Unstable diabetes

Hypoglycaemia and hyperglycaemia occur in both type 1 and type 2 diabetes. The aim of this section is to provide an overview of these acute complications in the context of the home / community setting. Refer to Hospitalisation – Section 4 to find out more about managing hypoglycaemia and hyperglycaemia in a hospital or health service setting.

Hypoglycaemia

Hypoglycaemia occurs when the blood glucose level falls to values low enough to cause symptoms and signs. When the level of glucose falls in the blood the cells in the periphery, and eventually the brain cells do not get adequate glucose to function. The value at which this occurs is defined at below 4mmol/L but probably differs according to the age and sex of the person, whether there are any associated medical conditions such as liver disease or cerebrovascular disease present and the rate at which blood glucose level has fallen. Significant hypoglycaemic symptoms tend not to occur until blood glucose levels fall below 4mmol/L.\(^1\)

There is significant physical and psychological morbidity associated with hypoglycaemia. Hypoglycaemia can be very frightening for the person and their family. Furthermore hypoglycaemia can lead to injury such as falling, an accident while driving and sometimes death. Health professionals play an important role in helping people to understand, prevent and manage hypoglycaemia.

Type 1 diabetes

Hypoglycaemia is very common for people with type 1 diabetes. For those who are wanting to improve or maintain target glycaemic control symptomatic hypoglycaemic episodes may occur on average 2 times a week. Severe hypoglycaemia may occur approximately 1 time per year.\(^1\) It has been estimated that 2-4% of deaths of people with type 1 diabetes have been attributed to hypoglycaemia.

Type 2 diabetes

The frequency of hypoglycaemia is substantially lower in type 2 diabetes as compared with type 1 diabetes. The rate of severe hypoglycaemia in type 2 diabetes are less than 10% of those in type 1 diabetes at the same level of A1c.\(^1\) Hypoglycaemia becomes more problematic for people with type 2 diabetes as their diabetes progresses and they become more and more insulin deficient. Deaths have been documented in people with type 2 diabetes who are on sulphonylurea medications.
Clinical features of hypoglycaemia

In people who do not have diabetes a counter-regulatory response is triggered as blood glucose levels drop. When the blood glucose level (BGL) drops to about 4.2mmol/L the secretion of endogenous insulin is suppressed. In type 1 diabetes this does not happen because they have no endogenous insulin and the injected (exogenous) insulin can not be suppressed. In people with type 2 diabetes the body can suppress some of the insulin because they are still producing their own insulin.\(^1\)

At about 3.7mmol/L the secretion of glucagon is increased and this results in the release of stored glucose. Other hormones such as epinephrine, cortisol and growth hormone are also released in order to raise the blood glucose.\(^1\)

The symptoms of hypoglycaemia can be classified into two groups.

1. Symptoms in response to adrenaline or the sympathetic nervous system (pale skin, sweating, shakiness, tingling especially around the lips, palpitations and a feeling of anxiety).
2. Symptoms due to decreased glucose in the brain (difficulty concentrating, confusion, inappropriate behavioural and psychological reactions, drowsiness, ultimately seizures and coma).

Hypoglycaemia can be defined on the basis of physiology using the terminology mild, moderate or severe (table 1).

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capable of self treating</td>
<td>May require prompting</td>
<td>Not capable of self-treatment</td>
</tr>
<tr>
<td>Tremors, palpitation, sweating, hunger, fatigue</td>
<td>Headache, mood changes, low attentiveness</td>
<td>Conscious or unconscious</td>
</tr>
</tbody>
</table>

Adrenergic Neuroglycopenic Neuroglycopenic

Hypoglycaemia at night is often slept through and not noticed. Symptoms of unnoticed nocturnal hypoglycaemia include:

- morning headaches
- hangover type feeling on waking
- nocturnal sweating.
Primary causes of hypoglycaemia

Hypoglycaemia is a risk for people who are taking glucose lowering medicines or insulin. There are a number of possible causes of hypoglycaemia that have been identified:

- missing a meal or snack
- inadequate carbohydrate intake
- delaying a meal (or enteral feeding)
- over-administration of insulin or oral hypoglycaemic agents
- prolonged physical activity with no food or adjustment of insulin
- excessive alcohol intake, especially on an empty stomach
- vomiting eg morning sickness.

In addition, hypoglycaemia has also been associated with:

- onset of menstruation cycle due to hormonal levels which decrease insulin requirement
- eating disorders such as anorexia nervosa and bulimia
- immediate post-partum period where a rapid decrease in placental hormones increases insulin effect
- autonomic neuropathy where there may be diminished epinephrine response or delayed gastric emptying
- extremes in weather temperature eg heat and cold.

Management

Hypoglycaemia must be treated promptly. People with diabetes should have a hypoglycaemia action plan which clearly steps out their management.

The following is a suggested protocol for the treatment of people with hypoglycaemia in the community. This protocol may be adapted for any hypoglycaemic situation. You should refer to Hospitalisation – Section 4 for the hypoglycaemia protocol for health services and hospitals.

Mild or moderate hypoglycaemia

If hypoglycaemia is suspected, check BGL.

Blood Glucose Level <4mmol/L treat as follows

**Step 1**
- 15gm fast acting carbohydrate (CHO)
  eg 150mls soft drink
  or 15g Glucose tablets
  or 6 jelly beans (glucose)
- Wait 5-10 minutes
- Repeat Step 1 if BGL still <4mmol/L
- If blood glucose level ≥4mmol/L, move to Step 2.

**Step 2**
- Slow acting CHO intake
  eg 4 water crackers or equivalent or
  1 piece of fruit or
  1 cup of milk or
  meal if only minutes away.
Severe hypoglycaemia

If confusion or loss of consciousness prevents safe administration of oral glucose then glucagon can be administered by a family member or ambulance officer.

Glucagon (GlucaGen®)

Glucagon is used to treat severe hypoglycaemia whereby a person is unable to swallow safely. A doctor will need to prescribe a GlucaGen Hypokit for use by the persons family / carers / friends.

Glucagon should be prescribed for all individuals who are at significant risk of severe hypoglycaemia eg past history of severe hypo or hypo unaware. Caregivers or family will require instruction.2

Glucagon is a hormone that increases glucose levels in the blood. It does this by releasing glucose from stored carbohydrate (glycogen) in the liver into the blood. This means that glucagon will only work to increase blood glucose if there are stores of glycogen in the liver.

What to teach in case of hypoglycaemia

People need to be informed that they will need a script and that they will need to check expiry dates. Ambulance cover and medic alert are recommended.

It is important to inform the person and their family that if they phone an ambulance they will be connected to a qualified SAAS call-taker. The call-taker will immediately assess the situation and can give step-by-step instructions over the phone. This can provide much needed support during a stressful event. The call taker will assess the severity and an ambulance will be dispatched if required. Visit the website www.saambulance.com.au for more information about the ambulance service.

If the person is unconscious, turn on to their side and get help immediately.

Advice for non-medical person: inject the dose of glucagon into the fatty tissue just below the skin of the thigh or buttocks.

- Adults and children above 25kg: inject full dose (marked on hypokit syringe as 1/1mL)
  Children below 25kg: inject half dose (marked on hypokit syringe as 1/2mL)
- The person will normally respond within 10-15 minutes to the injection of glucagon.
- Once conscious, follow usual guide for hypo treatment. Note: It is advisable not to give food immediately as the person may feel nauseous. Slow sips of a sweet drink is sufficient.
- People also often have a distressing headache after a severe hypo and they can be advised to sleep once BGLs are stabilised.
- After a severe hypo the liver stores of glucose may be depleted and so the person needs to be warned that they are at an increased risk of further hypos.
Storage

GlucaGen Hypokit should be stored at room temperature (eg less than 25°C).

Avoid freezing to prevent damage to the glass syringe.

The GlucaGen Hypokit powder vial should be protected from light.

The expiry date (“Expiry”) is printed on the pack. If passed this date, do not use it. Check the expiry date from time to time to make sure that the glucagon in your GlucaGen Hypokit has not expired.

The glucagon solution should be injected immediately after it is prepared. It should not be stored for later use.

For further information consult the Product Information leaflet. Information is also available from Novocare Customer Care Centre on 1800 668 626.

Monitor

Monitor person 15-30 minutes following treatment.

Check blood glucose level after 30 minutes from initial time. If blood glucose level is <4 repeat Steps 1 and 2 on page 3. It is necessary to ensure that the hypoglycaemia does not recur and blood glucose level remains within normal range.

Length of observation

The person should be aware that hypoglycaemia might reoccur and that increased testing for the next 24 hours may be needed. This will depend on the severity and duration of episode. Some form of fast acting, rapidly absorbed carbohydrate should be left with the person. After a severe episode of hypoglycaemia the next dose of medication may need to be modified and the person should discuss their needs with the appropriate health professional. The person should also be encouraged to determine the cause of the hypoglycaemia wherever possible to assist in preventing further episodes.

Hypoglycaemic unawareness

Some people with diabetes may not have any symptoms of hypoglycaemia. Unawareness of hypoglycaemia symptoms occurs more frequently in people who have had diabetes for many years or in people who maintain lower blood glucose levels. Diabetic neuropathy can also lead to hypoglycaemic unawareness.

People who may be `risk’ of hypoglycaemic unawareness are advised to monitor blood glucose levels more frequently and need to ensure meal patterns and exercise are matched. Some people may adjust their insulin dose by 10% depending on activity levels (see Maintaining a healthy lifestyle – Section 9). People need to discuss target blood glucose ranges with their GP / MO medical officer.

Education and support for partners / carers and the person themself are also important issues in managing hypoglycaemic unawareness.
Prevention of hypoglycaemia

Educating people at risk of hypoglycaemia regarding the signs and symptoms, causes and early treatment of hypoglycaemia is a mainstay of prevention.

People with diabetes should be instructed to carry some form of quick acting carbohydrate at all times. Educate people at risk to carry an identification card or wear a bracelet.

Advise people to check their blood glucose level or institute treatment at the first indication of possible hypoglycaemia.

If hypoglycaemia occurs frequently they must discuss this with the GP / MO so that some adjustment is made to their treatment plan. Adults trying to lose weight or maintain their current weight may need to have their medication dosage decreased.

Educate family members and close friends about hypoglycaemia and teach them when and how to measure blood glucose levels and the use of glucagon injection.

Educate people with diabetes who are at risk of hypoglycaemia to employ special care (eg increased monitoring, including 3am glucose checks) when activity and diet patterns are altered, when planning to drive or while driving.

Consider developing a ‘hypo’ action plan

Health professionals have an important role in assisting people to have a hypo action plan in place. A hypo kit is central to this action plan and the person can be asked to identify what foods would be most appropriate to keep in their hypo kit. You could consider working through a plan like the one below.

Example of a personalised ‘hypo plan’

<table>
<thead>
<tr>
<th>My ‘hypo’ plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>BG</td>
</tr>
<tr>
<td>Step 1</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Step 2</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Step 3</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Step 4</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>NB</td>
</tr>
</tbody>
</table>
Hyperglycaemia

Definition of hyperglycaemia

Hyperglycaemia is defined as a fasting blood glucose concentration of ≥7.0mmol/L and post prandial concentration of ≥11.1mmol/L. However, symptoms are more commonly evident when the blood glucose concentration is >15mmol/L.

Hyperglycaemia as a result of uncontrolled diabetes mellitus may ultimately lead to two types of metabolic disturbances, conditions known as diabetic ketoacidosis (DKA) and hyperglycaemic hyperosmolar state (HHS). Diabetic ketoacidosis is a serious life-threatening complication that results from uncontrolled type 1 diabetes. HHS is also a life-threatening emergency and is usually seen in the elderly or undiagnosed person with type 2 diabetes.

Primary causes

- insufficient insulin, omitting the insulin injection
- insufficient oral hypoglycaemic agents or omitting to take medications as prescribed
- excessive carbohydrate intake
- stress – physical stress increases the body’s energy demands, which increase the production of glucose and counter regulating hormones. Insulin or oral hypoglycaemic agents therefore are less effective
- infection and illnesses - gastroenteritis, myocardial infarction, urinary tract infection
- surgery
- rebound hyperglycaemia – Somogyi effect
- other medications, eg steroids such as prednisolone.

Assessment of hyperglycaemia

Assessment is crucial to prevent hyperglycaemia progressing to an advanced metabolic crisis. This can be prevented by early recognition of signs and symptoms and prompt treatment. To assess hyperglycaemia:

- perform blood glucose measurement
- in type 1 diabetes test ketones if blood glucose >15mmol/L, or are unwell. If urine ketone levels 3+ or blood ketone levels are above 1.5mmol/L or ketoacidosis suspected, contact the GP/MO or diabetes specialist (eg endocrinologist) immediately.
- continue to monitor blood glucose and ketones as ordered
- ensure medication is given as ordered
- observe for symptoms such as polyuria, polydipsia, polyphagia, lethargy or infections and monitor progress.
Advanced hyperglycaemia

If the symptoms of hyperglycaemia are not recognised and treated early, the hyperglycaemia may become advanced and lead to various emergency situations depending on the type of diabetes.

Ketoacidosis

Diabetic ketoacidosis (DKA) is a medical emergency which has a <5% mortality.\(^4\) It is preventable in people known to have type 1 diabetes and most cases of ketoacidosis occur in patients with undiagnosed type 1 diabetes.

Ketoacidosis results from the absence of insulin. Although small amounts of circulating insulin may be present, the presence of large amounts of the counter regulatory hormones such as glucagon, adrenaline and noradrenaline and cortisol, result in the insulin being less effective.

DKA consists of the biochemical triad of hyperglycaemia, ketonaemia and acidaemia.\(^4\) The following diagram depicts the development of diabetic ketoacidosis.

---

Pathophysiology of diabetic ketoacidosis\(^5\)

- Infection, Stress
- Missed insulin injection
  - Undiagnosed type 1 diabetes

- Glucagon and counter-regulatory hormone excess
- Insulin deficiency
- Reduced glucose uptake into tissues

- Lipolysis
  - Ketogenesis
- Glycogenolysis
  - Gluconeogenesis

- Ketosis
- Hyperglycaemia
- Acidosis
- Vomiting
- Osmotic diuresis
- Severe Dehydration
Precipitating factors

Precipitating factors vary from individual to individual but may include:

- Illness / infection.
- Inadequate insulin administration either by the MO or the person with diabetes. People with gastrointestinal infections often decrease or omit insulin when food intake is decreased. (The person must be educated regarding appropriate management during sick days and advised that adjustment of insulin dosages based on blood glucose levels may be required).
- First presentation of type 1 diabetes.

Features of ketoacidosis

The signs of diabetic ketoacidosis are hyperglycaemia, glycosuria, ketosis, dehydration and electrolyte imbalance.

**Glycosuria:** occurs as the concentration of glucose in the blood exceeds the renal threshold (ie capacity to reabsorb).

**Polyuria:** glucose in the urine acts as an osmotic diuretic, which can lead to dehydration if left untreated.

**Polydipsia:** thirst will occur as the body attempts to replace the lost fluid.

**Ketones:** as fats are broken down to supply energy, ketoacids accumulate in the blood stream causing ketosis and acidosis. Ketosis is also recognised by an acetone breath. The accumulation of ketones in the blood and excretion of ketones in the urine (ketonuria) leads to more electrolyte imbalance and dehydration.

**Gastrointestinal:** symptoms are nausea, vomiting, abdominal pain.

**Respiratory:** symptoms may include hyperpnoea (increased ventilation) and / or deep rapid breathing (Kussmaul's respirations) which produces a respiratory alkalosis as the body attempts to correct the metabolic acidosis.

Polyuria, ketonuria and acidosis cause **loss of body potassium.** However, acidosis causes potassium to move from the cells to the plasma. Hence, the circulating potassium may be low, normal or high.

If acidosis and hyperglycaemia continue, they may lead to **coma and death.**

Prevention

- Awareness of the early signs and symptoms of uncontrolled diabetes must be increased. People with diabetes and their family need education.
- The importance of ketone testing during illness should be stressed for people with type 1 diabetes.
- Management of sick days in the home situation with increased knowledge and skills is a major factor in prevention.
- Professional education with regard to proper diagnosis and treatment.
- Psychological intervention will need to be included as part of the treatment for those who have recurrent episodes requiring admission to hospital.
Hyperglycaemic hyperosmolar state (HHS)

HHS has a significant mortality rate of approximately 15%.

This complication of diabetes occurs more frequently in elderly people with type 2 diabetes and may occur as the presenting problem of undiagnosed diabetes. As in diabetic ketoacidosis it is a life threatening emergency. There is no ketoacidosis present since there is enough insulin to inhibit the breakdown of fat. Severe hyperglycaemia however causes osmotic diuresis, leading to severe dehydration, with polyuria, polydipsia and polyphagia.

If the person is unable to replace fluids, dehydration and mental impairment occurs. This is especially likely in the elderly. Hence this acute complication often occurs in the elderly on oral hypoglycaemic agents who may be inadequately monitored or not receiving adequate fluid intake and unable to communicate their need.

The high plasma osmolality and dehydration lead to:

- decreased skin turgor
- hypotension
- elevated body temperature
- drowsiness
- confusion
- convulsions
- coma.

Note: Kussmaul's respirations and acetone breath are not present.

Precipitating factors

These include:

- infection
- intercurrent illness such as myocardial infarction, acute airway disease
- medication, eg high dosage corticosteroids, excessive use of diuretics
- pancreatitis
- total parental nutrition
- renal dialysis
- severe burns.

Prevention is the key – education is the answer

To prevent hyperglycaemic hyperosmolar state (HHS) from occurring, identify those at high risk and ensure the older person is well hydrated.

Teach people with diabetes and family about warning signs and symptoms. Make sure they know about sick day management and when to seek advice. Health professionals should be aware of the appropriate management of people who are at risk.
Comparison of features of diabetic ketoacidosis and hyperglycaemic hyperosmolar state (HHS)

The following table highlights key areas related to the differing features of type 1 and type 2.6

<table>
<thead>
<tr>
<th>Feature</th>
<th>Ketoacidosis</th>
<th>Hyperglycaemic Hyperosmolar State</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of diabetes</td>
<td>Type 1</td>
<td>Type 2</td>
</tr>
<tr>
<td>Age of patient</td>
<td>Usually &lt;40 years</td>
<td>Usually &gt;40 years</td>
</tr>
<tr>
<td>Duration of symptoms</td>
<td>Usually &lt;2 days</td>
<td>Usually &gt;5 days</td>
</tr>
<tr>
<td>Glucose</td>
<td>Usually &lt;22mmol/L</td>
<td>Usually &gt;22mmol/L</td>
</tr>
<tr>
<td>Sodium</td>
<td>More likely to be normal or low</td>
<td>More likely to be normal or high</td>
</tr>
<tr>
<td>Potassium</td>
<td>High, normal or low</td>
<td>High, normal or low</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>Low</td>
<td>Normal</td>
</tr>
<tr>
<td>Urinary Ketones</td>
<td>4+’s on dip stick</td>
<td>May be present but not relevant</td>
</tr>
<tr>
<td>Blood ketones</td>
<td>&gt;1.5mmol/L</td>
<td>not applicable</td>
</tr>
<tr>
<td>Urinary pH</td>
<td>Low</td>
<td>Normal</td>
</tr>
<tr>
<td>Serum osmolality</td>
<td>Usually &lt;350mOsm/kg</td>
<td>Usually &gt;350mOsm/kg</td>
</tr>
<tr>
<td>Cerebral oedema</td>
<td>Often sub-clinical; occasionally</td>
<td>Not evaluated if subclinical;</td>
</tr>
<tr>
<td></td>
<td>clinical</td>
<td>rarely clinical</td>
</tr>
<tr>
<td>Prognosis</td>
<td>5% mortality</td>
<td>15% mortality</td>
</tr>
<tr>
<td>Subsequent course</td>
<td>Insulin therapy required in all</td>
<td>Ongoing insulin therapy often not</td>
</tr>
<tr>
<td></td>
<td>cases</td>
<td>required. May be required in the</td>
</tr>
<tr>
<td></td>
<td></td>
<td>long term.</td>
</tr>
</tbody>
</table>
Prevention of hyperglycaemic emergencies

- Medication should always be taken as prescribed.
- Notify the GP / MO if blood glucose concentration exceeds 15mmol/L, the person is unwell or ketones are moderate to large.
- Be aware of the early symptoms of hyperglycaemia before the condition progresses to a life-threatening situation.
- If the person is administering their own insulin, check their technique and knowledge.
- On days of illness, usual medication must be taken with usual diet / supplements and blood tested more frequently, eg 2 hourly. Extra medication may be required.

Sick day management

Note: This section is currently under review.


The ADEA Sick day guidelines are available for information about sick day management in type 2 diabetes

Other situations that cause unstable diabetes

Somogyi effect

Rebound hyperglycaemia or the Somogyi effect refers to morning hyperglycaemia that follows an episode of nocturnal hypoglycaemia.\(^5\)

This is a complex phenomenon that usually only occurs in type 1 diabetes. The Somogyi effect may partly reflect the release of counter-regulatory hormones such as glucagon, adrenaline, noradrenaline, cortisol, growth hormone stimulated by hypoglycaemia. These hormones stimulate the release of stored glucose from the liver, and also increase the manufacture of glucose by the liver. The person’s response to the hypoglycaemia episode may also contribute because people often eat more than is required to treat the hypo.

Clinical Presentation

Fasting hyperglycaemia, eg >15mmol/L for 3 consecutive mornings may be a sign of the Somogyi effect. High blood glucose level may occur at any time and even for 12-24 hours after a severe hypoglycaemic reaction.

Management

- Note any signs of nocturnal sweating or restlessness during the night.
- Perform blood glucose measurement during the night at 0300 hrs. With the Somogyi effect blood glucose will be low; with inadequate insulin activity blood glucose will be high.
- Treat hypoglycaemia <4mmol/L as per protocol.
- Document episode and action taken accurately in progress notes.
- Report to medical officer.
- Determine cause (has supper snack been given too early or inadequate carbohydrate or too much insulin).
- Continue to observe blood glucose patterns over a 24 hour period.
- Ensure medication / CHO intake is adjusted to prevent further episodes.

Honeymoon phase

The ‘honeymoon phase’ is a term used to describe the period of time immediately following initial diagnosis of type 1 diabetes.\(^5\) The beta cells may continue to produce insulin for a further 6 to 18 months. Often less insulin is needed and hypoglycaemia occurs. Young children occasionally require dilution of insulin because so little insulin is needed. C-peptide blood tests reflecting the amount of insulin secreted by the person’s pancreas can determine the extent of endogenous insulin production.
Dawn phenomenon

The ‘dawn phenomenon’ is characterised by unacceptably high fasting blood glucose levels and is more common in type 2 diabetes. Normally blood glucose levels rise from around 3.00am and gradually increase to a normal fasting level of 5.0mmol/L before breakfast. When this occurs in people with diabetes who have insufficient or ineffective endogenous insulin, a higher than normal fasting blood glucose level is found.

Treatment of the ‘dawn phenomenon’ requires additional insulin activity by either oral hypoglycaemic agents or insulin therapy but at the same time ensuring hypoglycaemia is avoided. It is also important to distinguish from the high fasting blood glucose levels which could be a result of the Somogyi effect.

Management involves regular home blood glucose monitoring with extra monitoring at 3.00am to ascertain the blood glucose levels and to assist with medication adjustments.

Lactic acidosis

Lactic acidosis is the accumulation of lactic acid in the body. The condition is rare and generally occurs in the older person.

The risk of lactic acidosis increases where there is decreased tissue perfusion associated with septicaemia or cardiovascular shock, or with alcohol abuse associated with renal or hepatic impairment. It may be aggravated by metformin therapy.

Signs of lactic acidosis include deep and rapid breathing, vomiting and abdominal pain. Metabolic acidosis is present but ketones are absent or minimal.

Lactic acidosis may be present in combination with ketoacidosis or non-ketotic hyperglycaemia.

Management is as for ketoacidosis, often with sodium bicarbonate to correct acidosis.
References


