Diabetic Ketoacidosis DKA

Resource Folder

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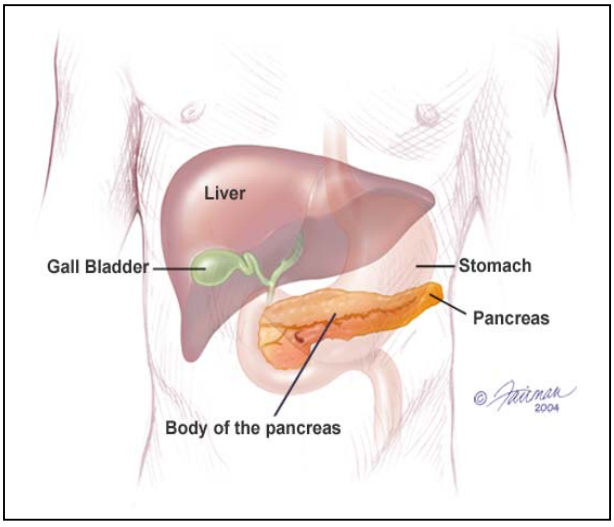
Purpose of resource folder

This resource folder has been compiled to assist nurses, medical staff and allied health professionals in the Intensive Care Unit at Nepean Hospital to understand the pathophysiology, clinical presentation and management of adults with diabetic ketoacidosis. It is for nurses new to the unit, for nurses who have not cared for a patient with diabetic ketoacidosis for some time and for anyone who wishes to expand their knowledge of diabetic ketoacidosis.

There are two parts to this resource folder. The first part is a quick guide to DKA management. In this part rationales for the treatment are not provided, but page numbers point to the relevant sections of the more comprehensive second part.



www.massgeneral.org/cancer/crr/types/gi/illustrations/pancreas.asp

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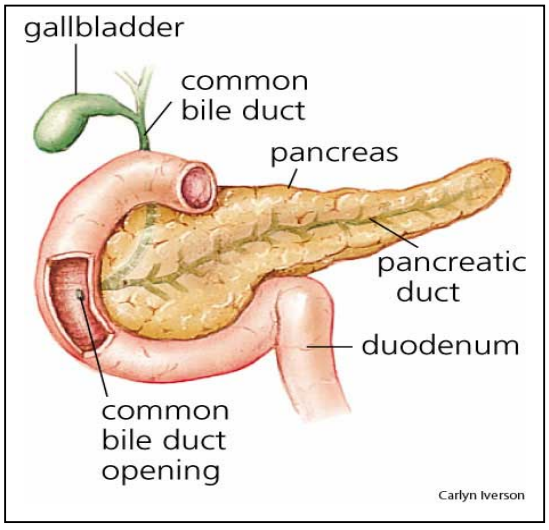


www.yourdictionary.com/images/ahd/jpg/A4pancre.jpg

DKA Quick Guide

Initial medical assessment and history done in ED (BSL > 11 mmol/L, dipstick ketonuria, venous pH < 7.30, bicarb < 18mmol/l). Patients admitted to ICU have moderate or severe DKA. Moderate DKA: HCO3: 10-15 mmol/L, pH 7.1 - 7.25, lethargic but responding appropriately, vomiting, tachycardic, hyperventilating. Severe DKA: HCO3 < 10mmol/L, pH <7.1, shock, reduced level of consciousness.

Principle	Observation, monitoring	Treatment
Primary survey	Assess airway and breathing. Assess circulation (see below) Assess level of consciousness	Consider intubation and ventilation if obtunded and airway is compromised. Insert Guedel's airway if indicated. Apply oxygen via Hudson mask/non-rebreather mask if hypoxic. Consider insertion of nasogastric tube if patient obtunded and vomiting.
Correct dehydration	Monitor hourly: HR, BP, RR, pulse oximetry, Glasgow Coma Score, observe for Kussmaul respiration. 4 hourly temperature. Assess degree of dehydration: neck veins, skin turgor, mucous membranes, tachycardia, hypotension, capillary refill, urine output. Strict fluid balance.	Place patient on cardiac monitor. Insert 2 large cannulas/CVC/PICC. Commence infusion of fluid: Hartmann's solution, Plasmalyte or N/saline 1000ml stat, at rate 1000-1500ml/h in first hour, then 250-1000ml/h depending on degree of dehydration. Adjust rate to achieve normal perfusion, normal CVP, normal MAP and urine output >0.5ml/kg/hr. Take bloods: BSL, ABG or venous blood gas, EUC, anion gap, serum osmolality, FBC, CMP, HbA1C, Blood cultures if Temp> 38.5^{o}C. Keep patient Nil By Mouth, may have ice to suck. Patient may commence oral intake when well enough (even if still a little ketotic). Page 14/21
Correct electrolyte imbalance	Check EUC 2 hourly, later 4 hourly. Check potassium before starting insulin therapy. Check that urine output is established before replacing potassium. Obtain 12-lead ECG to detect potassium-imbalance-related T-wave changes and ischaemia. Continue with cardiac monitoring during potassium replacement. Check iv-site. Check PO_4 and Mg levels regularly	Patient will have total body potassium depletion. If serum K < 3.3mmol/L, potassium replacement is started before commencing insulin therapy. Start potassium replacement as soon as serum K drops below 4.5mmol/L. Replace potassium at 10mmol/hr until serum K is > 4.0mmol/L. Potassium can be added to a burette, or infused separately if the IV resuscitation fluid rate is > 150ml/h (eg piggybacked from a syringe driver). Do not give potassium replacement if the serum K is > 5.0mmol/L. Sodium imbalance will correct itself with fluid resuscitation. Phosphate (as KH_2 PO_4) and magnesium replacement will be needed Page 16/23

Cont. Principle	Observation, monitoring	Treatment
Correct ketoacidosis	Check BSL hourly essentially until the ketones are gone. BSL may have to be checked ½ hourly if rapidly falling. Check for ketones and glucose in urine via dipstick and document positive/negative urine ketones. Check each urine portion if voiding. Check 4 hourly if catheterised. Monitor ABG hourly until pH is > 7.10, then 2 hourly. Check HCO3 on ABG and monitor rise in HCO3/improvement of acidosis. Check serum osmolality. Monitor Glasgow Coma Score as serum osmolality is falling. If Glasgow Coma Score is falling, alert doctor (cerebral oedema).	Prepare insulin infusion 50mls Actrapid in 50mls N/saline. Give bolus of 5 units of insulin intravenously. Commence insulin infusion at 0.1 units/kg/hour or 5 units/hour. **Insulin infusion stays at 5 units/ hour and is not to be reduced or ceased** even if BSL are normal or low! Commence 5% dextrose infusion once BSL < 15mmol/L at rate 80ml/h. If BSL continues to fall, increase 5% dextrose up to 250ml/h but do not reduce insulin. Consider 10% dextrose instead of large volumes of 5% dextrose. At this stage, BSL should be maintained between 10-15mmol/l for several hours (especially in children). Avoid BSL drop > 4mmol/L/hour. Consider insertion of an arterial line, alternatively venous pH is accurate. Consider insertion of urinary catheter. NB: Bicarbonate is not usually given, and should be reserved for QRS widening on the ECG due to hyperkalaemia or pre-arrest Page 23
Look for infection	Check WCC, CRP, Temp. Check microbiology. Chest x-ray, ultrasound, CT as required.	Obtain blood, sputum and urine cultures if the patient is febrile > 38º. Consider antimicrobial therapy. Page 27
Resolving ketosis and acidosis/ endpoint of treatment	Endpoint of treatment is not normoglycaemia, but correction of acidosis and ketosis. Continue BSL, ABG and urinalysis monitoring. Acidosis resolving when pH >7.3, HCO3 >18 mmol/L. Ketosis is resolved when ketones in urine are small or negative.	When ketoacidosis has resolved reduce insulin infusion to 0.05 units/kg/hour or 3.5 ml/hour. Patient may commence oral intake. Insulin infusion continues and subcutaneous split-dose insulin commenced concurrently. S/c and intravenous insulin have to overlap for at least 4 hours to avoid return of ketoacidosis. Involve endocrinologist. Page 27
Prevention of DKA	Evaluate Patient's knowledge about diabetes and management. Evaluate readiness for education.	Commence diabetic education if indicated. Arrange for diabetic educator. Involve Patient and family.

The role of insulin and glucagon

Glucose is the body's major source of energy. It is used to form adenosine tri-phosphate. Eventually all carbohydrates are broken down into glucose. Glucose is the only fuel that the brain can utilise, but it cannot be stored in the brain[10]. Therefore the body attempts to maintain normoglycaemia to provide a constant supply of glucose between meals. Glucose is stored in the liver and muscles in form of glycogen[10]. Glycogen is a polysaccharide made of many glucose molecules (figure 3). In the liver glycogen is easily broken down to glucose (glycogenolysis). In the muscle tissue glycogen is broken down into pyruvic acid or lactic acid in anaerobic conditions, which are then converted to glucose in the liver[10]. Insulin and glucagon are the chief hormones that control carbohydrate metabolism. Insulin is a powerful hypoglycaemic agent, whereas glucagon, its counterpart, is a hyperglycaemic agent (figure 6).

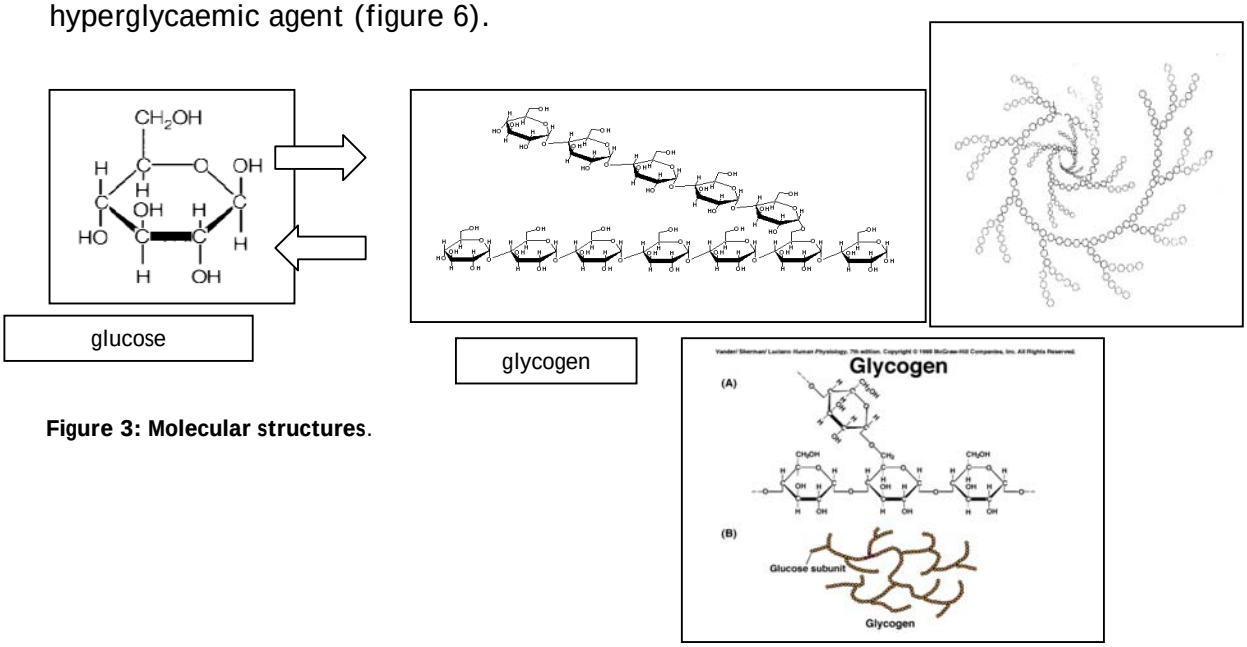


Figure 3: Molecular structures.

Glucagon, a 29-amino-acid polypeptide, is produced by the alpha-cells of the islets of Langerhans in the pancreas[10] (figure 4). Its main action takes place in the liver, where it promotes the breakdown of glycogen into glucose (glycogenolysis), the formation of new glucose from non-carbohydrate sources such as amino acids, fatty acids and lactic acid (gluconeogenesis), and the release of glucose into the bloodstream by the liver cells (hepatocytes). In adipose tissue it stimulates fat breakdown into

fatty acids and glycerol. Fatty acids are then metabolised in the liver and glycerol is used to form glucose[10]. All actions of glucagon are aimed at raising blood sugar levels. It helps to protect the body from hypoglycaemia.

The actions of insulin, on the other hand, are aimed at lowering blood glucose level. Insulin, a small 51-amino-acid protein, is produced in the beta cells of the islets of Langerhans in the pancreas[10] (figure 4). Insulin facilitates the passage of glucose from the bloodstream into the cells. Glucose can only cross the cell membrane when insulin binds with a receptor on the cell membrane. In the cell glucose is oxidised for energy. In the liver and muscle tissue insulin accelerates the conversion of glucose into glycogen (glycogenesis) and storage of glycogen (figure 5). Insulin slows the conversion of glycogen to glucose (glycogenolysis) and inhibits gluconeogenesis[8]. The net effect is that, in the presence of insulin, less glucose is released from the liver. Insulin also plays a role in fat and protein metabolism. It facilitates the conversion of fatty acids into fat (lipogenesis) and storage of fat in adipose tissue[10]. The breakdown of adipose tissue and the conversion of fat to ketone bodies are inhibited by insulin. Insulin stimulates protein synthesis and inhibits protein catabolism.

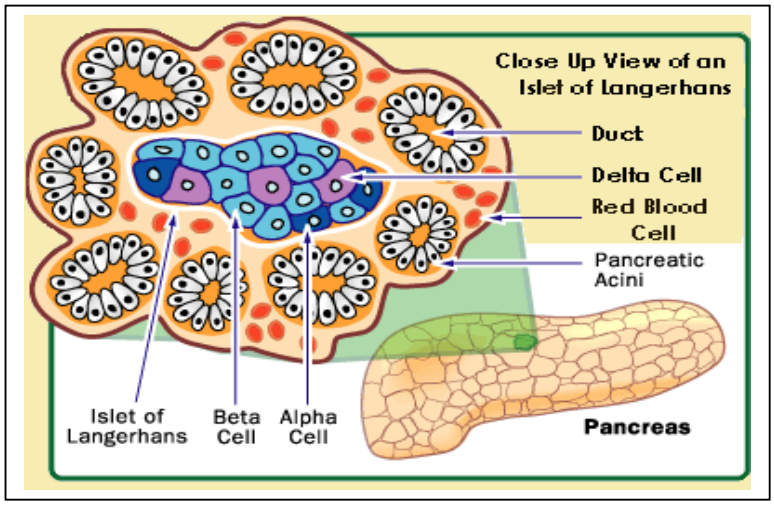


Figure 4: Islets of Langerhans.
www.rajeun.net/diabetes-pancreas.gif.

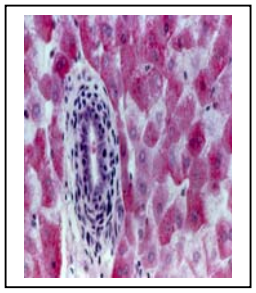


Figure 5: Glycogen in the liver.
www.oregonstate.edu/~hanba/Projector%20Slides/Liver%20Glycogen-2.jpg

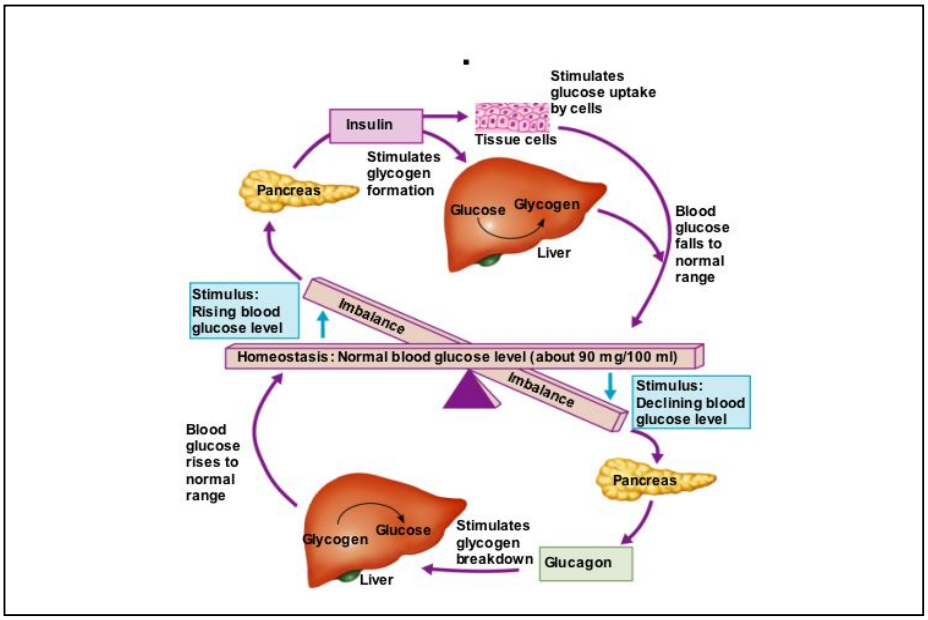


Figure 6: How insulin and glucagon control blood glucose homeostasis.
(90-100mg/dL is 4.9-5.5 mmol/L).

Diabetes mellitus: an overview

Diabetes mellitus is a chronic disease caused by the imbalance of insulin supply and demand. It leads to hyperglycaemia and abnormal carbohydrate, fat and protein metabolism.

Type I diabetes mellitus is caused by an autoimmune destruction of beta cells in the pancreas, which leads to an absolute insulin deficiency[12]. The initial presentation is characterised by sudden onset of hyperglycaemia, often with ketoacidosis, and occurs most often in children and younger adults. It is likely to develop through the following stages: genetic predisposition, environmental trigger/ viral infection/ stress, active autoimmunity, progressive beta-cell destruction, and clinical presentation of diabetes mellitus. Symptoms at the initial presentation of type 1 diabetes include polyuria, polydipsia, polyphagia, weight loss, and feeling unwell. Glucosuria is usually present. Treatment of type I diabetes entails a regimen of insulin injections and diet.

Type II diabetes mellitus has a gradual onset of hyperglycaemia and is the result of the development of resistance to the action of insulin and

insufficient insulin secretion[12]. The type II diabetes syndrome is characterised by obesity, hypertension, hyperlipidaemia and hyperglycaemia and mostly occurs in older adults. Genetic predisposition plays a role in the development of obesity and hypertension[1]. Type II diabetes can be managed with diet and lifestyle changes alone, or with diet and oral hypoglycaemic agents, or with diet, oral hypoglycaemic agents and insulin.

Long-term complications of diabetes

Chronic elevations of blood glucose can lead to diabetic nephropathy, diabetic neuropathy, ulcers and ischaemic damage in the feet, diabetic retinopathy and blindness, accelerated atherosclerosis, coronary artery disease, impaired immune function with increased infection and delayed wound healing. Diabetic nephropathy refers to the progressive microangiopathy (small blood vessel disease) involving sclerosis of glomeruli, nephrons and tubules (figure 7), leading to micro- and macro-albuminuria, decreased glomerular filtration rate, hypertension and eventually to renal failure[7]. In diabetic neuropathy, microangiopathy causes insufficient diffusion of nutrients and oxygen to sensory, autonomic and/ or motor nerve fibres, leading to damage in a single nerve or many nerves. Symptoms include sensory loss, tingling and burning, and weakness, often in a glove-and-stocking distribution[4].

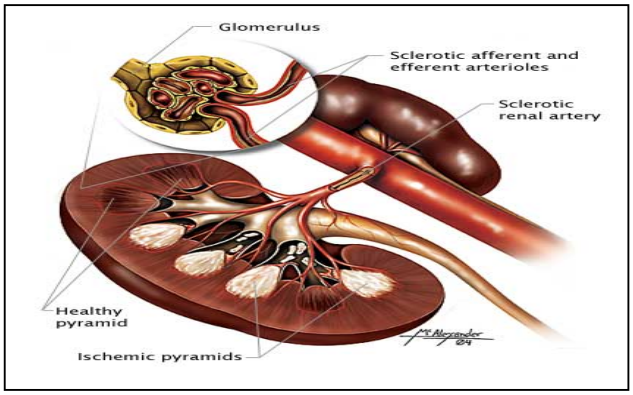


Figure 7: Diabetic nephropathy, showing sclerotic and ischaemic changes.
www.wildiris3.securesites.net/cms_prod/files/course/39nephropathy.jpg.

Epidemiology of diabetes

Diabetes is estimated to affect almost 1 million Australians aged 25 and over.

30% of Aborigines and Torres Strait Islanders have diabetes.

7% of non-indigenous people have diabetes.

194 million people worldwide have diabetes.

333 million people may have diabetes by 2025.

The annual cost to the Australian nation for diabetes exceeds $ 1.2 billion.

The annual cost for each individual with type II diabetes without complications is $4,025.

The annual cost for a diabetic with macro-vascular or micro-vascular complications is $9,645.

(www.health.gov.au/internet/wcms/publishing.nsf/content/pq-diabetes-stats. June 2006)

Incidence of DKA in Australia varies according to age and gender: 4.6-13.4 per 1000 diabetic cases/year[5].

Nepean ICU had 25 DKA admissions in 2005 and 18 DKA admissions in 2006 (Nepean Hospital, APACHE II Diagnosis data, ICU admissions, 23 January 2007).

Hyperglycaemic emergencies

Hyperglycaemic emergencies derive from an absolute or relative insulin deficiency[6] that leads to insufficient glucose uptake into the cells and concurrent breakdown of glycogen stores and new formation of glucose in the liver. Hyperglycaemic emergencies are life-threatening, and require immediate treatment in hospital, often with an admission to the Intensive Care Unit.

Hyperglycaemic hyperosmolar state (HHS) is mainly a complication of type II diabetes with minimal lipolysis (the breakdown of triglycerides into glycerol and fatty acids) and ketoacidosis. It has a slower onset than diabetic ketoacidosis, and mortality rate ranges from 10-35%. It is characterised by marked hyerglycaemia, hyperosmolality and severe dehydration[1].

Diabetic ketoacidosis (DKA) is mainly a complication of type I diabetes but incidence in type II diabetes are rising. DKA is characterised by hyperglycaemia, hyperosmolality, ketoacidosis and volume depletion. The mortality is 2-5% [6]. This resource folder deals with diabetic ketoacidosis.

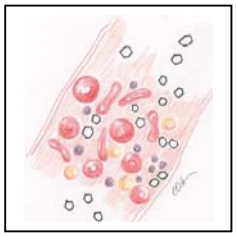
Diabetic Ketoacidosis DKA

Etiology and precipitating factors

DKA, primarily a type I diabetes complication, occurs mainly in younger adults and people in their teenage years. DKA can develop in a new-onset type I diabetic or a diabetic who misses insulin doses[9]. Often it occurs with poor insulin compliance and lack of knowledge about managing insulin administration in acute illness. The patient who is feeling unwell may believe that he/she does not need insulin while not eating.

Precipitating factors include medications and drugs that affect carbohydrate metabolism such as corticosteroids, thiazides, loop diuretics, sympathomimetics, anti-hypertensives, anti-histamines, tricyclic antidepressants, alcohol, cocaine and ecstasy[1]. Often DKA develops because of an acute illness or infection such as pneumonia or urinary tract infection[6]. Pregnancy, gastroenteritis, trauma, burns, surgery, sepsis, pancreatitis, stroke and silent myocardial infarction can also provoke DKA[1]. The patient fails to meet the increased insulin demand when these physical stressors occur. The stressors provoke an excessive release of counterregulatory hormones such as glucagon, catecholamines, cortisol and growth hormone and the elevation of pro-inflammatory cytokines[6]. In this 'fight-or-flight' stress response energy stores from fat, protein and glycogen are mobilised and new glucose is produced.

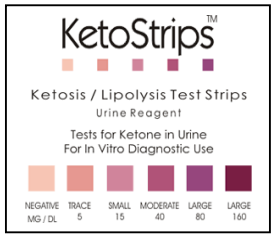
The 4 main characteristics of DKA



Hyperglycaemia

Insulin deficiency leads to accumulation of glucose in the blood as glucose cannot enter the cells. Normally insulin suppresses glucose production and lipolysis in the liver. Therefore insulin deficiency leads to hepatic glucose overproduction. Counter-regulatory hormones, glucagon, cortisol and catecholamines increase the glucose level through gluconeogenesis (formation of new glucose) and glycogenolysis (breakdown of complex glycogen into simple glucose). The process of gluconeogenesis is driven by the high availability of all the precursors: amino acids (from protein breakdown), lactate (from muscle glycogenolysis), and glycerol (from increased lipolysis).

It is thought that when serum osmolality is high, even less insulin is produced and insulin resistance increases[1]. These processes make it even more difficult for tissues to take up glucose. As a result hyperglycaemia worsens.



Ketosis and acidosis

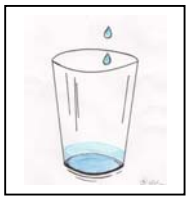
Insulin deficiency and elevated counter-regulatory hormones promote lipolysis in adipose tissue and inhibit lipogenesis, leading to increased release of fatty acids and glycerol. The liver is stimulated by glucagon to oxidise free fatty acids to ketone bodies such as beta-hydroxybutyrate and acetoacetate. The production of ketone bodies exceeds the ability of tissues to utilise them, resulting in ketonaemia[6]. Ketone bodies fully dissociate into

ketone anions and hydrogen ions. The body attempts to maintain extracellular pH by binding the hydrogen ions with bicarbonate ions thus depleting its alkali reserves[8]. Acidosis develops.

The respiratory system compensates for acidosis by increasing the depth and rate of breathing to exhale more carbon dioxide. This is called Kussmaul respiration. The breath has a fruity, acetone-like odour ("nail polish remover"), because the acetone ketones are exhaled.

The kidneys excrete ketone bodies (ketonuria), and large amounts of glucose spill over into the urine leading to osmotic diuresis, dehydration and haemoconcentration. This in turn causes tissue ischaemia and increased lactic acid production that worsens the acidosis[1]. Increased acidosis causes enzymes to become ineffective and metabolism decelerates. Even fewer ketone bodies are metabolised and acidosis worsens.

Acidosis can cause hypotension due to its vasodilating effect and negative effect on heart contractility[11].



Dehydration

Hyperglycaemia raises extracellular fluid osmolality. Water is drawn from the cell into the extracellular compartment and intracellular dehydration follows. Hyperosmolality is the main contributor to altered mental status, which can lead to coma[1]. Cellular dehydration and acid overload can also affect mental status.

The development of total body dehydration and sodium depletion is the result of increased urinary output and electrolyte losses. With marked hyperglycaemia the serum glucose threshold for glucose reabsorption in the kidneys of 10mmol/L is exceeded, and glucose is excreted in urine (glucosuria[6]). Glucosuria causes obligatory losses of water and electrolytes such as sodium, potassium, magnesium, calcium and phosphate (osmotic diuresis). Excretion of ketone anions also contributes to osmotic diuresis[6], and causes additional obligatory losses of urinary cations (sodium, potassium

and ammonium salts). Insulin deficiency per se might also contribute to renal losses of water and electrolytes, because insulin stimulates salt and water reabsorption by the nephron and phosphate reabsorption in the proximal tubule.

Acidosis can cause nausea and vomiting and this leads to further fluid loss. There is increased insensible fluid loss through Kussmaul respiration. Severe dehydration reduces renal blood flow and decreases glomerular filtration[8], and may progress to hypovolaemic shock.

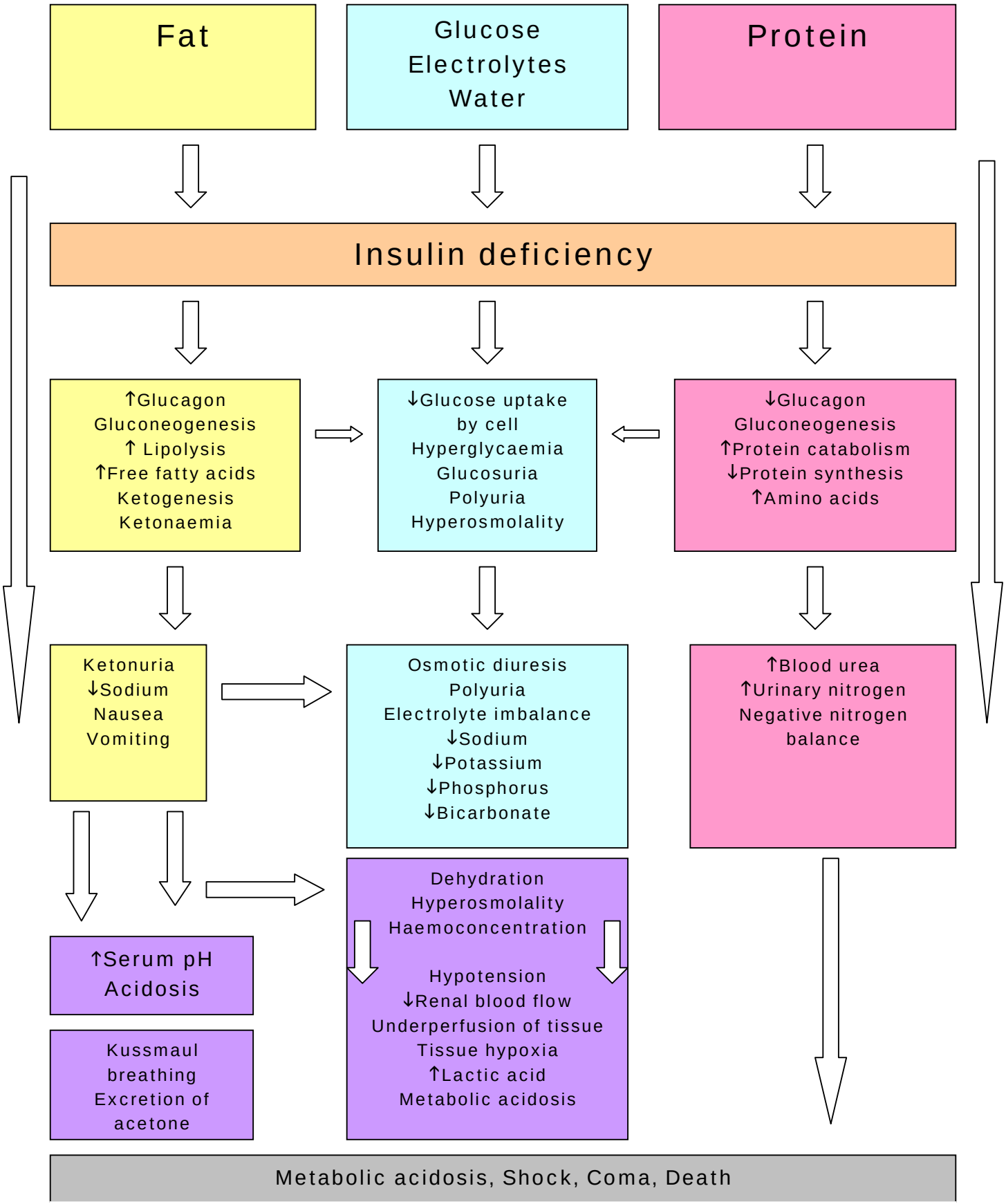
Electrolyte imbalance

Potassium is the electrolyte that is most affected in DKA. Acidosis causes hydrogen ions to move from the extracellular fluid into the intracellular space. Hydrogen movement into the cell promotes movement of potassium out of the cell into the extracellular compartment (including the intravascular space). Severe intracellular potassium depletion follows. As the liver is stimulated by the counterregulatory hormones to break down protein, nitrogen accumulates, causing a rise in blood urea nitrogen. Proteolysis leads to further loss of intracellular potassium and increases intravascular potassium[1].

The body excretes this mobilized potassium in urine by osmotic diuresis, and loses additional potassium through vomiting. Serum potassium readings can be normal or high, but this is misleading, because there is an intracellular and total body potassium deficit. Sodium, phosphate, chloride and bicarbonate are also lost in urine and vomitus.

Sodium levels are "lowered" (diluted) by the movement of water from the intracellular to the extracellular space in response to hyperglycaemia. A formula that 'corrects' the sodium level is:

Corrected Na = measured Na + 0.3(glucose – 5.5).



Pathophysiology of DKA adapted from Urden: Thelan's Critical Care Nursing: Diagnosis and Management. 5th ed. Cited in Nursing Consult. www.nursingconsult.com/das/book/body/64980806-2...2006.

Clinical presentation

- Feeling unwell for a short period, often less than 24 hours[6]
- Polydipsia and increased thirst
- Polyuria/ nocturia
- Polyphagia
- Weight loss
- Nausea and vomiting, vomitus can have coffee-ground colour due to haemorrhagic gastritis[6]
- Abdominal pain, due to dehydration and acidosis[1]
- Weakness
- Neurologic signs: restlessness, agitation, lethargy and drowsiness, coma. Increased osmolality is the main factor that contributes to altered mental status[1] (figure 9).
- Visual disturbances due to hyperglycaemia
- Deep and rapid breathing, known as Kussmaul breathing, may have acetone odour on breath.
- Signs of dehydration due to fluid loss through polyuria, vomiting and breathing: reduced skin turgor, dry mucous membranes
- Signs of hypovolaemia: tachycardia, hypotension, postural hypotension due to fluid loss over 3 litres[1].
- Mild hypothermia due to acidosis-induced peripheral vasodilation, warm dry skin. Fevers are rare despite infection. Severe hypothermia is a poor prognostic sign[9].

The nurse should have a high suspicion of DKA when a patient presents with unresponsiveness and hyperventilation. It could be first known onset of diabetes mellitus.

Laboratory findings

- Initial diagnosis of DKA: serum glucose level >11mmol/L, acidaemia, and presence of ketones in urine[6]
- Blood sugar level (BSL) hourly measures
  Initial blood glucose levels can be as high as 30-45mmol/L.
- Arterial blood gas (ABG) to measure degree of acidosis and degree of compensatory hypocarbia (PaCo2). Initially arterial pH, but following pH can be venous as venous pH correlates well with arterial pH[3] (venous pH is usually 0.03 units lower than arterial pH). When pH drops below 7.2 hyperventilation and hypocarbia are more pronounced[8]. Serum bicarbonate <18mmol/L, in severe DKA <15 mmol/L[6]
- Urinalysis (U/a) dipstick: testing for positive urine ketones (ketonuria) and glucose (glucosuria)

  Discussion point: Urine ketone test based on the nitoprusside reaction measures acetoacetate and acetone but not beta-hydroxybutyrate (B-OHB). U/a is unreliable as a marker for resolving of acidosis because ketone bodies can still be detected in urine long after ketoacidosis is resolved. Urine reflects changes over previous several hours, but not current state. Directly measured B-OHB is the preferred test for ketonaemia as B-OHB is the strongest and most prevalent acid in DKA (5). This test however, cannot be performed at Nepean Hospital. Capillary blood ketone testing would be a more reliable marker for ketoacidosis as it reflects real time (5).
- Urea and creatinine, indicators of renal function. Normal value for urea: 2.5-6.4mmol/l. Normal value for creatinine: 60-120μmol/l. Reduced renal blood flow results in decreased glomerular filtration rate and elevated urea and creatinine levels.
- Blood urea also elevated through protein catabolism
- Serum electrolytes:
- Potassium (particularly important!). Normal values: 3.5-5.0mmol/L. Serum potassium elevated due to extracellular shift of potassium caused by insulin deficiency and acidosis. Later, low serum potassium reflects the total body potassium depletion.

- Sodium (normal value: 136-145mmol/L) can be high due to osmotic diuresis and excessive water loss. It can be low due to increased amount of extracellular water in hyperosmolar state.
- Magnesium and phosphate: Magnesium (normal value: 0.07-1.10mmol/L) and phosphate (normal value: 0.80-1.50mmol/L) can be low due to loss in urine.
- Elevated anion gap [calculated as (sodium + potassium) minus (chloride + bicarbonate)]. Normal value <12mmol/L.

  Elevated anion gap is an indicator for metabolic acidosis. Elevated anion gap results from accumulation of keto-acid anions (mild anion gap >10mmol/L, moderate 12mmol/L, severe 16mmol/L). The accumulation of keto-acid-anions is not measured directly in laboratory. The amount of total cations (sodium and potassium) and most anions (chloride and bicarbonate) are measured. The excess of cations over anions provides a clue about the amount of unmeasured anions, such as keto-acids anions. This is called anion gap (8).
- Serum osmolality (normally 280-295 mosm/L) is elevated in DKA. Hyperosmolality is the main factor for decreased consciousness[1] (figure 9).
- Full blood count (FBC): Mild leucocytosis of 10,000-20,000 attributed to dehydration and stress. Severe leucocytosis >30,000 suggests infection[1].
- Serum amylase, serum lipase and liver enzymes to detect pancreatitis.
- Blood, urine and sputum cultures to detect source of infection.
- Cardiac enzymes to detect myocardial infarction
- Haemoglobin A1C, an indicator for quality of diabetes control, or new-onset diabetes[9]

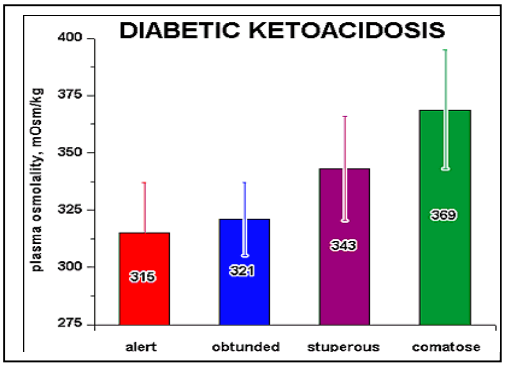


Figure 9: **Relationship between serum osmolality and level of consciousness**
www.endotext.org/diabetes/diabetes11/figures11/figure1.gif

Other Investigations

- 12-lead ECG to detect ischaemia and changes due to hyperkalaemia or hypokalaemia[3]
- Chest x-ray to detect pneumonia
- CT scan to detect neurological changes (eg if stroke is suspected)

Classification of DKA (adapted from 6 and 14)

	Mild	Moderate	Severe
Serum bicarbonate mmol/L	15-18	10-15	<10
Arterial pH	7.25-7.30	7.1-7.25	< 7.1
Anion gap	> 10	>12	>12
Serum glucose	>11	>11	>11
Mental status	alert	alert/drowsy	coma
Signs	clinically well	tachycardia	reduced periph pulses, tachycardia, shock

If the patient presents with a mild form of DKA, the patient can be managed on the ward. If the patient has moderate or severe form of DKA, admission to ICU is necessary.

Management of DKA

Oxygenation/ventilation

Airway and breathing remain the first priority. If the patient presents with reduced consciousness/coma (GCS<8) consider intubation and ventilation[14]. In obtunded patients airway can be temporarily maintained by insertion of Guedel's airway. Apply oxygen via Hudson mask or non-rebreather mask if indicated. Insert nasogastric tube and leave on free drainage if the patient is drowsy and vomiting or if patient has recurrent vomiting. Airway, breathing and level of consciousness have to be monitored throughout the treatment of DKA.

Fluid replacement

Circulation is the second priority. DKA patients are severely dehydrated and can be in hypovolaemic shock. Fluid replacement should be initiated immediately. Fluid resuscitation reduces hyperglycaemia, hyperosmolality, and counterregulatory hormones, particularly in the first few hours, thus reducing the resistance to insulin. Insulin therapy is therefore most effective when it is preceded by initial fluid and electrolyte replacement.

Two large-bore intravenous cannulas or a central venous catheter (such as PICC) should be inserted. The total body water deficit can be 10% of the body weight and more than 6 litres of fluid may have to be replaced. Immediate fluid resuscitation aims to restore intravascular volume and improve renal perfusion with crystalloid solutions, although colloids can be used if the patient is in hypovolaemic shock[2]. N/saline (0.9%NaCl) is most appropriate initially. Hartman's solution or Plasmalyte are also suitable (they have the advantage of providing a bicarbonate precursor). Exclusive use of normal saline often contributes to a hyperchloraemic acidosis some days later. If the patient is not cardiac-compromised, the initial bolus of fluid is 15-20ml/kg over an hour, which is equivalent to 1-1.5L in the first hour, and then 4-10ml/kg/hour for the following hours[1]. Ideally 50% of the total body water deficit should be replaced within the first eight hours and the other 50% within the following 24 hours. As a guide, serum osmolality should decrease by less than 3mOsm/L/hour. Careful monitoring of haemodynamic status (in unstable patients every 15 minutes), renal function, mental status and meticulous fluid balance are necessary to avoid fluid overload.

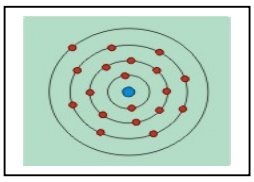
Intravenous fluids should be reduced as soon as the osmotic diuresis resolves, and urinary volumes decrease. Aggressive reduction of blood glucose and high rates of fluid resuscitation are associated with cerebral

oedema in 1% of children and adolescents. One recommendation limits fluid resuscitation in the first 4 hours of therapy to <50ml/kg isotonic solution. Fluid resuscitation also should be less aggressive in patients with heart failure.

Electrolyte replacement

Dehydration and osmotic diuresis cause enormous electrolyte shifts in cells and serum.

Potassium: Potassium is the major intracellular positive ion, responsible for maintenance of the electro-potential gradient of the cell membrane[15]. Hyperkalaemia may result from reduced renal function, but the patient is more likely to have total body potassium depletion[9]. Intracellular potassium depletion results from a lack of insulin, intracellular dehydration, acidosis and hydrogen ion shift. Vomiting can further cause potassium depletion. During DKA management insulin therapy, correction of acidosis and fluid resuscitation will decrease serum potassium levels. Potassium shifts into the cells with the passage of glucose. Therefore the potassium level has to be checked before starting insulin therapy[6]. The serum potassium level can indicate the severity of the potassium deficit. Serum potassium of 3mmol/L in an average adult suggests a deficit of 200mmol, serum potassium of 2.5mmol/L suggests a deficit of 300mmol and serum potassium of 2mmol/L suggests a deficit of 400mmol[15]. If potassium is <3.3mmol/L it has to be replaced before commencing insulin infusion[11]. Urinary output has to be confirmed prior to potassium replacement.



The potassium is replaced at 10mmol/hr until serum potassium is > 4.0mmol/l. The potassium can be added to a burette, or infused separately if the IV resuscitation fluid rate is > 150ml/h (eg piggybacked from a syringe driver). Potassium should not be replaced if the level is

>5.0mmol/L[6]. Serum potassium is monitored every 2 to 4 hours. During potassium replacement the patient has to be placed on a cardiac monitor for detection of arrhythmias and the iv-cannula site has to be inspected regularly to avoid tissue damage.

Sodium: Early "hyponatraemia" in DKA does not usually require specific treatment, it is an artefact arising from dilution by the hyperglycaemia-induced water shifts. As excess water moves out of the extracellular space with the correction of hyperglycaemia, the sodium level will return to normal.

Phosphate: Total body phosphate can be low due to loss from osmotic diuresis. Phosphate will move into cells with glucose and potassium once insulin therapy has started, and phosphate replacement is likely to be required if the serum levels are in the low end of the normal range, or just low. Hypophosphataemia of < 0.3mmol/l can cause respiratory muscle weakness, cardiac muscle weakness, decreased 2,3-DPG and a right-shift of the oxygen-haemoglobin-dissociation curve[13]. Phosphate can be given in the form of KH_2PO_4 at a rate of 10mmol/hr. The usual dose in 24 hours is 30-60mmol for an adult.

Insulin therapy

Insulin therapy is crucial to DKA management. It facilitates glucose uptake into the cell, correction of cell metabolism and acidosis. Insulin is initially given as an intravenous bolus of 0.1units/kg or a bolus of 5 or 10 units. Then a continuous insulin infusion of 50 units of Actrapid in 50ml N/Saline is commenced. The infusion rate is 5 units/hour, or 0.05-0.1 units/kg/hour for children[16]. The blood glucose level must be checked hourly until urinary ketones are gone, and than can be checked less frequently (2nd hrly and later 4th hrly).

Initially blood glucose can be as high as 30-45mmol/L. Insulin infusion should slowly reduce blood glucose level. The rate at which serum glucose falls should not exceed 4mmol/L per hour. This is important because if it falls too rapidly cerebral oedema may result through the influx of water into the brain cells[1]. This is because the intracellular change in osmolality lags behind the extracellular changes in osmolality. Cerebral oedema is rare in adults with DKA, and is most likely to occur in children with newly diagnosed diabetes. A slow normalisation of osmolality is desired. The patient, while acidotic, is kept nil by mouth[17] to maximize the speed at which ketoacidosis can resolve (food might slow resolution).

Once BSL has fallen <15mmol/L, a 5%-dextrose infusion is started at 80 ml/hour to slow the correction of the hyperglycaemia and prevent hypoglycaemia[16]. The BSL can be kept at 12-15mmol/l for several hours while the hyperosmolality and mental state improve. The dextrose infusion is titrated to the BSL (not vice versa!) and can be increased up to 250ml/hour if BSL is low. Alternatively 10% dextrose can be used instead of 5% dextrose if BSL falls too rapidly. The most important thing to remember is that the **insulin infusion rate stays constant and insulin infusion should never be discontinued** even if BSL becomes normal or low. The principle of titrating glucose infusion to the BSL and not titrating insulin to BSL, as we would usually do it, may be a difficult concept to grasp, but it is one of the major aspects in DKA management and cannot be emphasised enough. Insulin therapy suppresses fat catabolism and counteracts further ketone production. It facilitates metabolism of ketone acids, thus the correction of acidosis. If insulin were reduced or ceased prematurely, ketoacidosis would return and the patient's condition would deteriorate. Decreasing the insulin infusion rate should only be considered once ketoacidosis has resolved, and urinary ketones have disappeared. This is discussed later. Aim ultimately for a BSL of 6-10mmol/L.

!!

In summary the patient has three concurrent infusions: rehydration fluid, insulin infusion and dextrose infusion.

The use of bicarbonate

In acidosis myocardial contractility and catecholamine function are impaired. Multiple studies, however, have shown that the treatment of metabolic acidosis with sodium bicarbonate is not helpful[1]. Sodium bicarbonate infusion can cause paradoxical central nervous system acidosis, hypokalaemia and tissue hypoxia through decreased tissue oxygen uptake and a left-shift of the oxy-haemoglobin-dissociation curve. Bicarbonate is not routinely recommended if the initial pH is 6.9 or more, because the acidosis will correct with insulin therapy. Bicarbonate is regenerated as the ketone anions are metabolised. However, one clear indication for bicarbonate therapy is life-threatening hyperkalaemia.

Monitoring and nursing care

- Vital signs: blood pressure, pulse, respirations, pulse oximetry, level of consciousness, temperature.
- Hourly BSL until ketones have disappeared, then 2 hourly. If BSL falls rapidly, 1/2 hourly checks may be necessary.
- Hourly ABG to monitor pH, bicarbonate and potassium until pH is above 7.10 then 2 hourly until pH is above 7.30 or bicarbonate above 15.
- Insertion of an arterial line advised due to frequent blood sampling.
- Insertion of a PICC line is useful for the number of infusions
- Patient nil by mouth until acidosis is reversed. Acidosis can cause nausea and vomiting. Food intake could aggravate nausea and vomiting, increase BSL and make it difficult to titrate dextrose infusion to BSL.
- Assess fluid status: jugular venous pressure, peripheral perfusion, capillary refill, mucous membranes, pulse rate, urine output.
- Monitor other electrolytes, urea, creatinine 4 hourly.
- Consider insertion of urinary catheter.
- Strict fluid balance.
- Urinalysis. Check urine for ketones 2-4 hourly if catheterised or every portion voided. Be aware that it takes longer for ketones to disappear than for hyperglycaemia and acidosis to resolve. Check for glucose.
- Insertion of a nasogastric tube if patient is vomiting.
- Provide oral hydration with ice chips and frequent oral hygiene.
- Provide comfort measures and manage pain.
- Give reassurance to relieve anxiety.

Treatment of co-morbid precipitating factors

Commence anti-microbial therapy if indicated

Resolving acidosis, dehydration and hyperglycaemia

Generally the endpoint of treatment is not normoglycaemia but the correction of acidosis[3]. Acidosis is resolving when serum bicarbonate is >18mmol/L and blood pH >7.3. Resolution of ketosis takes longer than resolution of acidosis and hyperglycaemia. Correction of hyperglycaemia is achieved when blood glucose is <11mmol/L. When blood pH is above 7.3 and bicarbonate is >18mmol/L, the insulin infusion rate can be reduced to 0.05 units/kg/hour or to 3.5 units/h. Again it must be emphasised that the insulin infusion is not to be stopped. Ceasing the insulin infusion can lead to recurrence of ketoacidosis and deterioration of the patient's condition.

When acidosis has resolved, the patient may commence oral intake. However, if the patient cannot tolerate oral intake, dextrose infusion, N/saline infusion and intravenous insulin have to continue. If the patient is able to eat, insulin infusion continues and concurrent subcutaneous insulin is commenced. Insulin infusion should not cease until at least 2-4 hours after subcutaneous injection, because insulin has a short half-life and intravenous and subcutaneous insulin have to overlap[6]. Thus hyperglycaemia and recurrent ketoacidosis should be avoided. The patient is started on a multiple-dose split short-acting/ long-acting insulin regimen[9]. If the patient is a known diabetic and the current illness is of short term, the patient may revert to the previous insulin routine. If the illness of a known diabetic is severe and prolonged, insulin may have to be increased in this time of prolonged stress. The patient's endocrinologist should be involved in the management at this stage, or the new diabetic should be referred to an

endocrinologist. If the patient has not attended diabetic services for a long time, a newer and better insulin product may be introduced (Diabetic Services, Nepean Hospital, 8 January 2007, pers com).

Re-hydration with Hartmann's solution continues until euvolaemia is achieved. Euvolaemia is attained when blood pressure and pulse rate are normal and urine output is adequate, neck veins are visible, mucous membranes are moist, and skin turgor is normal. The goals of DKA manangement are re-hydration of all fluid compartments, normal tissue perfusion and kidney function, and normal cell metabolism.

Differential diagnosis

- Hyperglycaemic hyperosmolar state
- Alcoholic ketoacidosis diagnosed by history of an alcoholic binge and normal or low glucose levels.
- Starvation causing ketosis is not associated with acidosis, and blood glucose levels are normal or low.
- High-anion-gap metabolic acidosis including lactic acidosis, ingestion of salicylate, ethylene, glycol, paraldehyde[9].
- Renal failure.

Complications

- Hypoglycaemia or hyperglyaemia due to inadequate insulin therapy
- Hypokalaemia
- Fluid overload, non-cardiogenic pulmonary oedema
- ARDS
- Pancreatitis
- Rhabdomyolysis
- Cerebral oedema is rare (0.7-1% of DKA cases) but potentially fatal, occurring mainly in children and young adults. It leads to deteriorating consciousness, lethargy, headache, seizures, pupillary

changes. Severely raised intracranial pressure can lead to brain stem herniation, presenting with bradycardia and respiratory arrest[6]. Precipitating factors are a too rapid decline of serum osmolality and movement of water into brain cells. Mannitol should be given intravenously as a bolus of 0.5g/kg over 15 minutes[3].

Education and prevention

- Initiate preventative education for patient and family in ICU once condition is improving. Contact diabetic educator.
- Patient to learn the signs of deteriorating diabetes control and deterioration of health. Recognise the signs of DKA and know when to seek medical advice or present to hospital. Establish a good self-monitoring system at home: blood glucose testing, urine ketones.
- "Sick-day" management
- Managing medications
- Management of alcohol consumption
- Establish regular contact with diabetes educator, dietician, endocrinologist or GP.
- Aim for a good immunisation status.

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