: 30 mcg/day once or twice daily.

Note: The dosing of oral and nasal formulations is different owing to the difference in absorption rates.

The patient must have a phase of urinary dilution or breakthrough urination before the next dose to ensure that water intoxication does not result.

Nephrogenic diabetes insipidus
If no response to desmopressin.

Treat the underlying cause.

- Hydrochlorothiazide, oral, 0.5–1 mg/kg/dose 12 hourly.
- Ibuprofen, oral, 5 mg/kg/dose 12 hourly.

REFERRAL

» All cases for evaluation.

7.5 DIABETES MELLITUS

DESCRIPTION

A syndrome of abnormal carbohydrate metabolism, associated with a relative or absolute impairment of insulin secretion with varying degrees of peripheral resistance to the action of insulin.

7.5.1 TYPE 1 DIABETES MELLITUS

E10

DESCRIPTION

Most diabetic children have type 1 diabetes, and:

» have auto-immune destruction of the pancreatic beta cells as the underlying cause,
» have an absolute requirement for insulin therapy, and
» will develop diabetic ketoacidosis (DKA) if not given insulin.

DIAGNOSTIC CRITERIA

The following are criteria for the diagnosis of diabetes mellitus:

» Classical features of diabetes (polydipsia, polyuria, weight loss or failure to gain weight, weakness or tiredness, glycosuria, recurrent protracted infections, pruritis vulvae in a girl with diabetes) with a random serum glucose concentration ≥ 11.1 mmol/L; or
» Fasting plasma glucose ≥ 7.0 mmol/L (fasting defined as no caloric intake for at least 8 hours).
» An oral glucose tolerance test is generally not needed.

GENERAL AND SUPPORTIVE MEASURES

» Refer to a unit that is able to manage type 1 diabetic patients.
» Educate the child and caregiver about all aspects of the disease.
» A medical alert bracelet should be worn at all times.
» Follow-up by a medical practitioner or at a clinic/hospital should occur at least every 3 months.
» Monitor thyroid function annually.
» Screen for coeliac disease at diagnosis, and 3 years post diagnosis.
» Annual screening for dyslipidaemia, microalbuminuria, retinopathy and peripheral neuropathy 5 years after diagnosis in non-pubertal children and 2 years after diagnosis in pubertal children.

Diet: healthy lifelong eating habits

» Refer a newly diagnosed patient and family to a dietitian.
» Principles of the prudent diet:
  > Encourage children to reduce the intake of fats and salt and to increase dietary fibre content.
  > Provide all diabetics with a meal plan, e.g. ‘constant carbohydrate meal plan’ or ‘carbohydrates counting meal plan’. There is no one

'diabetic' diet. Individualise the diet giving consideration to usual eating habits and other lifestyle changes required.

> Six main nutrition factors contribute to better glucose control, i.e. lower HbA1c levels. These are:
1. Following a meal plan. Keep day-to-day intake consistent.
2. Avoiding extra snacks that are not part of the meal plan.
3. Avoiding over-treatment of low blood glucose levels (hypoglycaemia).
4. Prompt correction of high blood glucose levels.
5. Adjusting insulin levels for meals in patients using the 'carbohydrates counting meal plan'.
6. Consistency of night snacks.

CONSTANT CARBOHYDRATE MEAL PLAN

Consistency is the key. The amount of insulin, usually two or three doses per day, is kept relatively constant from day-to-day. Carbohydrates should be manipulated to match the relatively constant insulin dose. **If able to count carbohydrates, give 1 unit of insulin per 15 g of carbohydrate during the day:**

Units of insulin	Grams of carbohydrate per day
1.5–2.5 units	per 15 g carbohydrates for breakfast
1.2 units	per 15 g carbohydrates for supper
0.5 units	per 15 g carbohydrates during the night

The amount of carbohydrates (types can vary) should be kept about the same for each meal and snack from one day to the next.

As part of the educational process, the family must get used to reading food labels to know the grams (g) of carbohydrates being eaten. The dietitian may suggest a range of carbohydrates for each meal.

Examples of carbohydrate content of some foods
The following foods have 15 g of carbohydrate per serving:
1 cup = 250 mL

Food	Serving size
Whole wheat/brown bread	1 slice
Whole wheat/brown roll	½
Pita bread	½
Small wrap	1
Cooked porridge	½ cup
High fibre cereal	½ cup
Whole grain wheat biscuit	1

Whole wheat crispbread	4
Rye crispbread	2
Rice cakes (10 cm)	2
Whole wheat rusk	1
Cooked rice	½ cup
Cooked pasta	½ cup
Cooked couscous	½ cup
Cooked samp	½ cup
Cooked maize meal	½ cup
Cooked samp and beans	½ cup
Cooked crumbly maize meal or pap	½ cup
Cooked lentils/split peas/beans	½ cup
Baked beans	½ cup
Plain popped popcorn	1½ cups
Thick homemade soup	1 cup
Starchy vegetables	
Medium potato	1
Mash potato	½ cup
Sweet potato	¼ cup
Butternut/pumpkin	1 cup
Mixed vegetables with sweet corn	1 cup
Sweet corn	½ cup
Medium mealie	1
Peas	½ cup

» Tailor advice to the patient's lifestyle, economic circumstances and usual diet. Where possible, avoid drastic changes.
» Do not forbid any particular food as this may lead to disturbed attitudes to food, e.g. carbohydrates are not forbidden but can be taken before exercise, incorporated into a main meal or used as a source of energy during illness when children have a poor appetite.
» Diet should provide adequate nutrition for growth and development.

Dietary composition
Referral to a dietitian for an individualized meal plan to meet dietary requirements.

Timing of meals and snacks
Children receiving twice daily injections of combined short and intermediate acting insulin regimens need three main meals, and a snack, 2 hours after an insulin injection.
Eat meals and snacks at the same time each day. The timing of insulin injections may need to be adjusted according to the patient's own circumstances.

Preschool-aged children may have unpredictable eating habits and may require frequent small meals.

Exercise

» Regular exercise helps increase insulin sensitivity, maintains proper weight, blood pressure, blood glucose and blood lipid levels.
» Exercise must be regular, i.e. daily. The same amount of exercise should ideally be done at the same time of the day.
» Some form of carbohydrate is necessary before and after intense exercise to reduce the risk of hypoglycaemia. Blood glucose monitoring may be necessary before and after intense exercise.

Blood glucose testing, record keeping and review of records

» Glucometers with compatible strips and blood-letting devices.
» Encourage children to perform their own finger-prick blood glucose testing.
» Finger-pricks should be performed at the side of the fingertips.
» Encourage the child to monitor his/her blood glucose prior to each main meal and at bedtime. A daily record of all tests performed should be recorded in a logbook. Review the logbook frequently to ensure optimal insulin adjustments.
» More frequent blood glucose testing is indicated if the child is unwell, partaking in unusual amounts of physical activity or feels hypoglycaemic.
» For a basal-bolus regimen, testing can be done up to 6 times a day (180 strips/month) and for other regimens, 2–4 times daily (60–120 strips/month). If control is poor, more frequent testing is recommended with appropriate adjustment to therapy.

Acceptable glycaemic target range before and after meals

» Balance the ability of the family to avoid recurrent hypoglycaemia. A paediatrician should assist in setting practical goals. See table ‘Monitoring, control and adjustments’.
» Severe hypoglycaemia is the presence of recurrent and unpredictable hypoglycaemic episodes, requiring third party assistance. It leads to anxiety about repeated episodes and results in a poorer quality of life.
» Ideally, 80% of the pre-meal blood glucose values should fall within the target range during home monitoring, but targets may need to be altered based on the age of the child and the ability of the family.
» Infants, toddlers, and preschoolers are unable to recognise or communicate signs and symptoms of low blood glucose. They also have unpredictable eating habits.
» Some school-aged children and young adolescents have more predictable eating habits, but may be lacking in judgement. They are able to recognise or communicate signs and symptoms of low blood glucose.
» Most adolescents and young adults are able to recognise and treat low blood glucose reactions. They have predictable eating habits and are able to plan ahead.
» Acceptable target range:

> Before meals: 4–8 mmol/L.
> After meals: 5–10 mmol/L.

» Monitor HbA1c levels 3-monthly. The aim is to maintain HbA1c as close as possible to the recommended range, i.e. 6.5–7.5%. Aim for a lower HbA1c in patients who are adherent to home glucose monitoring.

Monitoring, control and adjustments

Level of control	**Optimal**	**Suboptimal** (need to take action)	**High-risk** (refer patient to specialised diabetic clinic)
Clinical assessment			
Raised blood glucose	No symptoms.	» polyuria*, » polydipsia*, and » enuresis*.	» blurred vision, » poor weight gain, » poor growth, » delayed puberty, » poor school attendance, » skin or genital infections, and » signs of vascular compromise.
Low blood glucose	Few, mild. No severe hypo-glycaemic episodes.	Severe hypoglycaemia (un-consciousness and/or convulsions).**	
Monitoring Biochemical assessment. Self-monitoring finger-prick glucose monitoring (mmol/L).			
AM fasting (pre-prandial)	4–6	> 8	> 9
Postprandial	5–10	10–14	> 14
Bed time	6.7–10.0	< 6.7*** or 10.0–11.0	< 4.4*** or > 11.0
Nocturnal	4.5–9.0	< 4.2*** or > 9.0	< 4*** or > 11
HbA1c	6.5–7.5	7.5–9.0	> 9

* In situations with polyuria, polydipsia and enuresis, adjust the doses of the insulin upwards. Dose adjustments should usually not be greater than 10% of the daily dose at any one time.
** Identify and address the specific reasons for hypoglycaemia, e.g. skipping meals or snacks. In specific situations where the lifestyle cannot be modified or there are recurrent episodes of severe hypoglycaemia, consider referral to a tertiary centre.

*** Consider hypoglycaemia unawareness in situations where there are consistently low readings and the patient does not report symptoms.

» Hypoglycaemia unawareness is dangerous. The insulin dose may need to be adjusted downwards if more than 30% of the readings during a single week are below the target values indicated.

Urine ketone testing

» Test urine for ketones in the following circumstances:
  > if vomiting occurs,
  > any time the blood glucose > 15 mmol/L, especially if the child is unwell and particularly if the blood glucose has been high for more than 24 hours,
  > if unusual drowsiness is present,
  > in the presence of high temperature, vomiting or diarrhoea, even when the glucose is < 15 mmol/L,
  > if abdominal pains occur, and
  > if the breathing is deep and rapid or smells of acetone.

MEDICINE TREATMENT

Insulin therapy

Principles of insulin therapy:

» To provide sufficient insulin throughout the 24-hour period to cover basal requirements.
» To deliver boluses of insulin in an attempt to match the glycaemic effect of meals.
» The most suitable areas for insulin injection are:
  > the upper, outer area of the arms,
  > the front and side of the thigh,
  > the upper, outer surface of the buttocks; and
  > the abdomen, except the area close to the navel.
» Establish a pattern for injecting, i.e. horizontally or vertically. Vary the site of injection according to this pattern. When the area has been fully covered move to another area.
» Patients doing strenuous exercise should not inject into their legs.

Insulin injection technique

Pinching the skin to give an insulin injection. A small pinch with the finger and thumb is enough.

» Insulin injection by syringe is usually given into deep subcutaneous tissue through a two-finger pinch of skin at an angle of 45–90 degrees.
» The subcutaneous fat layer should be thicker than the needle length.
» There is significant risk of accidental intramuscular injections with more rapid absorption, especially in lean individuals. This can be minimised by using a two-finger pinch technique, an injection angle of 90 degrees and use of 5 mm needles rather than longer needles in all ages.
» Withdraw the needle and release the skin fold on the count of ten.
» Disinfection of the skin is not necessary prior to insulin injections, however, injections should be given through clean, healthy skin.
» Needles should not be used for more than 6 injections.
» Prefilled insulin syringes are recommended for children. Pen devices delivering less than 1 unit should be available for selected patients.
» Thoroughly mix all insulin suspensions before injection by rolling or inverting the vial ten times so that the cloudy suspension mixes thoroughly and uniformly.

Duration of action of standard insulins

Insulin	Onset of action	Peak action	Effective duration
Regular/short-acting	30–60 minutes	2–4 hours	5–8 hours
Intermediate-acting	2–4 hours	4–12 hours	12–20 hours

Choice of insulin regimen

» No insulin injection regimen satisfactorily mimics normal physiology. The choice of insulin regimen should be individualised and will depend on age, duration of diabetes, lifestyle (dietary patterns, exercise schedules, school, work commitments, etc.), targets of glycaemic control, and particularly, individual patient/family preferences.

» The choice of an insulin regimen is determined by the patient's circumstances. Depending on the patient's scope to undertake insulin therapy, a number of alternatives will allow insulin therapy to be tailored to their lifestyle. Discussion with parents should provide the basis for such important decisions.
» It is not possible to prescribe a single best regimen for preschool and primary school children. Individualise the choice of regimen according to family circumstances.
» Multiple daily injections provide for the best glycaemic control in young people with type 1 diabetes. If manageable, the basal-bolus regimen should be the regimen of choice. A twice daily injection regimen is not recommended, but 3 injections a day is a good alternative.

Questions to be considered when choosing a regimen

What scope does the patient have for insulin therapy?

» Will the patient be able to undertake, financially and culturally, an advanced insulin regimen if necessary?
» Is a responsible person available to give insulin injections at all times of the day or only at certain times?
» How goal-orientated is the patient/caregiver in terms of diabetes control?

What is the patient's eating pattern?

» What is the typical pattern of meals?
» What type of food do they typically eat at each meal, and how much?
» Is their eating pattern relatively constant, or does it vary?
» Can and will they change their eating habits?

All chosen insulin regimens should be supported by comprehensive education appropriate for the age, maturity and individual needs of the child and family.

Selecting an insulin regimen

Total daily insulin dose

This is individualised and varies according to age, puberty development, stress and individual variability. The usual range is 0.5–1 units/kg/day, but may be higher or lower.

The aim is to select a regimen that allows the achievement of glycaemic control without disabling hypoglycaemia. This also requires a comprehensive support programme for the child and family enabling the implementation of an appropriate diet and other care strategies. These include home blood glucose monitoring and the ability to recognise and manage hypoglycaemic episodes. Where glycaemic control is not achieved despite an adequate support programme, consider referral to a tertiary centre**.**

Insulin regimens

Consult with a paediatric endocrinologist or paediatrician with experience in diabetes care. Repeated consultations are indicated when glycaemic control targets are not achieved.

Basal-bolus regimen

- Short-acting insulin 15–30 minutes before a meal or rapid-acting insulin with main meals, e.g. breakfast, lunch and main evening meal; intermediate-acting insulin before bed.
- Normally, 30–40% of the total daily dose of insulin is given at bedtime as intermediate-acting insulin. The remaining insulin is given prior to breakfast, lunch and evening meal in the form of short-acting insulin.

Basal-bolus regimen Short-acting insulin is indicated in the child (especially < 5 years of age) with erratic eating habits despite adequate education.		
Breakfast	Short-acting insulin	20% of total daily dose (if able to count carbohydrates: give 1 unit per 15 g)
Lunch	Short-acting insulin	20% of total daily dose
Supper	Short-acting insulin	20% of total daily dose
At night (± 21h00)	Intermediate-acting insulin (ideally this ought to be a basal insulin acting over 24 hours)	40% of total daily dose

Three injections daily regimen

- A mixture of short- and intermediate-acting (premixed 70:30) insulin before breakfast; short-acting insulin alone before an afternoon snack or main evening meal; intermediate-acting insulin before bed; or variations of this regimen may be used at times.
- This requires that the caregiver is aware of three different insulin preparations and can differentiate between them.

Three injections daily regimen		
Breakfast	Short-acting insulin (30% of morning dose) + Intermediate-acting insulin (70% of morning dose)	$^2/_3$ of total daily dose
Supper	Short-acting insulin ($^1/_3$ of evening dose)	$^1/_3$ of total daily dose
At night (± 21h00)	Intermediate-acting insulin ($^2/_3$ of evening dose)	

None of these regimens can be optimised without frequent assessment of blood glucose monitoring.

Achieving a balance between food intake, insulin levels and energy expenditure is an essential pre-requisite for achieving glycaemic control.

Adjustment of insulin dosage for 3 injections daily regimen
The insulin dose should not be changed after a single abnormal blood glucose reading.

Adjust the dose only once a pattern has been established. The dose to be adjusted depends on the time of abnormal glucose readings, as indicated in the table below:

	Timing of the unsatisfactory blood glucose level			
	Before breakfast	**Before lunch**	**Before supper**	**At ± 21h00**
Three injections daily regimen				
Insulin dose to be **increased** if *glucose too high*	21h00 dose: intermediate-acting insulin	Breakfast dose: short-acting insulin	Breakfast dose: intermediate-acting insulin	Supper dose: short-acting insulin
Insulin dose to be **decreased** if *glucose too low*				
	Timing of the unsatisfactory blood glucose level			
	Before breakfast	**2 hours after breakfast**	**2 hours after lunch**	**At ± 21h00**
Basal-bolus regimen				
Insulin dose to be **increased** if *glucose too high*	21h00 dose: intermediate-acting insulin	Breakfast dose: rapid (or short-acting) insulin	Lunch dose: rapid (or short-acting) insulin	Supper dose: Rapid-acting (or short-acting) insulin
Insulin dose to be **decreased** if *glucose too low*				

REFERRAL

» Management of all children with diabetes should be supervised by a paediatrician with experience in managing diabetes in the young and should involve a multidisciplinary team, i.e. paediatrician, dietician, nurse educator, psychologist, ophthalmologist at a regional hospital.
» Complications.
» Uncontrolled diabetics, such as children with unpredictable blood glucose control, nocturnal or frequent hypoglycaemic events or children who do not reach their therapeutic goals for consideration of analogue insulin.
» Periodic screening of eyes by an ophthalmologist:
  > prepubertal onset of diabetes: 5 years after onset and annually thereafter;
  > pubertal onset of diabetes: 2 years after onset and annually thereafter.

7.5.1.1 GUIDELINES FOR MANAGEMENT OF DIABETICS ON SICK DAYS

DESCRIPTION

Illness associated with fever tends to raise blood glucose because of higher levels of stress hormones, gluconeogenesis and insulin resistance.

Illness associated with vomiting and/or diarrhoea may lower blood glucose, with the possibility of hypoglycaemia and the development of starvation ketones.

DIAGNOSTIC CRITERIA

» Unstable blood glucose measurements because of illness, stress or starvation.
» Increased insulin requirements are induced by a catabolic state and stress.
» Ketonuria may indicate the following:
  > In the presence of hyperglycaemia, it is indicative of severe insulin deficiency and calls for urgent therapy to prevent progression into ketoacidosis.
  > In the presence of low blood glucose levels, it is indicative of a starvation state or is the result of a counter-regulatory response to hypoglycaemia.

GENERAL AND SUPPORTIVE MEASURES

» Monitor glucose more frequently.
» Test urine for ketones.
» Ensure adequate intake of calories and fluids on sick days to prevent ketogenesis. If insufficient calories are consumed, ketones will appear in

the urine without hyperglycaemia. In this circumstance encourage the patient to eat whatever he/she feels like.

» Treat the underlying intercurrent illness.

» Special circumstances:

> Gastroenteritis:
If hypoglycaemia occurs especially with gastroenteritis, and there is mild ketonuria, ensure that the child takes regular frequent amounts of carbohydrate, using oral rehydration solution or intravenous fluids.

> Loss of appetite:
Replace meals with easily digestible food and sugar-containing fluids.

> Vomiting:
If the patient has difficulty eating or keeping food down and the blood glucose is < 10 mmol/L, encourage the patient to take sugar-containing liquids. Give small volumes. Some glucose will be absorbed. If there is no vomiting, increase the amount of liquid.

MEDICINE TREATMENT

Insulin therapy

Insulin must be given every day. Insulin injections should not be omitted because of sickness and/or vomiting. If vomiting occurs, IV fluids may be needed to avoid hypoglycaemia.

During an infection, the daily requirement of insulin may rise by up to 25%.

Generally, the body will require more energy during illness. Insulin allows more glucose to enter the cells, providing more energy to fight infection.

General guidelines when giving extra insulin:

» If the blood glucose is > 14 mmol/L and capillary beta-hydroxybutyrate ≥ 1.5 mmol/L or if ketones > 1+ in the urine, the patient must seek urgent medical attention.

» If no ketonaemia/ketonuria:

> Blood glucose 14–22 mmol/L: Add 5% of total daily dose (TDD) of insulin or 0.05 u/kg to ordinary bolus.

> Blood glucose > 22 mmol/L: Add 10% of TDD of insulin or 0.1 u/kg to ordinary bolus; drink sugar-free fluids.

Check blood glucose and ketones every 2 hours; repeat additional insulin if needed every 2–4 hours.

Extra fluids

In addition to taking extra insulin, extra sugar-free fluids are important to prevent dehydration. If blood glucose < 10 mmol/L (if intake is poor), sugar-containing fluid should be given (to prevent ketosis).

REFERRAL

» In a child with inter-current illness, **urgent** specialist medical or nursing advice must be obtained when:
  > the patient is unable to carry out the advice regarding sick days,
  > the diagnosis is unclear,
  > vomiting is persistent, particularly in young children,
  > blood glucose continues to rise despite increased insulin,
  > hypoglycaemia is severe,
  > ketonuria is heavy or persistent, and
  > the child is becoming exhausted, is confused, hyperventilating, dehydrated or has severe abdominal pain.

7.5.2 DIABETES MELLITUS, INSULIN DEPENDENT: ACUTE COMPLICATIONS

E10

7.5.2.1 CEREBRAL OEDEMA IN DIABETIC KETOACIDOSIS (DKA)

G93.6

DESCRIPTION

A condition of brain swelling during the course of treatment for DKA.

Cerebral oedema usually occurs 4–12 hours after the initiation of treatment, but may be present at the time of diagnosis. It often follows an initial period of clinical and biochemical improvement.

Cerebral oedema causes significant neurological morbidity and has a mortality of approximately 80%.

The cause of cerebral oedema during treatment remains unclear. However, very rapid reduction in intravascular osmolality may aggravate the process. Therefore, rehydration should occur more slowly in children with DKA than in other causes of dehydration.

DIAGNOSTIC CRITERIA

Clinical

» Signs and symptoms of cerebral oedema include:
  > headache,
  > confusion,
  > irritability and restlessness,
  > reduced consciousness,
  > papilloedema (late sign),
  > hypoxaemia, and
  > specific neurological signs and raised intracranial pressure.

» The risk of cerebral oedema is increased if urea levels are increased or if the PCO_2 is persistently low, i.e. < 20 mmHg (2.7 kPa).

GENERAL AND SUPPORTIVE MEASURES

» Admit to ICU, if possible, or to a centre experienced with managing this condition.
» Restrict intravenous fluids to ⅔ maintenance and replace deficit over 72 hours rather than 48 hours pending ICU admission.
» Elevate the head of the bed.
» Exclude hypoglycaemia.
» Do not use bicarbonate.
» Exclude thrombosis, intracranial haemorrhage or infection.
» Do not delay treatment while waiting for a CT scan to confirm cerebral oedema.

MEDICINE TREATMENT

For the management of cerebral oedema, see Chapter 13: The Nervous System, section 13.3: Status Epilepticus (convulsive), cerebral oedema.

7.5.2.2 DIABETIC KETOACIDOSIS

E10.1

DESCRIPTION

Diabetic ketoacidosis (DKA) occurs with relative or absolute insulin deficiency, either caused by non-adherence to insulin regimens or by excessive secretion of counter-regulatory hormones during stress, e.g. infection, trauma and surgery.

DIAGNOSTIC CRITERIA

» Heavy glycosuria (3+ or more).
» Hyperglycaemia, i.e. blood glucose > 11 mmol/L, ketonuria 2+.
» Blood gas: pH < 7.3, bicarbonate < 15 mmol/L.
» Polyuria, polydipsia and dehydration.
» Kussmaul respiration, nausea, vomiting, abdominal pain and depressed level of consciousness are all late signs.

Note:
In rare cases, blood glucose is not elevated.
Children with mild dehydration and not clinically unwell usually tolerate oral rehydration and subcutaneous insulin.
See section 7.5.1.1: Guidelines for management of diabetics on sick days.

GENERAL AND SUPPORTIVE MEASURES

» Admit all children and adolescents to an ICU or ward experienced in the management of DKA in children and adolescents, if possible.
» Ensure a patent airway.
» If the child is comatosed, secure the airway and insert a urinary catheter.

» If comatosed or has recurrent vomiting, insert an oro-/nasogastric tube and apply free drainage.

MEDICINE TREATMENT

Seek specialist advice early in the management.

If hypoxaemic:

- Oxygen via facemask.

The objectives of fluid and sodium replacement therapy in diabetic ketoacidosis are:

» To restore circulating volume.
» To replace sodium and water deficits from extracellular and intracellular compartments.
» To restore glomerular filtration rate to enhance clearance of glucose and ketones from the blood.
» To reduce the risk of cerebral oedema.

Fluids

a: Fluids for resuscitation in shock:

- Sodium chloride 0.9%, IV, 10–20 mL/kg over 10–30 minutes.
  - Repeat if shock persists.

b: Fluid requirements after resuscitation:

Maintenance (over 24 hrs)

≤ 10 kg	100 ml/kg/24 hrs
11–20 kg	1000 ml + 50 ml/kg/24 hrs for each kg from 11–20 kg
> 20 kg	1500 ml + 20 ml/kg/24 hrs for each kg > 20 kg

Obese children: Use ideal body weight for height.

+

Rehydration (over 48 hours)

5% dehydrated	50 ml/kg/48 hrs
10% dehydrated	100 ml/kg/48 hrs

Review at least 2 hourly.

+/-

Ongoing losses

Replace urine loss in excess of 2 ml/kg/hour	= urine output (in ml/kg/hr) - 2 ml/kg/hr

Review at least 2 hourly**.**

Examples of fluid volumes for the **subsequent phase** of rehydration (i.e. maintenance + 5% of body weight/24 hours).

Body weight (kg)	Maintenance (mL/24 hour)	Maintenance + 5% of body weight (mL/24 hrs)	Maintenance + 5% of body weight (mL/hour)
4	325	530	22
5	405	650	27
6	485	790	33
7	570	920	38
8	640	1040	43
9	710	1160	48
10	780	1280	53
11	840	1390	58
12	890	1490	62
13	940	1590	66
14	990	1690	70
15	1030	1780	74
16	1070	1870	78
17	1120	1970	82
18	1150	2050	85
19	1190	2140	89
20	1230	2230	93
22	1300	2400	100
24	1360	2560	107
26	1430	2730	114
28	1490	2890	120
30	1560	3060	128
32	1620	3220	134
34	1680	3360	140
36	1730	3460	144
38	1790	3580	149
40	1850	3700	154
45	1980	3960	165
50	2100	4200	175
55	2210	4420	184
60	2320	4640	193
65	2410	4820	201
70	2500	5000	208
75	2590	5180	216
80	2690	5380	224

Note: Sodium chloride 0.9% is preferred for resuscitation and the initial phase of rehydration. However, to prevent the occurrence of hyperchloraemic acidosis switch to sodium chloride 0.45%/dextrose 5% after blood glucose has fallen to 12 mmol/L or less. Monitor sodium and chloride (on VBG) 4–6 hourly and adjust maintenance fluids as necessary.

Note: One of the danger signals for cerebral oedema is a precipitous drop in the serum sodium level.

Bicarbonate

Bicarbonate use is associated with increased risk of cerebral oedema. It should not be used routinely to improve acidosis.

Caution
Consult a specialist before administering any bicarbonate solution.

Potassium

Commence potassium replacement immediately unless patient has anuria. If the serum potassium is high, start replacement after the patient has passed urine.

Early addition of potassium in the fluid regimen (KCl 15% 20 mL in 1 L = 40 mmol/L) is essential even if the serum concentration is normal as insulin will drive glucose and potassium into the cells.

DKA protocol:

Two-bag system – Alternative fluid and electrolyte treatment

Under supervision of a specialist.

The two-bag system consists of 2 bags of identical electrolyte content but different dextrose concentrations, 0% and 10%, administered simultaneously into a single IV line. Variations in dextrose delivery are achieved through changing the proportions of the 2 bags contributing to the total rate, which is determined by the degree of dehydration.

- Sodium chloride 0.9%, IV, 10–20 mL/kg.
  - May be repeated if necessary.
  - Then switch to the two-bag system.

LoE II [2,3]

Bag 1 (dextrose 0%)	Bag 2 (dextrose 10%)
• Sodium chloride 0.45%, 1 L **PLUS** • Potassium chloride, 20 mL	• Dextrose 10%, 1 L **PLUS** • Sodium chloride 5%, 90 mL **PLUS** • Potassium chloride, 20 mL

Run these two riders for easy titration of dextrose from dextrose 10% to dextrose 0%:

Fluid	Blood glucose > 15 mmol/L	Blood glucose 10–15 mmol/L	Blood glucose < 10 mmol/L
Bag 1	100%	50%	0%
Bag 2	0%	50%	100%

Insulin

- Insulin, short-acting, 0.05–0.1 units/kg/hour as a continuous IV infusion.

- Add insulin, 50 units (0.5 mL) to 50 mL sodium chloride 0.9% in a syringe pump to get a solution of 1 unit/mL.
- Use a separate cannula and line for insulin administration.
- Do not add insulin to the fluid bag administering maintenance and rehydration fluids.

If the rate of blood glucose fall exceeds 5 mmol/L/hour or the blood glucose falls to 17 mmol/L:

- Add a dextrose-containing fluid.
- Do not stop the insulin infusion while dextrose is being infused.

If the blood glucose falls below 5 mmol/L:

- Give a bolus of 2 mL/kg of dextrose 10% and increase the concentration of dextrose in the infusion.

Continue with IV insulin until:

- the base deficit is < 5 or bicarbonate is ≥ 15 mmol/L,
- there is no ketonuria, and
- the blood glucose is ≤ 10 mmol/L.

Alternative to insulin infusion

Where there are no facilities for insulin infusion, e.g. no syringe pumps, staff constraints, etc.:

- Insulin, short-acting, IV, 0.1 units/kg, hourly.

Changing from intravenous to subcutaneous insulin

Continue with intravenous fluids until the child is drinking well and able to tolerate snacks. When oral fluids are tolerated, reduce intravenous fluids. Subcutaneous insulin can be started once the child is well hydrated and able to tolerate a normal diet.

The most convenient time to change to subcutaneous insulin is just before a meal. Administer the first dose of subcutaneous insulin 30 minutes before the meal and continue with the insulin infusion for 90 minutes after the subcutaneous injection to prevent rebound hyperglycaemia.

In newly diagnosed diabetics, basal-bolus regimen is started as described in section 7.5.1: Type 1 Diabetes Mellitus – Insulin regimens, in a low range dose:

- Prepubertal children: 0.7 units/kg.
- Pubertal children: 1 unit/kg.

In established diabetics, give maintenance insulin.

Give supplemental subcutaneous short-acting insulin before meals if the blood glucose > 11 mmol/L:

Blood glucose (mmol/L)	Short-acting insulin (units/kg/dose)
11–12	0.06
13–16	0.09
16	0.12

REFERRAL

» No improvement.
» Deterioration of condition, i.e.:
  > pH < 7.1,
  > hyperventilation,
  > shock,
  > depressed level of consciousness,
  > persistent vomiting, and
  > age < 5 years.
» Rising blood glucose.

7.5.2.3 HYPOGLYCAEMIA IN DIABETICS

E16.0

DESCRIPTION

Autonomic symptoms (hunger, nausea, anxiety, pallor, palpitations, sweating, trembling) usually precede neuroglycopaenic symptoms (impaired thinking, change of mood, irritability, dizziness, headache, tiredness, confusion, and later convulsions and coma). Patients with frequent hypoglycaemic episodes develop hypoglycaemia unawareness, where the symptoms above do not occur despite a dangerously low blood glucose level.

Causes of hypoglycaemia include:

» A missed or delayed snack or meal.
» Exercise without appropriate dietary preparation.
» Alcohol.
» Overdose of insulin.
» Impaired food absorption, e.g. gastroenteritis.
» Addison's disease. Recurrent hypoglycaemia may necessitate investigation for this condition.
» Coeliac disease.

Nocturnal hypoglycaemia

Nightmares and headaches may be suggestive of nocturnal hypoglycaemia. Blood glucose concentrations fall to their lowest levels between 02h00 and 04h00.

DIAGNOSTIC CRITERIA

» Blood glucose < 3.5–4.0 mmol/L with symptoms in a known diabetic patient. Good glycaemic control is likely to be associated with occasional hypoglycaemic episodes.
» Grading of severity:
  Mild (Grade 1)
    > Child or adolescent is aware of, responds to and self-treats the hypoglycaemia.

> Children < 6 years of age can rarely be classified as grade 1 because they are unable to help themselves.

Moderate (Grade 2)

> Child or adolescent cannot respond to hypoglycaemia and requires help from someone else, but oral treatment is successful.

Severe (Grade 3)

> Child or adolescent is semiconscious or unconscious with or without convulsions and may require parenteral therapy with glucagon or intravenous glucose.

GENERAL AND SUPPORTIVE MEASURES

» Determine the underlying cause.
» Patient education on diabetes and its complications.

MEDICINE TREATMENT

Mild or moderate hypoglycaemia

Immediate oral, rapidly absorbed, simple carbohydrate, e.g.:

- Glucose, oral, 5–15 g or 1–3 level teaspoons of sugar (depending on the child's age) in a small amount of water.
  - Wait 10–15 minutes.
  - If blood glucose has not risen by 3–4 mmol/L, repeat above.
  - As symptoms improve, the next meal or oral complex carbohydrate should be ingested, e.g. fruit, bread, cereal, milk, etc.

Severe hypoglycaemia

Outside hospital

- Glucagon, IM/SC.
  - If < 12 years of age: 0.5 mg.
  - If > 12 years of age: 1.0 mg.

If glucagon is not available:

A teaspoon of sugar moistened with water placed under the tongue every 20 minutes until patient awakes.

LoE II[4]

In hospital

If there is an unsatisfactory response or inability to take oral carbohydrate and signs of disorientation, stupor, convulsions or coma:

- Dextrose 10%, IV, 2–5 mL/kg.
  - Dilute dextrose 50% solution to 10% strength before use, i.e. dextrose 50% 1 mL + water for injection 4 mL = 5 mL 10% dextrose solution.

If IV dextrose cannot be given:

- Glucagon, IM/SC.
  - If < 12 years of age: 0.5 mg.
  - If > 12 years of age: 1.0 mg.

Monitor blood glucose every 15 minutes until stable, then repeat 1–2 hourly. Keep blood glucose between 6 and 8 mmol/L.

REFERRAL

» Recurrent episodes of hypoglycaemia.

7.5.2.4 DIABETIC NEPHROPATHY

E10.21

DIAGNOSTIC CRITERIA

» Persistent micro-albuminuria:
  > Three specimens over a 3–6 month period all show increased albumin:creatinine ratio on a spot urine:
    - males: > 2.5 mg/mmol,
    - females: > 3.5 mg/mmol.

» Screening for micro-albuminuria should start from:
  > Prepubertal children: 5 years post diabetes diagnosis.
  > Pubertal children: 2 years post diabetes diagnosis.

GENERAL AND SUPPORTIVE MEASURES

» Optimise diabetes control.
» Monitor blood pressure.

MEDICINE TREATMENT

If urinary albumin:creatinine ratio is persistently above reference range for sex:

- ACE inhibitor, e.g.:
  - Enalapril, oral, 0.1 mg/kg/dose as a single dose or two divided doses.
  - Maximum dose: 0.5 mg/kg or 40 mg/day.
    Note: Exclude non-diabetic nephropathy.

Note: Discuss patient with an endocrinologist or nephrologist if there is a poor response to ACE inhibitor and improved glycaemic control.

7.5.2.5 DYSLIPIDAEMIA

E78.9

DESCRIPTION

Dyslipidaemia is a broad term used to describe disorders of lipid metabolism that may be classified according to the Frederickson classification.

Phenotype	Elevated particles	Lipid increased	Frequency
I	Chylomicron	TG	Rare
IIA	LDL	LDL-C	Common
IIB	LDL and VLDL	LDL-C, TG	Common
III	IDL	TC, TG	Rare
IV	VLDL	TG	Common
V	Chylomicron and VLDL	TG	Uncommon

The three common types of dyslipidaemia are important because they are associated with an increased risk of cardiovascular disease due to atherosclerosis.

DIAGNOSTIC CRITERIA

Children with severe hypercholesterolaemia may present with xanthomas or myocardial infarction but most children with hypercholesterolaemia will be asymptomatic in childhood.

Children should be screened for dyslipidaemia if any of the following are present:

» Family history of premature cardiac disease or dyslipidaemia.
  > Children should be screened from 8 years. Children should be screened earlier than 8 years if homozygous familial hypercholesterolaemia is suspected.
» A medical condition associated with dyslipidaemia: diabetes mellitus, nephrotic syndrome, liver disease, obesity.

INVESTIGATIONS

» Exclude causes of secondary hyperlipidaemia.
» In most cases, non-fasting total cholesterol is determined in children at risk.
  If the level is higher than the upper limit, a lipid profile is done after 12 hours of fasting.
  > Upper limit of serum cholesterol and triglycerides: Total cholesterol 5.2 mmol/L.
  > Triglycerides (after 12 hours of fasting):
    - influenced by lifestyle – needs attention if > 1.68 mmol/L,
    - pancreatitis risk if > 10 mmol/L.

GENERAL AND SUPPORTIVE MEASURES

Manage secondary causes of hyperlipidaemia according to guidelines.
Schedule for integrated cardiovascular health promotion in children:

» **Obesity**
  > See Chapter 7: Endocrine System, section 7.15: Obesity.

» **Blood pressure**
  > With a family history of hypertension < 55 years of age: routine BP measurement from 3 years of age, once a year.
  > If BP ≥ 95th percentile for sex, age, and height percentile, follow-up and investigate if persistently elevated.
» **Diet**
  > Refer to a dietician.
  > Learning healthy eating habits is an important preventative measure.
  > Moderate salt intake.
» **Physical activity**
  > Encourage active child-parent play.
  > Limit child's sedentary behaviour such as time watching television and playing video computer games to a maximum of 2 hours per day or 14 hours per week.
  > Children should not be allowed to eat while watching television, i.e. no 'grazing'.
  > Organised sport 5 times per week for at least 20–30 minute periods.
» **Smoking**
  > Encourage members of the household who smoke to stop.

MEDICINE TREATMENT

Consider medicine treatment only after failure of general and supportive measures to lower the cholesterol over 6–12 months.
Children should be at least 8 years of age for consideration of pharmacological intervention.
If LDL-C remains above 4.1 mmol/L in children with 2 or more risk factors, or above 4.9 mmol/L regardless of the presence of risk factors, refer to a paediatric specialist for consideration of statins:
Risk factors: smoking, hypertension, BMI ≥ 95th percentile (Z-score ≥ +1.96), HDL-C < 1 mmol/L, diabetes mellitus, renal disease, male sex.

- Statins, e.g.:
  - Simvastatin, oral, 10 mg at night.

Secondary hypercholesterolaemia due to nephrotic syndrome
See Chapter 6: Nephrological/Urological Disorders, section 6.3: Nephrotic syndrome.

REFERRAL

» Children with homozygous familial hypercholesterolaemia.
» Children under 10 years of age with dyslipidaemia unresponsive to appropriate lifestyle interventions.
» Children with inadequate response to statins.

7.5.3 DIABETES MELLITUS IN ADOLESCENTS

E10

DESCRIPTION

Adolescence is the period between 10 and 19 years of age. The adolescent and the transition should be managed with special planning, i.e.:

» the admission policy of the hospital,
» observing the wishes of the adolescent,
» emotional and physical maturity considerations, and
» the presence of any co-existing medical, surgical or psychiatric disorder that may be more appropriately managed in the paediatric service.

Aggression and agitation may be features of poorly controlled diabetes.

GENERAL AND SUPPORTIVE MEASURES

Promote:

» normal growth and pubertal development,
» psychological development,
» maintenance of glycaemic control and adherence,
» avoidance of risk-taking behaviours (smoking, substance abuse), and
» sex education.

Adolescents with diabetes may have concomitant behavioural and psychiatric disorders. Anxiety disorders are common in adolescents and should be differentiated from hypoglycaemic and hyperglycaemic episodes.

MEDICINE TREATMENT

Failure of current insulin regimens may be attributed to the endocrine changes of puberty which results in poor glycaemic control.
Insulin resistance occurs during puberty, being maximal in late puberty.
Other causes of poor glycaemic control include family dynamics (e.g. resistance to parental supervision), emotional lability and risk-taking behaviour (e.g. intentionally neglecting to inject and substance abuse).

Normal insulin requirements during puberty:

- 1.0–1.4 units/kg/day.

This may occasionally be higher (up to 2.0 units/kg/day), but as a general rule, a higher requirement generally necessitates the search for non-adherence and poor absorption through injections in lipohypertrophy sites.

After puberty, the insulin requirements fall to prepubertal levels.
Failure to reduce insulin requirements in the late adolescent stages may result in excessive weight gain.

7.5.4 DIABETES MELLITUS, TYPE 2

E11

DESCRIPTION

Type 2 diabetes develops when insulin secretion cannot meet the increased demand posed by insulin resistance. Type 2 diabetes may be associated with hyperlipidaemia, hypertension, acanthosis nigricans, ovarian hyperandrogenism and non-alcoholic fatty liver disease (features of insulin resistance).

DIAGNOSTIC CRITERIA

Clinical

» Obesity or overweight.
» Children with a strong family history of type 2 diabetes, usually in adolescents with BMI > 95th centile without auto-antibodies to islet cells and normal serum C-peptide levels.
» Ketoacidosis is unusual in type 2 diabetes.
» A fasting plasma glucose > 7.0 mmol/L.
» Type 2 diabetics may have minimal symptoms or signs for months or even years before the diagnosis.

Investigations

To confirm diagnosis:

» Symptoms of diabetes.

PLUS

» Fasting plasma glucose > 7.0 mmol/L.

OR

» Random plasma glucose > 11.0 mmol/L.

OR

» No symptoms, but an abnormal 2-hour serum glucose level on the oral glucose tolerance test:
  > Ingestion of 1.75 g/kg (maximum 75 g) of glucose dissolved in water.
  > Serum glucose > 11.0 mmol/L 2 hours post ingestion of oral glucose.

GENERAL AND SUPPORTIVE MEASURES

» Lifestyle modification:
  Manage patients who are not ill at diagnosis initially with advice on nutrition and exercise, but most will eventually require medicine therapy.
» Education on routine blood glucose monitoring. A logbook with all blood glucose readings should be kept. In most cases, fasting, pre-breakfast measurement and a 2-hour postprandial dinner measurement are sufficient.
» Initial medicine treatment is determined by symptoms, severity of hyperglycaemia and presence of ketosis. This should be decided in consultation with a specialist who is experienced in treating these children.

MEDICINE TREATMENT
Refer for initiation of therapy.

7.6 HYPOGLYCAEMIA IN CHILDREN
E16.2

DESCRIPTION
Infants and small children have relatively limited glycogen stores with larger brain/body ratios than adults and are, therefore, at greater risk of hypoglycaemia during starvation.

The causes of hypoglycaemia (outside the neonatal period) include:

- » hypopituitarism,
- » growth hormone deficiency,
- » hyper-insulinaemia,
- » malnutrition,
- » liver dysfunction,
- » severe illness with poor intake,
- » accelerated starvation (ketotic hypoglycaemia),
- » medicine, e.g. insulin, alcohol, aspirin, beta-blockers, oral hypoglycaemic agents, quinine.
- » adrenal insufficiency,
- » hypothyroidism,
- » inborn errors of metabolism,
- » sepsis,
- » malaria,

DIAGNOSTIC CRITERIA
Clinical
- » Acute autonomic symptoms: hunger, nausea, anxiety, pallor, palpitations, sweating, trembling.
- » Neuroglycopaenic symptoms: impaired thinking, change of mood, irritability, dizziness, headache, tiredness, confusion, and later, convulsions and coma.
- » Patients are often asymptomatic, especially younger children, who may be completely asymptomatic or present only with a behaviour change.

Investigations
- » Serum glucose concentration < 2.6 mmol/L.
- » Hypoglycaemia is a clinical emergency requiring prompt therapy. However, if possible, draw a blood sample for investigation prior to the administration of glucose. Collect 5 mL of blood in a plain tube at the earliest opportunity and send for separation and storage of plasma at –20°C. Such samples may provide clear biochemical evidence of the cause of the hypoglycaemic episode thus avoiding having to subject the child to further investigations.

MEDICINE TREATMENT
After collection of initial blood samples:

- Dextrose 10%, IV, 2–5 mL/kg.
  - Dilute dextrose 50% solution before use to 10% strength.

(1 mL/kg of dextrose 50% plus 4 mL/kg of water for injection, gives 10% dextrose solution).

Stabilisation

- Sodium chloride 0.9%/dextrose 5%.
- Increasing the dextrose concentration in the fluid to 7.5% or 10% may be necessary:
  - To increase from 5% to 10% dextrose concentration in 1 L of fluid, add 100 mL 50% dextrose water.
  - 10 mL 50% DW increases dextrose concentration of 100 mL of fluid by 5%.

For persistent hypoglycaemia consider the underlying cause, e.g. hyper-insulinism or adrenal insufficiency (see section 7.3: Adrenal insufficiency, acute.). For persistent hypoglycaemia in the neonate, see Chapter 19: Prematurity and Neonatal Conditions. An inappropriately high insulin or C-peptide level at the time of the confirmed hypoglycaemia is also strongly suggestive of hyper-insulinism.

If hyper-insulinism is suspected, administer:

- Glucagon, IM/SC.
  - If < 12 years of age: 0.5 mg.
  - If > 12 years of age: 1.0 mg.

OR

- Diazoxide, orally, 5 mg/kg/day in three divided doses; may increase to 15 mg/kg/day.

LoE III[5,6,7]

Ongoing treatment

Intravenous fluid therapy as needed.
Start oral feeds as soon as possible.

REFERRAL

» All patients with confirmed hypoglycaemia not explained by intercurrent illness or drugs.
» All neonates with persisting or recurrent hypoglycaemia.
» Suspected hyper-insulinism.

7.7 GROWTH DISORDERS

R62

DESCRIPTION

Pathological growth failure may be suspected if a child is short relative to his/her peers and, his/her parents and possibly disproportionate to his/her weight. It is confirmed by a reduced growth velocity. This could be due to endocrine causes, chronic or bone disease or dysmorphic syndromes.

Idiopathic short stature may be due to constitutional delay in growth and puberty or familial short stature. Constitutional delay in growth is defined by short stature with a disproportionately short trunk and a bone age that is significantly delayed relative to chronological age. Familial short stature is determined by genetic potential and a bone age equivalent to chronological age. Both have a normal growth velocity.

DIAGNOSTIC CRITERIA

» Measure and plot the child's height and weight on growth charts. Routine monitoring of height and weight for growth assists in timely diagnosis and treatment, and thus ensures maximum benefit.
» A child is regarded as short if his/her height-for-age Z-score is below –2 for age and sex.
» To further evaluate short stature, assess parental height. Target height:
  > for a boy = (father's height + (mother's height + 13 cm)) ÷ 2; range 10 cm above and below target height.
  > for a girl = ((father's height – 13 cm) + mother's height) ÷ 2; range 9 cm above and below target height.
» If the child's predicted final height is below the target height range, monitor growth velocity over 6 months to 1 year.
» If the child's height-for-age Z-score is below –3, refer immediately.
» Growth failure occurs when the child's height deviates further from Z-score of –2 over a period of 1 year or the growth velocity is below 25th percentile for gender and age.

GENERAL AND SUPPORTIVE MEASURES

» Identify and manage non-endocrine causes of stunted growth, e.g.:
  > intra-uterine growth retardation,
  > chronic disease,
  > psychosocial deprivation, and
  > skeletal dysplasia and other dysmorphic syndromes.

REFERRAL

» Height-for-age Z-score below –3.
» Height 10 cm or more below target height.
» Growth failure (height deviates further from Z-score of –2 over a period of 1 year) or the growth velocity is below 25th percentile for gender and age.
» Suspected endocrine causes as suggested by a child who is short with a normal or high BMI.
» A dysmorphic child with an unidentified syndrome.
» Untreated chronic disease.

7.8 HYPOCALCAEMIA IN CHILDREN

E83.5

DESCRIPTION

The main causes of hypocalcaemia in children are:

» vitamin D deficiency,
» calcium deficiency,
» magnesium deficiency,
» reduced parathyroid hormone production or resistance,
» impaired renal function, and
» hyperventilation.

DIAGNOSTIC CRITERIA

Clinical

» Signs and symptoms of tetany include:
  > paraesthesia,
  > cramps,
  > carpopedal spasm,
  > laryngospasm,
  > positive Chvostek's sign,
  > positive Trousseau's sign,
  > weakness,
  > lethargy,
  > prolonged QT interval on the ECG.

Investigations

» Blood levels to establish cause:
  > calcium,
  > albumin,
  > phosphate,
  > magnesium,
  > ALP,
  > 25-hydroxyvitamin D.

MEDICINE TREATMENT

Acute hypocalcaemia

- Calcium gluconate 10%, IV, 1–2 mL/kg administered over 5–10 minutes, 6–8 hourly.
  - Maximum dose: 10 mL.
  - ECG monitoring is advised.

If hypomagnesaemic:

- Magnesium sulphate 50%, IV/IM, 0.2 mL/kg every 12–24 hours.

Chronic therapy

Long-term therapy depends on the cause.

Manage hypophosphataemia or hyperphosphataemia, depending on the cause of hypocalcaemia, before long-term calcium is initiated.

- Calcium, elemental, oral, 45–65 mg/kg/day until a normal calcium level is achieved (given with meals).
  - Maintenance dose: 30 mg/kg/day.

If vitamin D deficient:

- Vitamin D, oral:

Under 6 months	2500 IU/day
6 months–12 years	5000 IU/day
12–18 years	10 000 IU/day

For hypoparathyroidism and pseudohypoparathyroidism:

- Calcitriol, oral, 0.01–0.04 mcg/kg/day.

OR

- Alfacalcidol, oral, 0.05 mcg/kg/day.
  - If < 20 kg: 0.05 mcg/kg/day.
  - If > 20 kg: 1 mcg/day.

REFERRAL

» Chronic hypocalcaemia.

7.9 HYPERKALAEMIA

E87.5

See Chapter 6: Nephrological/Urological Conditions, section 6.4: Acute kidney injury (renal failure, acute).

7.10 HYPOKALAEMIA

E87.6

DESCRIPTION

Causes include:

» prolonged decreased intake and protein energy malnutrition,
» increased renal excretion: renal tubular acidosis, amphotericin B and diuretics,
» increased extra-renal losses,
» transmembrane shifts: $ß_2$ stimulants, alkalosis; and
» mineralocorticoid excess.

DIAGNOSTIC CRITERIA

Clinical

» Cardiac arrhythmias, especially with digitalis.
» Neuromuscular dysfunction, e.g. muscle weakness.
» Renal: impairment of urine concentrating or diluting ability.

Investigations

» Serum potassium < 3.0 mmol/L.

MEDICINE TREATMENT

See Chapter 2: Alimentary Tract, section 2.2.4: Diarrhoea, acute.

Severe respiratory paralysis and or cardiac arrhythmias:

- Potassium chloride, IV, < 1 mEq/kg/hour.
  - ECG monitoring.
  - Potassium concentration should not be > 40 mmol/L/infusion.
  - Never give potassium as an IV bolus.

Less critical situations to correct potassium deficit over 2–3 days:

- Potassium chloride, oral, 2–6 mEq/kg/day.

Note: 1 g KCl = 13 mEq; 1 mL 15% KCl = 2 mmol; 1 mEq = 1 mmol.

7.11 HYPOPITUITARISM

E23.0

DESCRIPTION

Multiple or isolated deficiencies of adrenocorticoid hormone (ACTH), luteinising hormone, thyroid stimulating hormone, prolactin, and growth hormone manifesting as hypoglycaemia, abnormal body proportions and failure to grow and develop. If the posterior pituitary is involved (ADH deficiency), then this condition is known as panhypopituitarism.

The deficiency may be due to:

» congenital abnormalities with/without midline structural abnormalities of the brain,
» central nervous system tumours, e.g. craniopharyngioma, histiocytosis; and
» complications of radiation therapy.

DIAGNOSTIC CRITERIA

Clinical

» Neonates with hypopituitarism may present with:
  > persistent hypoglycaemia,
  > cholestatic jaundice (related to low cortisol), and
  > micropenis.
» Short stature with normal or high BMI.
» Polydipsia, polyuria, nocturia and enuresis in the case of panhypopituitarism.

Investigations

» Endocrine evaluation with pituitary function tests under specialist supervision.
» Confirm diagnosis in older children with stimulation tests.

MEDICINE TREATMENT

To correct hypoglycaemia:

- Hydrocortisone, IV, 2–3 mg/kg.

REFERRAL

» All patients after stabilisation of hypoglycaemia.

7.12 HYPOTHYROIDISM, CONGENITAL

E03.1

DESCRIPTION

Congenital deficiency of thyroid hormone due to:

» aplasia/hypoplasia or ectopia of the thyroid gland,
» thyroglobulin defects,
» defects in thyroid hormone biosynthesis, or
» intrauterine exposure to antithyroid medicines.

Congenital hypothyroidism is one of the common treatable causes of preventable intellectual disability in children. Congenital hypothyroidism must be treated as early as possible to avoid intellectual impairment. Symptoms and signs in neonates are unreliable, thus screening is essential for ensuring early intervention.

DIAGNOSTIC CRITERIA

Clinical

» Prolonged unconjugated hyperbilirubinaemia.
» Feeding difficulties.
» Lethargy
» Somnolence
» Abdominal distension.
» Umbilical hernia.
» Subnormal temperature.
» Periorbital oedema.
» Delayed dentition.
» Broad hands.
» Coarse, scanty hair.
» Hoarse voice and goitre.
» Oedema of the extremities and genitals.
» Bradycardia
» Anaemia
» Apnoeic episodes.
» Coarse cry.
» Constipation
» Wide open fontanelles.
» Enlarged tongue.
» Short and thick neck.
» Dry skin.
» Hypotonia.
» Delayed physical and mental development.

Investigations

» When suspected, perform a TSH test.
  > If elevated, perform a free T_4.

Delay in diagnosis and treatment is associated with irreversible neurodevelopmental damage**.**

GENERAL AND SUPPORTIVE MEASURES

» Routine screening of all newborns for congenital hypothyroidism.
» Growth and neurodevelopmental assessment.
» Regular follow-up.

MEDICINE TREATMENT

For neonates, start as soon as possible, ideally within the first three weeks after birth:

- Levothyroxine, oral, 10–15 mcg/kg as a single daily dose on an empty stomach.
  - Adjust dosage to blood levels of free T_4 (in the upper-half of the reference range) and normalise the TSH, especially in the first 3 years of life. Check TSH only 6 weeks after adjusting the thyroxine dose.
  - Continue treatment indefinitely.

REFERRAL

» All patients for confirmation of diagnosis, but initiation of therapy should not be delayed.

7.13 HYPOTHYROIDISM IN OLDER CHILDREN AND ADOLESCENTS

E03.9

DESCRIPTION

Acquired hypothyroidism in childhood and adolescents may be due to:

» auto-immune thyroiditis,
» goitrogen induced,
» iodine deficiency,
» post surgery,
» radioactive iodine,
» infiltrations,
» medicines.

DIAGNOSTIC CRITERIA

Clinical

» Low growth velocity or short stature with short limbs associated with a normal or elevated BMI.

» Subtle features with cold intolerance, dry skin, brittle hair, pallor and myxoedema.

Investigations

» Elevated TSH and low thyroxine levels.

MEDICINE TREATMENT

- Levothyroxine, oral, once daily on an empty stomach.

1–6 months	8–10 mcg/kg
6–12 months	6–8 mcg/kg
1–5 years	5–6 mcg/kg
6–12 years	4–5 mcg/kg
Over 12 years	2–3 mcg/kg

REFERRAL

» All cases for investigation and initiation of therapy.

7.14 HYPERTHYROIDISM, GRAVES DISEASE

E05.9/E05.0

DESCRIPTION

Hyperthyroidism is a pathological syndrome in which tissue is exposed to excessive amounts of circulating thyroid hormones.

The most common cause is Grave's disease, although thyroiditis may also present with thyrotoxicosis.

DIAGNOSTIC CRITERIA

Clinical

» Poor school performance.
» Warm moist hands.
» Thyromegaly
» Tremor
» Proptosis
» Fatigue
» Tachycardia
» Nervousness or anxiety.
» Weight loss.
» Palpitations
» Heat intolerance.

Investigations

» Elevated thyroxine (T_4) and suppressed TSH.

MEDICINE TREATMENT

- Carbimazole, oral, 0.5 mg/kg once daily.

AND

To block sympathetic hyperactivity:

- Atenolol, oral, 1–2 mg/kg as a single daily dose.

For children less than 10 kg:

- Propranolol, oral, 0.2–0.5 mg/kg 6–12 hourly.
  - Maximum dose: 1.5 mg/kg/dose 6–12 hourly.

REFERRAL

» All patients for confirmation of diagnosis, initiation and follow-up of therapy.

7.15 OBESITY

E66

DESCRIPTION

Most children with obesity do not have an underlying pathological cause and have so-called 'simple obesity', i.e. both weight and height are increased.

In children with pathological obesity, the height is not usually increased when compared to parental height. Causes of pathological obesity include syndromes, hypothalamic damage, endocrine abnormalities, immobility, impaired skeletal growth or medicines.

There has been a dramatic increase in the prevalence of childhood overweight and its resultant comorbidities.

DIAGNOSTIC CRITERIA

Clinical

» Measurement of weight alone is inadequate given the influence of height on weight.

» Assess severity using body mass index (BMI):

$$\text{Body mass index} = \frac{\text{weight (kg)}}{[\text{height (m)}]^2}$$

» The BMI varies with age. Use sex-specific BMI charts for accurate diagnosis. Obesity is defined by a Z-score > +2; overweight by a Z-score between +1 to + 2. Contrary to WHO teaching, the same cut-offs should be used at all ages of obesity.

» In general, obesity is likely if BMI:
> 19 kg/m^2 at age 5 years,
> 23 kg/m^2 at age 10 years, and
> 25 kg/m^2 at age 18 years.

Investigations

» Fasting glucose and lipid profile.

» ALT, AST, GGT.

GENERAL AND SUPPORTIVE MEASURES

» Weight control by:
> education about the nature of obesity and its long term consequences;

- > healthy eating, e.g. regular meal times, avoidance of excessive 'snacking', fried foods, added fats and sugars and high energy drinks while encouraging foods with high fibre content, with modest calorie restriction;
- > increasing physical activity;
- > reduce sedentary time, e.g. TV watching, computer games, videogames or time on the telephone;
- > parental guidance in managing abnormal behaviour, e.g. temper-tantrums.

» Weight loss down to an 'ideal body weight for height' is unrealistic. Prevention of further weight gain may produce significant longer-term benefits. If the patient is over 7 years, or if complications are present, aim for a weight loss of 0.5 kg/month. Ideally, target BMI should be in the overweight range.

MEDICINE TREATMENT

Look for and manage complications such as hyperlipidaemia, hypertension, sleep apnoea, slipped upper femoral epiphysis and non-alcoholic fatty liver. Insulin resistance is another important complication, and this is a key factor in the pathogenesis of metabolic syndrome. Metabolic syndrome is a cluster of cardiovascular and diabetes risk factors such as central abdominal obesity, dyslipidaemia, glucose intolerance, and hypertension (particularly common in patients on ARVs).

Refer to Chapter 4: Cardiovascular System, sections 4.10: Dyslipidaemia and 4.11: Hypertension in children; and section 7.5: Diabetes Mellitus.

REFERRAL

» All cases of pathological and morbid simple obesity (as defined by a Z-score > +3).
» Severe/progressive obesity < 2 years.
» Serious co-morbidity requiring weight loss.

7.16 DISORDERS OF PUBERTY

E30

DESCRIPTION

Abnormally early or late development of signs of puberty including the development of breasts (in girls) or enlargement of external genitalia (boys) and sexual hair growth.
Often associated with an abnormality of growth velocity.

DIAGNOSTIC CRITERIA

» Puberty begins after 9 years and usually not later than 14 years in males.

» Puberty begins after 8 years and usually not later than 13.5 years in females.
» Precocity or delay of puberty occurring outside these ages needs investigation.

Investigations
» Puberty staging.
» Radiological bone age.
» Endocrine investigation.

GENERAL AND SUPPORTIVE MEASURES
» Psychological support.
» Treat the cause, e.g. tumours.

REFERRAL
» All.

7.17 POLYCYSTIC OVARY SYNDROME
E28. 2

DESCRIPTION
Characterised by excessive androgen activity, with many having abnormal insulin activity.

DIAGNOSTIC CRITERIA
Clinical
» Hirsutism
» Acne
» Oligomenorrhoea or amenorrhoea due to chronic anovulation.
» Female pattern alopecia.
» Overweight or obese.

Investigations
» Polycystic ovaries on ultrasound.

GENERAL AND SUPPORTIVE MEASURES
» Assess and monitor for long-term health complications, including:
  > impaired glucose tolerance,
  > insulin resistance,
  > type 2 diabetes,
  > dyslipidaemia,
  > obesity,
  > fatty liver,
  > depression, and
  > infertility.

» Lifestyle changes in nutrition and exercise to reduce weight.

REFERRAL

All suspected cases for assessment and management

References

[1] Caldato MCF, Fernandes VT, Kater CE. One-year clinical evaluation of single morning dose prednisolone therapy for 21-Hydroxylase Deficiency. Arq Bras Endocrinol Metab. 2004;48(5):705-712.

[2] So TY, et. al. Evaluation of the Two-Bag System for Fluid Management in Paediatric Patients with Diabetic Ketoacidosis. J Pediatr Pharmacol Ther. 2009;14:100-105.

[3] Grimberg A, et. al. The 'two bag system' for variable intravenous dextrose and fluid administration: benefits in diabetic ketoacidosis management. J Pediatr. 1999;134(3):376-378.

[4] Sublingual sugar for hypoglycaemia in children with severe malaria: A pilot clinical study. Malaria Journal. 2008;7:242.

[5] Aynsley-Green A, et. al. Practical management of hyperinsulinism in infancy. Arch Dis Child Fetal Neonatal Ed. 2000;82:F98-F107.

[6] Güemes M, Hussain K. Hyperinsulinemic Hypoglycemia. Pediatr Clin N Am. 2015;62: 1017-1036.

[7] The British National Formulary for Children, 2020-2021. BMJ group, Pharmaceutical Press, RCPCH Publications Ltd. 2014.