Glucose control in the intensive care unit (ICU) may be particularly difficult because of the presenting illness, patient co-morbidities, erratic oral intake, changes in renal or liver function and changes in medication e.g. stopping metformin or commencing steroids.

The monitoring and control of the blood glucose level is vital for all critical care patients. Patients will fall into one of the following categories although there may be some ‘cross-over’ in these:

- Known type 1 diabetics with intercurrent illness
- Known type 2 diabetics with intercurrent illness
- Patients presenting with diabetic ketoacidosis (DKA)
- Patients presenting with hyperosmolar hyperglycaemia (HHS)
- Non-diabetic patients with glycaemic control compromised by acute illness → stress hyperglycaemia
- Drug induced hyperglycaemia e.g. steroids
- Surgery – due to fasting requirements, IV insulin and a glucose infusion is started in type 1 diabetics.

**Insulin therapy may also be required in the following**

- Patients admitted with gestational diabetes

The Joint British Diabetes Societies Guidelines suggest that there is limited evidence for a threshold for starting intravenous insulin in medically unwell patients. However, in certain scenarios such as in the context of ICU, acute myocardial infarction, or acute stroke, it is recommended that initiation of insulin therapy should be considered if the capillary blood glucose (BG) concentration is greater than 10mmol/l.

A consensus target glucose range is 6 to 10mmol/l for patients with diabetes is also recommended, with a range of 4 to 12mmol/l deemed acceptable.

**Goals of treatment**

- Optimise glucose control
- Alleviate symptoms
- Prevent or delay complications
Hyperglycaemia

Hyperglycaemia is a commonly encountered issue in the ICU setting. The presence of hyperglycaemia is associated with increased morbidity and mortality, regardless of the reason for admission e.g. acute myocardial infarction, stroke, surgery, sepsis.

The increased risk of hyperglycaemia is often attributed to diabetes. However mortality rates are higher in patients with new hyperglycaemia and in patients with no history of diabetes than in patients with hyperglycaemia and known diabetes. In patients with pre-existing diabetes mellitus, the presence of hyperglycaemia has not been consistently associated with a worse prognosis.

Hyperglycaemia in a hospitalised patient may reflect poor chronic diabetes control and be similar to preadmission glucose levels for that patient, represent a transient physiologic response to an intercurrent illness (stress hyperglycaemia) or a be a combination of the two. Hyperglycaemia is associated with increased inflammation, susceptibility to infection and organ dysfunction.

Stress hyperglycaemia

Stress hyperglycaemia is a very common feature in the ICU setting and is known to be a marker of critical illness severity.

The pathophysiology of stress hyperglycaemia is thought to reflect temporary insulin resistance coupled with relative insulin deficiency, in that plasma concentrations are inadequate to compensate for hyperglycaemia.

Insulin resistance is driven by the stress response to critical illness initiating an overwhelming activation of pro-inflammatory mediators (e.g. tumour necrosis factor-α, interleukin-6) and counter-regulatory hormone excess (glucagon, cortisol, catecholamines) which lead to excessive hepatic gluconeogenesis and down-regulation of insulin-mediated GLUT-4 glucose transporters.
Understanding type 1 diabetes

Diabetes occurs when the blood glucose is too high. Blood glucose is an important source of energy and is mainly derived from the food that is eaten. Insulin is a hormone made by the pancreas and helps the glucose in the blood to get into the cells and be used for energy. Glucagon is another hormone that works closely with insulin to control blood glucose levels.

Diabetes is an auto-immune condition. In most individuals with type 1 diabetes, the body’s immune system, which normally fights infection, attacks and destroys the cells in the pancreas that make insulin. As a result, the pancreas stops making insulin.

Without insulin, glucose can’t get into the cells and this results in the blood glucose rising above normal. **People with type 1 diabetes need to take insulin every day to stay alive.** This means that their **insulin therapy should never be stopped** i.e. usual subcutaneous therapy or continuous intravenous insulin (if not able to take subcutaneous therapy as normal).

Who is more likely to develop type 1 diabetes?

Type 1 diabetes typically occurs in children and young adults, although it can appear at any age. **10% of people diagnosed with diabetes will have type 1.** Having a parent or a sibling with the disease may increase the chance of developing type 1 diabetes.

What are the symptoms of type 1 diabetes?

Symptoms of type 1 diabetes are serious and usually happen quickly, over a few days to weeks. Symptoms can include:

- Increased thirst and urination
- Increased hunger
- Unexplained weight loss
- Fatigue
- Blurred vision

Sometimes, the **first symptoms of type 1 diabetes** are signs of a life-threatening condition referred to as **diabetic ketoacidosis** (DKA).

Some symptoms of DKA include:

- Breath that smells fruity
- Dry or flushed skin
- Nausea or vomiting
- Stomach pain
- Breathing problems
- Concentration problems/confusion
What health problems can people with type 1 diabetes develop?

Over time, high blood glucose leads to:

- Heart disease
- Stroke
- Kidney disease
- Eye problems
- Dental disease
- Nerve damage
- Foot problems
- Depression
- Sleep apnoea

What is the role of insulin?

Insulin is a key to unlock the door to the cells and allows glucose to enter the cells.
Understanding type 2 diabetes

In type 2 diabetes, the body doesn’t produce enough insulin or doesn’t use insulin well. Too much glucose stays in the blood and not enough reaches the cells.

Who is more likely to develop type 2 diabetes?

Type 2 diabetes can occur at any age. However, it occurs most often in middle-aged and older people. **90% of people with diabetes will have type 2.**

The risk of developing type 2 diabetes increases when aged ≥ 45 years, where there is a family history of diabetes, or in overweight or obese individuals.

Diabetes is more common in people who are African American, Hispanic/Latino, American Indian, Asian American or Pacific Islander.

How are patients with type 2 diabetes managed?

- Lifestyle changes e.g. losing weight, smoking cessation, increasing physical activity, blood pressure control, monitoring cholesterol levels.
- Diabetes medicines e.g. metformin
- Combination of diabetes medicines e.g. oral medication and subcutaneous insulin therapy.
## Summary of differences between Type 1 and Type 2 Diabetes

<table>
<thead>
<tr>
<th>Type 1 Diabetes</th>
<th>Type 2 Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>What is type 1?</strong></td>
<td><strong>What is type 2?</strong></td>
</tr>
<tr>
<td>The body doesn’t produce insulin</td>
<td>Either the body does not produce enough insulin or the body does not react to insulin</td>
</tr>
<tr>
<td><strong>Warning signs</strong></td>
<td><strong>Warning signs</strong></td>
</tr>
<tr>
<td>Increase thirst and urination, constant hunger, weight loss, blurred vision and extreme tiredness</td>
<td>Fatigue, slow wound healing, pain/numbness in hands/feet. Symptoms can be mild and go unnoticed</td>
</tr>
<tr>
<td><strong>Caused by</strong></td>
<td><strong>Caused by</strong></td>
</tr>
<tr>
<td>Genetics, environmental (e.g. viruses) and auto-immune factors e.g. Coeliac Disease is more common in type 1 diabetes. Therefore it cannot be prevented.</td>
<td>Lifestyle, genetics and aging. Therefore it may be prevented with a healthy lifestyle including eating sensibly and exercise.</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td><strong>Treatment</strong></td>
</tr>
</tbody>
</table>

### Summary of insulin production in normal pathology, type1 and type 2 diabetes

Insulin is also indicated for patients with secondary diabetes due to pancreatic insufficiency, including from cystic fibrosis, chronic pancreatitis, or after pancreatectomy.
Gestational diabetes

- Gestational diabetes is a type of diabetes that affects pregnant women, usually during the second or third trimester.
- Women with gestational diabetes don’t have diabetes before their pregnancy, and after giving birth it usually goes away.
- In some women diabetes may be diagnosed in the first trimester, and in these cases the condition most likely existed before pregnancy.
- Gestational diabetes is usually diagnosed through a blood test at 24–28 weeks into pregnancy. It occurs in 3-5% of all pregnancies or approximately

What causes gestational diabetes?

During pregnancy, maternal cells have increased insulin resistance, due to elevated levels of human placental lactogen, progesterone, and oestrogen. This mild increase in insulin resistance is protective, and allows glucose absorption to be prioritised in the foetus, however in some patients, this mild resistance can be combined with insulin resistance, leading to persistent hyperglycaemia

Who is at risk of gestational diabetes?

Women can significantly reduce their risk of developing gestational diabetes by managing their weight, eating healthily and keeping active. Any woman can develop gestational diabetes during pregnancy, but there is an increased risk if the individual:

- Is overweight/obese with a body mass index (BMI) > 30
- Has had a very large baby in a previous pregnancy ≥ 10 lb
- Has had gestational diabetes before.
- Has a family history of diabetes (parent, brother or sister)
- Family origins are south Asian, Chinese, African-Caribbean or Middle Eastern

Symptoms of gestational diabetes

Gestational diabetes doesn't usually cause any symptoms. Most cases are only picked up during the first antenatal appointment at around weeks 8 to 12 of the pregnancy. A screening test or oral glucose tolerance test is normally carried out if the individual has one or more risk factors for gestational diabetes.

Some women may develop the following symptoms if their blood glucose level gets too high:

- Increased thirst
- Frequency of urination
- Dry mouth
- Tiredness

But some of these symptoms are also common during pregnancy and aren’t necessarily a sign of a problem.
How gestational diabetes can affect the pregnancy

Most women with gestational diabetes have otherwise normal pregnancies with healthy babies. However, gestational diabetes can cause problems such as:

- The baby growing larger than usual - this may lead to difficulties during the delivery and increases the likelihood of needing induced labour or a caesarean section.
- Polyhydramnios - too much amniotic fluid in the womb which can cause premature labour or problems at delivery.
- Premature birth - giving birth before the 37th week of pregnancy.
- Pre-eclampsia - a condition that causes high blood pressure during pregnancy and can lead to pregnancy complications if not treated.
- Following birth, the baby may develop low blood glucose or jaundice which may require treatment.
- Having gestational diabetes means that there is an increased risk for developing type 2 diabetes in the future.

Treatment of gestational diabetes

- In women with gestational diabetes, the chances of having problems with the pregnancy can be reduced by controlling blood glucose levels. Blood testing kits are given to monitor glucose levels.
- Blood glucose levels can be reduced by changes in diet and exercise. But the majority of women will need medication as well if changes in diet and exercise don't reduce blood sugar enough. This may be tablets or insulin injections.
- The individual will be more closely monitored during the pregnancy and birth to check for any potential problems. In some cases, earlier delivery may be recommended if there are concerns about the mother’s or the baby's health or if the blood glucose levels haven't been well controlled.
- The HbA1c is a well-validated measure of glycaemia over the previous 8 to 12 weeks and can be translated into an estimated average glucose concentration during this time.
- A1c goals in patients with diabetes should be tailored to the individual, balancing the demonstrated benefits with regard to prevention and delay in micro- and macrovascular complications with the risk of hypoglycaemia.
- A1c should be tested every 3 to 6 months to assess chronic glucose control.
- The HbA1c chart below shows that the target HbA1c for people with Type 1 diabetes is less than 58mmol/mol.
- Very high blood glucose levels will put the patient at risk of developing Diabetic Ketoacidosis (DKA) if left untreated.
- Lowering the HbA1c by just 10mmol/mol reduces the risk of complications by 20%

![HbA1c Chart]

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**The blood Glucose and Ketone monitoring system**

- To perform a test, simply insert a strip into the meter’s port, apply a small drop of blood and wait for the countdown to complete.
- For convenience, the sample may be applied to either the top or end of the test strip. The test will not start until adequate sample has been applied.
- Scanning the barcode label on each test strip foil packet prior to use automatically calibrates the meter and checks the expiry date, helping ensure reliable and accurate test results.
- A warning can also be displayed to an operator whose ID is set to expire in the near future. To renew user access: perform a high and low control test and then re-dock the glucometer.
Control Solutions

Control solutions are used to perform regular quality control checks on the meter to ensure it is functioning correctly.

High & Low Control Testing

- Must be done once every 24 hrs.
- Ensure the meter is positioned horizontal on a level surface for the procedure.
- Opened solutions expire in 90 days (3 months) so label the bottles with the date of opening.
- Replace the correct colour of cap on the bottle.
- Do not scan one test strip foil packet’s barcode and use a test strip from another foil packet. This may cause incorrect results to be generated.
- When a sample for ketones is required, the operator must first perform the quality control testing procedure.

Blood glucose test strips

Blood ketone test strips

These test strips have chemistry to specifically measure β-hydroxybutyrate, the primary ketone produced when a patient is developing ketoacidosis.
Battery compartment

- 2 AA batteries are needed to power the meter.
- If the meter display is blank or completely grey this means that there is no or little battery supply so new batteries need to be installed.

Docking the glucometer into its station

- This needs to be done at least once daily and this is carried out by the night staff after the QC testing procedure has been completed.
- Once the glucometer is correctly installed into the docking station, the upload will commence and the ‘Data Uploading’ message will appear.
- In the event of last upload incomplete: An error has occurred during last data transfer. This screen will appear when you turn on the meter → Place the meter into the docking station to complete the upload. Once the meter has successfully been docked, the warning will disappear.

Blood sampling

- Blood samples used for blood glucose measurement may be taken from arterial or venous blood.
- For venous samples, check that the infusion line does not contain glucose.
- Finger-prick samples are less accurate in hypotensive patients, in patients receiving high-dose vasopressors, peripheral oedema and in patients with hyperosmolar hyperglycaemia state (HHS)
- If the blood glucose result is not as expected or if extremely low i.e. < 4.0 mmol/l or extremely high > 15.0mmol/l, **best practice** is to repeat the sample and send a blood sample in a yellow-top blood tube to the lab.
Exclusions to using the variable rate intravenous insulin infusion

- Diabetic Ketoacidosis (DKA)
- Hyperosmolar Hyperglycaemic State (HHS)
- Paediatrics

Key safety measures when using an intravenous insulin infusion

- A dedicated cannula is used solely for the intravenous insulin infusion.
- No other medication is administered through this cannula other than 10% glucose (if required)
- Bolus medications must never be given through the dedicated cannula.
- A y-connector with 2 non-return (anti-siphon) valves must be used when the 10% glucose infusion is connected: never use 3-way taps.
- An insulin syringe must always be used to measure and prepare insulin for an IV infusion. IV syringes must never be used for insulin administration.
- The term ‘units’ is used in all contexts. Abbreviations such as ‘u’ or ‘iu’ are never used.
- Care must be taken to avoid any prolonged disconnections/interruptions of the IV insulin infusion as the half-life of actrapid is just a few minutes.
- Always record the syringe driver’s identification number on the pump chart. If there is a problem with the syringe driver the identification number is important for the medical physics department to correctly obtain the faulty equipment.

Safety checks that should be taken when the blood glucose does not respond to IV insulin as expected

The following should be carried out if there is no decrease in the blood glucose for 2 or more hourly checks

- Check that the insulin infusion line is securely connected to the venous line.
- Check that the infusion line contains a non-return valve (if 10% glucose infusion is being used).
- Check that the clamps are open on the syringe infusion lines/y-connector lines/central line port.
- Check the venous line: Is it patent? Could there be a problem with the bionector? Is the peripheral or central line kinked?
- Check that the hourly volume infused on the pump chart corresponds with the volume infused on the syringe graduations.
- If the pump has been alarming high resistance the insulin won’t be delivered: check the pressure limit on the syringe driver and increase to 600mmHg as necessary and check the venous line for patency.
- Subcutaneous emphysema could trigger a high resistance alarm: check the central site for any signs of subcutaneous swelling.
- Could this be an infusion pump problem? → stop the infusion pump and complete a medical physics referral form quoting the infusion pump’s identification number.
- Prepare a new 50ml syringe with 50 units actrapid diluted to a total volume of 50ml using 0.9% sodium chloride.
- Document any infusion pump related issues and complete Datix as appropriate.
Blood glucose trigger for initiating an intravenous insulin infusion in the ICU

If the blood glucose is > 10mmol/l for 2 consecutive samples → commence IV insulin infusion

- All Insulin Dependent Diabetics (IDD) will commence on regimen 1 and the regimen increased as needed. This may mean that IDDs may later require regimen 2 or 3 depending on blood glucose results.

- All other patients presenting with a blood glucose > 10mmol/l for 2 consecutive samples will commence on regimen 2 and the regimen increased or decreased as needed. This may mean that some patients may require regimen 1 or 3 depending on blood glucose results.

Some form of glucose load is essential whilst the patient is receiving an IV insulin infusion

- Glucose load can relate to enteral nutrition (EN), total parenteral nutrition (TPN) or a continuous infusion of 10% glucose at a rate of 50ml/hr.

- In the context of EN, the patient must be reliably absorbing a minimum of 40ml/hr with no signs of large gastric aspirates or vomiting/diarrhoea – otherwise a background infusion of 10% glucose will be required.

- If the patient is fluid restricted: reduce the glucose 10% infusion to 15ml/hr or use a higher concentration of glucose e.g. 20%

- Sedation break: if EN is stopped and the patient continues to require the IV insulin infusion → immediately start 10% glucose infusion at a rate of 50ml/hr. This must be done especially for insulin dependent diabetics.

Frequency of blood glucose monitoring and special precautions whilst on IV insulin infusion

- Hourly blood glucose sampling is recommended whilst the patient is receiving an IV insulin infusion: this is a national recommendation.

- Hourly blood glucose sampling is recommended during the first 24 hours of treatment.

- Hourly blood glucose sampling is mandatory whenever regimen 3 is used. It is also recommended that an electronic timer is used to prompt hourly testing.

- If blood glucose samples are maintained within the range of 6.1 to 10.0 mmol/l for 4 consecutive samples and the patient continues on regimen 1 or 2 – then it may be feasible to change to 2-hourly monitoring – provided that there are no signs of vomiting/diarrhoea or change in nutrition plan during this period.

- During the first few hours of commencing haemofiltration: citrate or phoxilium bags don’t contain glucose. This shouldn’t normally be a problem but as a precaution it is advised to monitor the blood glucose closely during the early stages of haemofiltration.

- Clearance of toxins as haemofiltration is initiated: clearance of toxins/inflammatory mediators often leads to reduced vasopressor requirements. This, may in turn, lead to a decrease in the patient’s blood glucose.
Advice for stopping the IV insulin infusion or when to attempt trial off insulin

1. Whenever hypoglycaemia occurs i.e. blood glucose < 4.0 mmol/l
   - Stop the IV insulin infusion immediately and promptly treat hypoglycaemia with a rescue bolus of iv glucose 50% via the central line or a large bore peripheral cannula → inform medical staff.
   - If the patient doesn’t have a central line or a large bore peripheral cannula: the alternative is to administer 75ml of 20% glucose via a small bore peripheral cannula as 50% glucose is more concentrated.
   - Confirm any blood glucose < 4.0 mmol/l with a lab measurement but do not delay treatment of any obvious signs of hypoglycaemia → send lab glucose in yellow top blood tube.
   - Recheck the patient’s blood glucose after 15 minutes.
   - Once the blood glucose is > 4.0 mmol/l → restart the insulin infusion within 20 minutes.
   - Consider changing to an alternative regimen to give less insulin e.g. change from regimen 2 to regimen 1.
   - Reflect and act on any factors that may have contributed to the hypoglycaemic event e.g. EN switched off due to vomiting but oversight in not commencing 10% glucose infusion at 50ml/hr.

2. IDDM patients or patients with pancreatic pathology – a more cautious approach is recommended.
   - Never stop the intravenous insulin infusion just because the blood sugars are within normal range.
   - If the blood glucose has been maintained within the range of 4.0 and 7.0 mmol/l on regimen 1 for a period of 24 hours → have a conversation with medical staff regarding reduced IV insulin requirements as conversion to subcutaneous i.e. long-acting insulin may be appropriate.
   - If medical staff agree to convert to the subcutaneous route – check that the long-acting insulin is given as prescribed 1 hour prior to discontinuation of IV insulin.
   - Refer the patient to the Diabetic Team if this hasn’t already been done.

3. Stopping or attempting trial off in all other patients.
   - If 4 consecutive samples are within the range of 4.0 and 7.0mmol/l on regimen 1 → then stop the IV insulin infusion. Recheck the blood glucose 4 hours after stopping.
   - Recommence the IV insulin infusion when the blood glucose is > 10.0 mmol/l for 2 consecutive recordings or as parameters agreed by medical staff – document these parameters in the ICU chart’s alert box or on the blood glucose monitoring chart.
Measures for avoiding hypoglycaemia and hyperglycaemia whilst the patient is receiving an IV insulin infusion

- Continuous feeding is essential and the patient should be receiving one of the following: (1) 50ml/hr IV infusion of 10% glucose or (2) TPN or (3) the patient is reliably absorbing a minimum of 40ml/hr EN.

- If the patient is not reliably absorbing EN at a minimum rate of 40ml/hr or if there are signs of vomiting and +/- diarrhoea → an IV infusion containing 10% glucose at rate of 50ml/hrs should be commenced until EN is reliably ≥ 40ml/hr.

- Careful attention to frequency of blood glucose monitoring.

- Mindful attention to following the recommended infusion rate. Nursing staff need to check the infusion rate table every time a new blood glucose level is documented. Ensuring the patient is given the correct dose/infusion rate is an important step in avoiding extremes of blood glucose levels – otherwise a drug error has been made.

- If there are concerns that the patient’s blood glucose level is trending towards hypoglycaemia, a rescue bolus of 20ml IV glucose 50% can be given as per protocol. For example, if the blood glucose is 4.1mmol/l, rather than risk the chance of hypoglycaemia, nursing staff can administer this glucose bolus. Nursing staff can also consider switching to a lower regimen as per protocol to give less insulin.

- When the blood glucose is continuing to rise above 11.0 mmol/l on 2 or more consecutive occasions there is a need to change to a higher regimen to give more insulin. Remember insulin is the key to unlocking the cells and allowing glucose to enter the cells. This may mean increasing from regimen 1 to regimen 2 or increasing from regimen 2 to regimen 3. Using higher infusion rates earlier may help achieve better glucose control.

- Strict hourly monitoring is required whilst on regimen 3 and it is recommended that an electronic timer is used as a prompt to maintaining hourly frequency of testing.

- It may also be useful to use the electronic timer when the blood glucose is between the range of 4.0 to 6.0mmol/l to avoid the risk of hypoglycaemia.
Blood glucose regulation and hypoglycaemia

- The level of blood glucose is monitored by the islets of Langerhans in the pancreas.
- The pancreas makes 2 hormones: **insulin** and **glucagon**.
- Insulin is produced in the beta cells and is released when blood glucose levels are high.
- Glucagon is produced by the alpha cells and is released when blood glucose levels are low.
- Other hormones which affect glucose metabolism include **cortisol** (controlled by ACTH) and **adrenaline** (controlled by the medulla oblongata and the sympathetic nervous system).

The physiologic response to hypoglycaemia

Hypoglycaemia is a transient biochemical condition caused by a mismatch of insulin and glucose concentration. The body reacts to low blood glucose levels by defence reactions called counter regulation.

**The autonomic nervous system co-operates with many different hormones:**

- Adrenaline
- Glucagon
- Cortisol
- Growth hormone

**Influence from the liver:**

The liver acts as a store for glucose. Liver cells can release glucose into the blood from glycogen stores when the blood glucose is low. This release of glucose will be impaired where glycogen levels are low. This is most likely in patients who:

- Are malnourished
- Have had repeated episodes of hypoglycaemia
- Have severe liver disease
- Have consumed alcohol to excess

**Autonomic symptoms:**

The symptoms of hypoglycaemia can vary. Firstly there are autonomic symptoms. As the blood glucose level falls, the patient will experience symptoms associated with the activation of the autonomic nervous system and include the following:

- Trembling
- Anxiety
- Palpitations
- Numbness or tingling
- Irritability
- Hunger
- Pale and sweaty
- Feeling vulnerable and afraid.
Neuroglycopenic symptoms:
As the blood glucose falls further, the brain becomes short of glucose. This usually occurs as the blood glucose falls towards 2mmol/l. The following neuroglycopenic symptoms may be present:

- Problems with concentration, co-ordination and weakness.
- Slurred speech.
- Problems with vision.
- A loss of consciousness.
- Seizures.

Signs of hypoglycaemia
Signs of hypoglycaemia may be difficult to detect in critically ill patients and especially in those that are sedated but the following may be demonstrated:

- Sudden hypotension
- Sudden resistance to inotropes
- Sudden tachycardia
- Sudden sweating
- Loss of consciousness, including seizure activity/tremoring.
- If any of the above symptoms are present → check the blood glucose to exclude hypoglycaemia.

Consider the following patient groups that may be at increased risk of hypoglycaemia

- Pre-existing diabetes with poor control/previous history of hypoglycaemia
- Severe liver failure or adrenal failure may precipitate hypoglycaemia (+/- insulin therapy)

Consider the following factors that may contribute to hypoglycaemia
Episodes of hypoglycaemia are associated with the following:

- Deviation from the recommended dose → check the IV insulin infusion rate table when every new blood sugar is obtained. The correct dose i.e. infusion rated must be given to avoid generating drug error (wrong dose of insulin is given)
- Deviation from recommended frequency of monitoring: hourly blood glucose monitoring is recommended especially whenever regimen 3 is used.
- Unintended NG tube displacement/removal or disconnections/interruption in EN or TPN → immediately commence IV infusion of 10% glucose at a rate of 50ml/hr.
- Sedation interruption: if EN is stopped and IV insulin is still required → commence IV infusion of 10% glucose at a rate of 50ml/hr.
- Have there been recent episodes of vomiting/diarrhoea/other losses? e.g. large output from drains.
- Is EN being reliably absorbed? Has there been a change in the patient’s feeding regime?
- Reduction in drug dose e.g. corticosteroids.
- Review all of the above risk factors to avoid a further episode.
Consider the following factors that may contribute to hyperglycaemia

- Check that the arterial transducer fluid bag contains sodium chloride 0.9%
- Insecure connection of the IV insulin line to the venous port/cannula
- Increasing dose of vasoactive infusion e.g. high noradrenaline infusion rates.
- Failure to increase to a higher regimen as per protocol → remember insulin is the key to unlocking the cells.
- Patients with pre-existing diabetes.
- Obese patients/patients with a high body mass index (BMI)
- Acute myocardial infarction
- Stroke
- Intermittent steroid administration
- Total parenteral nutrition (TPN)
- Seizure activity
- Evolving DKA
- Any new drug that has been introduced – check the time of drug administration against the time of random occurrence of hyperglycaemia
- Underlying infection: temperature change, abnormal white cell count, increased CRP.
- Interruption of IV insulin: actrapid insulin has a short half-life of just a few minutes.

Management of blood glucose > 11.0mmol/l for 2 consecutive samples whilst on iv insulin infusion

- Check that the arterial transducer fluid bag contains sodium chloride 0.9%
- Check that the IV insulin line has a secure connection to the venous cannula/port
- When the blood glucose continues to rise above 11.0mmol/l for 2 or more consecutive occasions → change to a higher regimen to give more insulin → remember insulin is the key to unlocking the cells. If the patient is already on regimen 1 this means increasing to regimen 2. If the patient is already on regimen 2 this means increasing to regimen 3.
- Strict hourly blood glucose monitoring is mandatory when regimen 3 is used – use the electronic timer to prompt testing each hour.
- Discuss with medical staff regarding appropriateness for considering higher blood glucose target range. Document any revised target range on the patient’s monitoring chart.
- Patients that are known to be type 1 or type 2 diabetics should be referred to the Diabetic Team as resuming long-acting insulin therapy may help achieve greater glucose control and reduce the need for regimen 3.
Management of blood glucose levels persisting between 14.9 to 19.9 or increasing beyond 20mmol/l

Firstly, there is a need to consider Diabetic Ketoacidosis (DKA) when the blood glucose falls within this range

DKA is indicated by a combination of the following

- Ketonaemia: blood ketones ≥ 3.0mmol/l or significant ketonuria (more than 2+ on standard urine sticks)
- Blood glucose > 11.0mmol/l or known diabetes mellitus
- Bicarbonate (HCO3) < 15.0mmol/l and/or venous pH < 7.3
- Inform medical staff if any of the above is evident.

When the diagnosis of DKA is made the patient should then change to fixed rate insulin infusion and commenced on the DKA Care Pathway

Secondly, there is a need to consider Hyperosmolar Hyperglycaemic State (HHS)

A precise definition for HHS does not exist but it is usually diagnosed by the following characteristic features that differentiate it from other hyperglycaemic states such as DKA:

- Hypovolaemia
- Marked hyperglycaemia ≥ 30mmol/l without significant hyperketonaemia ( < 3mmol/l) or without significant acidosis (pH > 7.3, bicarbonate > 15mmol/l)
- Osmolality usually 320 mosmol/kg or more.

When DKA/HSS is excluded but the blood glucose level persists between 14.9 to 19.9 or increases > 20mmol/l the following should be undertaken

- Confirm that the arterial transducer fluid bag contains 0.9% sodium chloride.
- Check that the IV insulin line is securely connected.
- Inform medical staff
- Reduce the 10% glucose infusion to 25ml/hr. Switch the infusion rate back to 50ml/hr when the blood glucose is ≤ 13.9mmol/l
- If the patient is fluid restricted → reduce the 10% glucose infusion to 15ml/hr or use a higher concentration of glucose as necessary e.g. 20% glucose.
Understanding Diabetic Ketoacidosis

Introduction

- DKA is an acute metabolic complication of diabetes which happens when the body runs out of insulin.
- DKA is most common in type 1 diabetes and often a common factor when first diagnosed with type 1 diabetes.
- However, people with type 2 diabetes that produce very little of their own insulin may also be affected.
- Ketoacidosis is a serious short term complication which can result in unconsciousness or even death if it is not treated quickly.
- Cerebral oedema remains the most common cause of mortality, particularly in young children and adolescents.
- The main causes of mortality in the adult population include severe hypokalaemia, adult respiratory distress syndrome, and co-morbid states such as pneumonia, acute myocardial infarction and sepsis.

DKA pathophysiology

- DKA is a metabolic disorder, which is characterised by hyperglycaemia, ketonaemia and acidosis that is a consequence of absolute or relative insulin deficiency.
- The lack of insulin means the body is unable to utilise glucose. This leads to accumulation of glucose within the blood resulting in hyperglycaemia.
- As glucose cannot be used there is an increase in hepatic glucose production through the breakdown of glycogen stores (glycogenolysis) and increased formation of glucose from other substrates (gluconeogenesis).
- This is coupled with an increase in counter-regulatory hormone release (e.g. cortisol, glucagon, growth hormone), which exacerbates the hyperglycaemia and drives the production of alternative energy sources.
- The lack of utility of glucose leads to the break down of fats (lipolysis) that increases serum free fatty acids. Fatty acids can be used as an alternative energy source through ketogenesis.
- This increase the levels of ketone bodies (acetone, beta-hydroxybutyrate and acetoacetate) within the blood leading to ketonaemia. The main ketone body within DKA is 3-beta-hydroxbutyrate. Ketone bodies are weak acids, which can lead to significant acidosis and severe illness in increasing quantities.
- As DKA progresses, the large amount of plasma glucose leads to osmotic diuresis and profound hypovolaemia that is exacerbated by vomiting. This can lead to major electrolyte derangements, reduced consciousness and eventually death if not managed urgently.
Precipitants

In most cases of DKA, there is an underlying precipitant in patients with a pre-existing diagnosis of diabetes.

It is essential to manage the diabetic emergency, but also to consider the underlying precipitant and manage this appropriately e.g. antibiotics for infection.

The main precipitants of DKA are

- Infection
- Non-compliance – missing insulin injections
- Inappropriate dose alteration
- New diagnosis of diabetes
- Myocardial infarction
- Excessive alcohol consumption

Symptoms of DKA

Diabetic ketoacidosis may itself be the symptom of undiagnosed type 1 diabetes

Typical symptoms of DKA include

- Vomiting
- Dehydration
- An unusual smell on the breath
- Deep laboured breathing (called kussmaul breathing) or hyperventilation
- Rapid heartbeat
- Confusion and disorientation
- Coma

Symptoms of DKA usually evolve over a 24 hour period if blood glucose levels become and remain too high
**Diagnosis of DKA**

**Serious complications of DKA and their treatment**

1. **Hypokalaemia and hyperkalaemia**
   - Hypokalaemia and hyperkalaemia are potentially life threatening conditions during the management of DKA.
   - There is a risk of acute pre-renal kidney injury associated with severe dehydration and it is therefore recommended that NO potassium be prescribed with the initial fluid resuscitation or if the serum potassium level remains above 5.5mmol/l.
   - A normal or even elevated serum potassium concentration may be seen due to the extracellular shift of potassium in acidotic conditions, and this poorly reflects the patient’s total potassium stores. However, potassium will almost fall as the DKA is treated with insulin.

2. **Hypoglycaemia**
   - The blood glucose may fall very rapidly as ketoacidosis is corrected and a common mistake is to allow the blood glucose to drop to hypoglycaemic levels.
   - This may result in a rebound ketosis driven by counter-regulatory hormones. Rebound ketosis lengthens duration of treatment.
   - Severe hypoglycaemia is also associated with cardiac arrhythmias, acute brain injury and death. Once the blood glucose falls to 14.0mmol/l, intravenous 10% glucose needs to be commenced alongside the 0.9% sodium chloride solution to prevent hypoglycaemia.

3. **Cerebral oedema**
   - Cerebral oedema causing symptoms is relatively uncommon in adults during DKA although asymptomatic cerebral oedema may be a common occurrence.
   - The observation that cerebral oedema usually occurs within a few hours of initiation of treatment has led to the speculation that it is iatrogenic. However, this is disputed since subclinical cerebral oedema may be present before treatment is started.
   - The exact cause of the phenomenon is unknown; previous work in animals and humans have suggested that hypo perfusion with subsequent reperfusion may be the mechanism operating.

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**Metabolic treatment targets:**

A number of metabolic treatment target should be achieved during the management of DKA:

1. Blood ketones – falling at least by 0.5 mmol/l/hr
2. Bicarbonate – rising by at least 3.0 mmol/l/hr
3. Blood glucose – falling by at least 3.0 mmol/l/hr
- **Cerebral oedema associated with DKA is more common in children than in adults.** In the UK, previous data suggested that around 70 to 80% of diabetes-related deaths in children under 12 years of age were as a result of cerebral oedema. The UK control study of cerebral oedema complicating DKA showed that children who developed cerebral oedema were more acidotic, and after severity of acidosis was corrected, for, insulin administration in the first hour and volume of fluid administered over the first 4 hours was associated with increased risk. Retrospective evidence has shown increased risk for cerebral oedema after bicarbonate administration.

4. **Pulmonary oedema**
- Pulmonary oedema has only been rarely reported in DKA. As with cerebral oedema, the observation that pulmonary oedema usually occurs within a few hours of initiation of treatment has led to the speculation that the complication is iatrogenic and that rapid infusion of crystalloids over a short period of time increases the likelihood of this complication.
- Elderly patients and those with impaired cardiac function are at particular risk and appropriate non-invasive or invasive monitoring should be considered.

**Hyperosmolar Hyperglycaemic State (HHS)**

**Background:**

- The hyperosmolar hyperglycaemic state (HHS) is a medical emergency.
- HHS is different from diabetic ketoacidosis (DKA) and treatment requires a different approach.
- Previously called hyperosmolar non ketotic (HONK) coma, it was apparent that most of these patients were not comatose but were extremely ill. Changing the name to HHS allows for the fact that some people with severely raised blood glucose may also be mildly ketotic and acidotic.
- Although typically occurring in the elderly HHS is presenting in ever younger adults and teenagers, often as the **initial presentation of type 2 diabetes** mellitus.
- HHS has a higher mortality than DKA and may be complicated by vascular complications e.g. myocardial infarction, stroke or peripheral arterial thrombosis.
- Seizures, cerebral oedema and central pontine myelinolysis (CPM) are uncommon but well-described complications of HHS.
- There is some evidence that rapid changes in osmolality during treatment may be the precipitant of CPM. Cerebral oedema is rare in HHS but it is thought that it may occur from rapid lowering of glucose levels and a rapid drop in osmolality.
- Whilst DKA presents within hours of onset, **HHS comes on over many days**, and consequently the **dehydration and metabolic disturbances are more extreme**.
In HHS, the relative lack of insulin is coupled with a rise in counterregulatory hormones (e.g. cortisol, growth hormone, glucagon) that leads to a profound rise in glucose.

These patients retain a certain level of insulin, which prevents the development of ketosis that is the predominant problem in DKA.

However, the level of insulin is inadequate to prevent profound hyperglycaemia.
The excessive glucose leads to **massive osmotic diuresis** within the kidneys with the **loss of essential electrolytes** such as sodium and potassium. This is because the proximal tubules within the kidneys only have a certain capacity for reabsorption of glucose. Once this is reached, the remaining glucose is passed through the renal nephrons causing diuresis. As water is lost, there is **profound dehydration** and **reduced circulating volume**, resulting in hyperosmolarity and marked hyperglycaemia. Patients with HHS may have up to a 9 litre deficit of water.

The increase in osmolality increases compensatory mechanisms such as release of antidiuretic hormone (ADH) and stimulation of thirst. However, if this cannot compensate for the renal water loss (e.g. elderly patients with co-morbidities) then hypovolaemia develops with progression to acute kidney injury, electrolyte disturbances, hypotension and coma.

**Precipitants of HHS**

A number of underlying conditions are known to precipitate development of HHS, although **most cases represent a new diagnosis of type 2 diabetes mellitus.**

**Common precipitants of HHS include**

- Infection, High-dose steroids
- Myocardial infarction, vomiting.
- Stroke, poor treatment concordance.
Assessment of severity

Patients with HHS are complex and often have multiple co-morbidities so require intensive monitoring. The presence of one or more of the following may indicate the need for admission to a high dependency unit, where the insertion of a central venous catheter to aid assessment of fluid status and immediate senior review by a clinician skilled in the management of HHS should be considered:

- Osmolality greater than 350 mosmol/kg.
- Sodium above 160 mmol/l
- Venous/arterial pH below 7.1
- Hypokalaemia < 3.5 mmol/l or hyperkalaemia > 6 mmol/l on admission
- Glasgow Coma Scale less than 12 or abnormal
- APVU (Alert, Voice, Pain, Unresponsive) scale
- Oxygen saturation below 92% on air (assuming normal baseline respiratory function)
- Systolic BP below 90 mmHg
- Pulse over 100 or below 60 bpm
- Urine output less than 0.5ml/kg/hr
- Serum creatinine > 200 micromol/l
- Hypothermia
- Macrovascular event e.g. myocardial infarction or stroke
- Other serious co-morbidity.

Treatment of HHS

The goals of treatment of HHS are to treat the underlying cause and to gradually and safely:

- Normalise the osmolality
- Replace fluid and electrolyte losses
- Normalise blood glucose

Other goals include prevention of:

- Arterial or venous thrombosis. Vascular complications may occur because the severe dehydration of HHS leads to hypotension and hyperviscosity of the blood, both of which predispose patients to thromboembolic events of the coronary, cerebral, pulmonary and/or mesenteric beds.
- Other potential complications e.g. cerebral oedema/central pontine myelinolysis
- Foot ulceration.
Key principles

- Measure or calculate osmolality (2Na+ + glucose + urea) frequently to monitor treatment response. Generally hourly blood glucose, Na+, K+, urea and calculated osmolality for the first 6 hours then 2 hourly if gradual decline in osmolality is observed. Aim to achieve a gradual decline in osmolality (3 to 8 mosmol/kg/hr).

- Use IV 0.9% sodium chloride solution as the principle fluid to restore circulating volume and reverse dehydration. The target is to achieve positive fluid balance of 2 to 3 litres by 6 hours. Only switch to 0.45% sodium chloride if the osmolality is not declining despite adequate positive fluid balance.

<table>
<thead>
<tr>
<th>Problem</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osmolality declining at appropriate rate but Na+ increasing</td>
<td>Continue with 0.9% sodium chloride</td>
</tr>
<tr>
<td>If plasma Na+ and osmolality increasing or declining at less than 3 mosmol/kg/hr</td>
<td>Check fluid balance – if positive fluid balance is inadequate – increase rate of infusion of 0.9% sodium chloride</td>
</tr>
<tr>
<td>If osmolality increasing and fluid balance adequate</td>
<td>Consider switching to 0.45% sodium chloride at same rate</td>
</tr>
<tr>
<td>If osmolality falling at rate exceeding 8 mosmol/kg/hr</td>
<td>Consider reducing infusion rate of IV fluids and/or insulin infusion if already commenced</td>
</tr>
</tbody>
</table>
- An initial rise in sodium is expected and is not in itself an indication for hypotonic fluids. Thereafter the rate of fall of plasma sodium should not exceed 10mmol/l in 24 hours. If plasma Na+ increasing but osmolality declining at appropriate rate, continue 0.9% sodium chloride.
- The fall in blood glucose should be no more than 5mmol/l/hr. Insulin should only be commenced if there is evidence of significant ketonaemia ( > 1mmol/l) or ketonuria (2+ or more). If so, insulin should be commenced as a fixed rate intravenous insulin infusion (FRIII) at 0.05 units/kg/hr.

<table>
<thead>
<tr>
<th>Problem</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood glucose falling less than 5mmol/l/hr</td>
<td>Check fluid balance</td>
</tr>
<tr>
<td>If positive balance inadequate</td>
<td>Increase rate of infusion of 0.9% sodium chloride</td>
</tr>
<tr>
<td>If positive balance adequate</td>
<td>Commence low dose IV insulin or if already running increase rate to 0.1 unit/kg/hr</td>
</tr>
</tbody>
</table>

Management of patient with HHS from 24 hours to day 3

Expectation – patient should be steadily recovering, beginning to eat and drink, biochemistry back to normal

- Ensure that clinical and biochemical parameters are improving or have normalised
- Continue IV fluids until eating and drinking normally.
- Change to variable rate insulin infusion if not eating and drinking.
- Convert to appropriate subcutaneous regime when biochemically stable.
- Encourage early mobilisation.
- Daily U/Es.
- Remove CVC and urinary catheter when clinically appropriate.
- Assess for signs of fluid overload or cerebral oedema.
- Assess for evidence of continuing sepsis.
- Daily foot checks.
- Continue low molecular weight heparin until day of discharge (consider extended treatment in very high risk patients)
- Ensure patient has been reviewed by the Diabetes Team.
Transitioning patients from Intravenous Insulin to Subcutaneous insulin

The transition from intravenous to subcutaneous long-acting insulin is an important step in the care of a patient, usually occurring when the patient has improved significantly.

Indications that it is safe to transition from IV to SC insulin

- Normal anion gap and resolution of acidosis in DKA
- Not on high-dose vasopressors i.e. ≤ 10 mls/hr of 4mg in 50ml noradrenaline.
- Stable nutrition plan or patient is eating/drinking or fully absorbing enteral feed or receiving TPN.

Converting from VRIII to Subcutaneous Long-acting Insulin in Type 1 or Type 2 Diabetics

- Calculate the intravenous insulin requirements over the previous 24 hours. Next subtract 2/3rds from the total iv insulin requirements and divide by 2 to obtain the total long-acting levemir dose.

- Example for patient prescribed levemir (often prescribed twice daily)
  - Total intravenous insulin for previous 24 hours = 60 units
  - 2/3rds of 60 = 40 units
  - Divide 40 units further by 2 to obtain the total long-acting dose i.e. 20 units.
  - Now assign 2/3rds of the 20 units for the morning dose i.e. 13 units at 0800hrs and the remaining 1/3rd i.e. 7 units is given at 20.00hrs
  - Early referral to the Diabetic Team

- There should always be an overlap between the VRIII and injection of subcutaneous insulin. The long-acting insulin dose is administered one hour prior to intravenous insulin discontinuation.

- The overlap is designed to prevent rebound hyperglycaemia due to the short half-life i.e. <10minutes of short-acting insulin. Premature disconnection is associated with iatrogenic DKA.

- Frequency of blood sugar monitoring
  - A blood glucose level is obtained 2 hours after the long-acting subcutaneous insulin has been given. Avoid collecting the blood glucose level earlier than 2 hours.
  - Thereafter, blood sugars are monitored at a minimum frequency of 2 hours for the next 24hrs.
  - If blood sugars remain stable for 24 hours, have a conversation with medical staff regarding decreasing frequency of monitoring.

- Some patients may redevelop hyperglycaemia and this should be managed as follows
  - In the event of a single glucose level > 17mmol/l → check blood for ketones and if negative, restart the VRIII protocol and commence on regimen 1. Increase to higher regimen as per protocol as appropriate.
  - In the event of 3 consecutive blood glucose levels > 11.0mmol/l → restart the VRIII protocol and commence on regimen 1. Increase to higher regimen as per protocol as appropriate.
  - The long-acting insulin dose should not be withheld as it will help achieve more stable control.
Contingency Planning for Patients receiving long-acting insulin

If theatre is planned
- Reduce the levemir dose by 20%
- Start 10% glucose infusion and maintain at 50ml/hr
- Continue with IV insulin infusion

If nutrition is interrupted and/or nausea and vomiting
- Start 10% glucose infusion and maintain at 50ml/hr.

Sick day rules
- Do not stop the long-acting insulin
- Monitor the blood glucose every 2 hours
- Check blood for ketones if blood sugar > 15mmol/l
- If patient can eat: eat as normally as able.
- If unable to eat, replace meals with fluids. Each of the following contains around 10g carbohydrates:
  - 400ml milk
  - 200ml carton fruit juice
  - 150 to 200ml non-diet fizzy drink
  - 1 scoop ice cream
  - 1 small carton yogurt (120g)
- If patient can drink: aim for 100ml of water or sugar-free fluid every hour if not fluid restricted
- If patient is unable to eat or drink: restart 10% glucose infusion at 50ml/hr
- If patient can eat: eat as normally as able.
- Where possible rest the patient and avoid strenuous exercise or over-exertion.

Discharging from ICU
- If not already done – refer to the Diabetic Team. This needs to be done before the patient is transferred to another ward area.
NICE guidance [NG19] states that every patient with diabetes should have a foot examination within 24 hours of admission. Any new foot ulcer, swelling or discolouration requires urgent referral.

Renal disease also contributes to delayed wound healing and increased potential for subsequent amputation. An eGFR ≤ 15 has been introduced as an additional risk factor for foot ulceration.

All patients with diabetes/on dialysis should have their feet examined and their pressure relief needs assessed daily.

All of the above are recognised in the Diabetic Foot Risk Stratification and Triage System introduced by the Scottish Diabetes Foot Action Group (2016)
**Definition of diabetic foot**

- The term diabetic foot complications encompasses the conditions of diabetic foot ulcer i.e. a full-thickness epithelial defect below/distal to the ankle.

- And includes diabetic foot infections i.e. any soft-tissue or bone infection occurring in the diabetic foot including osteomyelitis.

**Complications of diabetic foot and why it’s important to assess and refer as appropriate**

- Diabetic foot complications, including ulcers and infections, are a common and costly complication of diabetes mellitus.

- The majority of diabetic foot ulcers are caused by repetitive trauma sustained during activity on a structurally abnormal, insensate foot.

- Ulcers act as a port of entry for bacterial infections. Preventing and/or healing ulcers helps prevent infections and thereby minimise limb loss risk. Initial assessment and early management are important strategies for minimising further complications.

- Leg amputation should be avoidable in the majority of cases and is rarely the first-choice option for ambulatory patients.
Assessment, intervention and management is based on the following:

**Check**

For any signs of skin breakdown or discolouration:

- Between the toes including apices
- The soles and the top of the feet including the heels
- Is there an ulcer or gangrene present?
- Touch the Toes Test → is there reduced sensation?
- Is action required?

**Protect**

Use a heel protector if at risk due to:

- Reduced sensation – previous ulcer or amputation
- Bed bound or fragile skin

**Refer**

Ulceration, gangrene, major concerns:

- Refer to the Diabetes Specialist Podiatrist (contact via switchboard)
Perform ‘Touch the Toes’ test:

1. Explain the procedure to the patient and remove any socks and slippers.
2. Ask the patient to close their eyes.
3. Tell the patient you are going to touch their toes.
4. Ask them to tell you which foot you touched, left or right.
5. Using your index finger, gently touch toe no.1 for 2 seconds. The touch must be carried out just once and should be light as a feather and very brief. Do not press, prod or poke.
6. Touch each toe only once – there is no second chance – if it is not felt this must be recorded by circling ‘N’ on the chart.
7. Continue until you have assessed all 6 toes as indicated on the diagram i.e. 1st toe, 3rd toe and 5th toe.
8. If the patient cannot feel 2 or more toes they have reduced sensation and are at risk of a diabetic foot ulcer. Their feet should be checked for ulceration and protected from damage with a heel protector e.g. prevalon boot.
How to use an insulin pen

- Check that the insulin is as prescribed.
- Rapid acting insulin should be clear. Don’t use if it has particles or is discoloured.
- Long acting insulin will appear cloudy. Roll between your hands until the white powder has disappeared. Or you can turn the pen up and down gently a few times.

Remove the cap and then roll the pen between your palms

Wipe the tip of the pen with an alcohol swab. Remove the protective pull tab from the needle and screw the needle on to the pen. Remove the needle cap.

Next step is to clear air from the needle. Looking at the dose window, turn the dosage knob to 1 or 2 units.

Next step is priming. Holding the pen up with the needle pointing upwards, then press the injection button all the way until you see a drop of insulin at the needle tip. The dosage knob should be back at zero after completing this step. The priming procedure is important as it helps to clear the dead space of the pen and ensures that the patient receives the correct and full dose as prescribed.

Next dial the insulin dose. Turn the dosage knob to dial the number of units of insulin you need. Select the injection site.
**Insulin types**

Insulin is made in different ways:

- **Human insulin** – this is synthetic and made in a laboratory to be like insulin made in the body.

- **Analogue insulin** - the insulin molecule is like a string of beads. Scientists have managed to alter the position of some of these beads to create genetically engineered insulin known as analogues. An analogue refers to something that is similar to something else. Therefore “insulin” analogues are analogues that have been designed to mimic the body’s natural pattern of insulin release. These synthetic-made insulins are called analogues of human insulin. However, they have minor structural or amino acid changes that give them desirable characteristics when injected under the skin. Once absorbed, they act on cells like human insulin, but are absorbed from fatty tissue more predictably. There are short-acting and long-acting analogue insulins available.

- **Animal insulin** – this isn’t used much anymore, but some people find that insulin from animals works best for them. It is usually from cow or pig.

**Characteristics of insulin**

Insulin has 3 characteristics:

1. **Onset** is the length of time before insulin reaches the bloodstream and begins lowering blood glucose.

2. **Peaktime** is the time during which insulin is at maximum strength in terms of lowering blood glucose.

3. **Duration** is how long insulin continues to lower blood glucose.

4. Diagram below describes the different types of insulin and how they can affect the recipient. Within each category, there are different formulations that may vary the onset, peak or duration.
**Rapid acting analogues**

- Commonly used rapid acting insulins include: Novarapid, Humalog, Apidra.
- Duration of clinically effective action **4 hours**.
- Can be injected immediately before meals or up to 15 minutes after.
- Fewer hypoglycaemic events.

**Short-acting (soluble) insulins**

- Commonly used short-acting insulins include: Actapid, Humulin S.
- Onset 30 to 45 minutes
- Peak 2 to 4 hours
- Duration 5 to 8 hours
- Used pre-meals combined with intermediate or long-acting background insulin.
Intermediate acting insulins

- Intermediate acting insulins include Insulatard, Humulin I
- Onset of action 2 to 4 hours
- Peak action 4 to 6 hours
- Duration 8 to 14 hours
- Can be used daily/twice daily on its own or in combination with analogue or short acting insulin.
- These insulins tend to be cloudy in appearance and need to be mixed well before use.

Long-acting peakless basal analogues

Lantus and Levemir are currently the only products in this category.

- Lantus duration of action 18 to 24 hours (once daily)
- Levemir duration of action 12 to 18 hours (may be given once or twice daily)
- The long-acting insulins mimic endogenous basal insulin secretion, but their duration of action may last up to 36 hours. They achieve a steady-state level after 2 to 4 days to produce a constant level of insulin.
Sites for injecting insulin

- Lipohypertrophy is when fatty lumps appear on the surface of the skin and is a fairly common side effect of insulin injections.
- Lipohypertrophy can affect insulin absorption. Insulin may not be absorbed so well and this may increase glucose variability.

What is lipohypertrophy?

- Appropriate site rotation: injecting the same site too often can cause skin problems and impair insulin absorption.
- Using a new needle for every injection: even after just 1 or 2 uses, syringes and pens can become dull. Sharp needles cause the least amount of trauma to the skin.
- Regular inspection of the injection sites.

Lipohypertrophy can be avoided by:
Injection technique:

- Insert the needle straight into the fat, at a 90 degree angle to the skin.
- Slowly push the end button all the way down until it stops.
- Hold the needle under the skin for 10 seconds. Remove the needle from the skin and check the injection site. If any medication or blood appears on the skin, apply gentle pressure.
- If using an insulin pen, check to make sure that you see a 0 in the dose window to confirm that the full dose was given.
- If using an insulin pen, remove the needle from the pen and dispose of the needle in a sharps container. If using an insulin syringe – close the needle protector guard and dispose of the needle into a sharps container.

Injection storage:

Insulin vials are not for sharing with others – they are for single patient use only.

Unopened insulin:

- Insulin that is unopened and not in use should be stored in the refrigerator. Unopened insulin stored in the refrigerator is valid until the expiration date shown on the packaging.

Opened insulin:

- When opened, insulin vials/cartridges can be stored at room temperature. In use vials/cartridges should be kept in the drug cupboard by the patient’s bed space – and not stored in the fridge.
- Insulin is very sensitive to sunlight, indoor lighting and to extremely hot or cold temperature.
- In use insulin vials/cartridges are discarded after 28 days.

Opened or punctured vials found in the fridge:

- Dispose of any open vials that are stored in the fridge. OPEN means the insulin cap has been removed and the rubber stopper has been punctured.
- Insulin vials should also be disposed of the following signs are observed: discoloration, frosting, appearance of crystals or clumps in the insulin.