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Acid-Base Physiology

8.1 Lactic Acidosis

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Lactic acidosis is a common cause of metabolic acidosis. [1,2,3]

8.1.1 Daily Production of Lactate

Each day the body has an excess production of about 1500 mmols of lactate (about 20 mmols/kg/day) which enters the blood stream and is subsequently metabolised mostly in the liver. This internal cycling with production by the tissues and transport to and metabolism by the liver and kidney is known as the Cori cycle. This normal process does not represent any net fixed acid production which requires excretion from the body.

All tissues can produce lactate under anaerobic conditions but tissues with active glycolysis produce excess lactate from glucose under normal conditions and this lactate tends to spill over into the blood. Lactate is produced from pyruvate in a reaction catalysed by lactate dehydrogenase:

Pyruvate + NADH + H^+ <=> Lactate + NAD^+

This reaction is so rapid that pyruvate and lactate can be considered to be always in an equilibrium situation. Normally the ratio of lactate to pyruvate in the cell is 10 to 1. The ratio [NADH]/[NAD^+] by the Law of Mass Action determines the balance between lactate and pyruvate. This ratio is also used to denote the redox state within the cytoplasm. Lactic acid has a pK value of about 4 so it is fully dissociated into lactate and H^+ at body pH. In the extracellular fluid, the H^+ titrates bicarbonate on a one for one basis.

8.1.2 Tissue Production & Metabolism

Lactate is released from cells into the ISF and blood.

Tissues Producing Excess Lactate

At rest, the tissues which normally produce excess lactate are:

- skin - 25% of production
- red cells - 20%
- brain - 20%
- muscle - 25%
- gut - 10%

During heavy exercise, the skeletal muscles contribute most of the much increased circulating lactate. [4,5]

During pregnancy, the placenta is an important producer of lactate which passes into both the maternal and the foetal circulations.

Lactate is metabolised predominantly in the liver (60%) and kidney (30%)[6]. Half is converted to glucose (gluconeogenesis) and half is further metabolised to CO_2 and water in the citric acid cycle. The result is no net production of H^+ (or of the lactate anion) for excretion from the body. Other tissues can use lactate as a substrate and oxidise it to CO_2 and water but it is only the liver and kidney that have the enzymes that can convert lactate to glucose.

Note:

- The balance between release into the bloodstream and hepatorenal uptake maintains plasma lactate at about one mmol/l.
- The renal threshold for lactate is about 5 to 6 mmols/l so at normal plasma levels, no lactate is excreted into the urine.
- The small amount of lactate that is filtered (180mmol/day) is fully reabsorbed.

8.1.3 Mechanisms involved in Lactic Acidosis

Lactic acidosis can occur due to:

- excessive tissue lactate production
- impaired hepatic metabolism of lactate

In most clinical cases it is probable that both processes are contributing to the development of the acidosis. The liver has a large capacity to metabolise lactate so increased peripheral production alone is unlikely to lead to other than transient acidosis. The situation is analogous to a respiratory acidosis where increased CO_2 production alone is rarely responsible because of the efficient ventilatory regulation of pCO_2. Impaired ventilation (impaired excretion of CO_2) is almost invariably present and responsible for a respiratory acidosis.

In situations where lactic acidosis is clearly due to excessive production alone (such as severe exercise or convulsions), the acidosis usually resolves (due to hepatic metabolism) within about an hour once the precipitating disorder is no longer present. In severe exercise, lactate levels can rise to very high levels eg up to 30 mmol/l. Respiratory compensation for the acidosis may not be significant because of the short time involved. However, there are other causes of hyperventilation present and arterial pCO_2 is typically reduced providing partial compensation. For example, exercise results in markedly increased ventilation and the cause of this is largely unknown. The arterial pCO_2 usually falls with exercise and this is not considered to be due to the lactic acidosis as it occurs even in less severe exercise where there is little excess lactate produced.

A continuing lactic acidosis means that there is continuing production of lactate that exceeds the liver's capacity to metabolise it. This may be due to clearly very excessive production (eg convulsions) with a normal liver at one extreme, or to increased production in associated with greatly impaired hepatic capacity to metabolise it (eg due to cirrhosis, sepsis, hypoperfusion due hypovolaemia or hypotension, hypothermia, or some combinations of adverse factors) at the other extreme.

8.1.4 Definitions

Definitions differ concerning the blood level at which a lactic acidosis is regarded as 'significant'. For our purposes:

Hyperlactaemia: a level from 2 mmols/l to 5 mmol/l.

Severe Lactic Acidosis: when levels are greater than 5 mmols/l

As levels rise above 5mmols/l, the associated mortality rate can become very high. A serious lactic acidosis can be present without much noticeable elevation of the anion gap. This is because the lactate levels associated with high mortality (say 6 to 10 mmols/l) may not cause much change in a derived variable (the anion gap) which has a 95% reference range of +/-5mmols/l.

The brief and often very high lactate levels that occur with severe exercise or generalised convulsions (eg up to 30 mmol/l) are associated with an extremely low mortality rate. Indeed the mortality rate in these causes is usually extremely low. A lactate level of 15 mmols/l in an elderly ill septic patient in an Intensive Care Unit would be associated with a very high risk of death.

The absolute lactate level (alone) is not a good predictor of outcome unless the cause of the high level is also considered.

Lactate can be converted to glucose in the liver and kidney. This part of the Cori cycle is an example of gluconeogenesis.

Anaerobic glycolysis produces lactate and equivalent amounts of H^+ from ATP hydrolysis. If both these reactions are combined, then there is effectively a net production of equal amounts of lactate and H^+ but the low pKa of lactic acid dissociation means that lactic acid (the undissociated form) is present only in miniscule amounts.

8.1.5 Causes of Lactic Acidosis

Lactic acidosis is commonly classified into either Type A or Type B (Cohen & Woods, 1976) with the main differentiating point being the adequacy of tissue oxygen delivery. In both types, the fundamental problem is the inability of the mitochondria to deal with the amount of pyruvate with which they are presented.

Type A lactic acidosis refers to circumstances where the clinical assessment is that tissue oxygen delivery is inadequate. This is the most common clinical situation. The inadequate oxygen supply slows mitochondrial metabolism and pyruvate is converted to lactate (and NADH to NAD^+) The conversion of NADH to NAD^+ is important as it regenerates NAD^+ needed for glycolysis to continue. This situation is known as anaerobic metabolism and results in a small net ATP production: two moles of ATP per mole of glucose. The mitochondrial reactions are presumed to be intact but unable to function because of inadequate oxygen If hypoxaemia is the only factor present, it needs to be severe (eg paO_2 < 35mmHg) to precipitate lactic acidosis because of the protection afforded by the body's compensatory mechanisms which increase tissue blood flow. Similarly anaemia needs to be severe (eg [Hb] <5G%) if present alone because tissue blood flow is increased in compensation.

Reduced perfusion is the most important factor in causing impaired oxygen delivery in type A lactic acidosis.

Anaemia or hypoxaemia alone is not sufficient unless severe or associated with reduced perfusion.

Type B lactic acidosis refers to situations in which there is no clinical evidence of reduction in tissue oxygen delivery. Carbohydrate metabolism is disordered for some reason and excess lactic acid is formed. Research using more sophisticated methods to assess tissue perfusion have now shown that occult tissue hypoperfusion is present in many cases of Type B acidosis.

An **ischaemic bowel** can produce large amounts of lactate. Mesenteric ischaemia can cause a severe lactic acidosis even if perfusion in the rest of the body is adequate. This situation can easily be overlooked especially in those cases where abdominal clinical signs are minimal.

Phenformin is a biguanide oral hypoglycaemic agent which was associated with a severe form of Type B lactic acidosis. The incidence was highest among diabetics with renal insufficiency where blood levels are highest. The mechanism of action is not fully established but the drug probably interferes with mitochondrial function. High levels of phenformin significantly depress myocardial contractility. The decrease in cardiac output undoubtably contributes a major component of tissue hypoperfusion to many cases.

Other factors predisposing to development of lactic acidosis are sepsis, liver failure and some malignancies.

Patients with cirrhosis often have a much reduced ability to take up and metabolise lactate. Despite this, patients with chronic hepatic disease alone do not commonly develop lactic acidosis unless other factors such as sepsis, shock, bleeding or ethanol abuse are also present. So, the development of lactic acidosis in patients with cirrhosis suggests severe liver damage and the presence of other factors. In this setting, death rates are high.

Any factor which stimulates glycolysis (eg catecholamine administration, cocaine) will lead to an increased lactate production. Lactic acidosis occurs in up to 10% of patients presenting with diabetic ketoacidosis. This may be due to poor peripheral perfusion or phenformin administration but may occur without the presence of these factors.

Classification of Some Causes of Lactic Acidosis (Cohen & Woods, 1976)

Type A Lactic Acidosis : Clinical Evidence of Inadequate Tissue Oxygen Delivery

- Anaerobic muscular activity (eg sprinting[7], generalised convulsions)
- Tissue hypoperfusion (eg shock -septic, cardiogenic or hypovolaemic; hypotension; cardiac arrest; acute heart failure; regional hypoperfusion esp mesenteric ischaemia; malaria[8,9])
- Reduced tissue oxygen delivery or utilisation (eg hypoxaemia, carbon monoxide poisoning, severe anaemia)

Type B Lactic Acidosis: No Clinical Evidence of Inadequate Tissue Oxygen Delivery

- **type B1** : Associated with underlying diseases (eg ketoacidosis, leukaemia, lymphoma, AIDS)
- **type B2**: Assoc with drugs & toxins (eg phenformin, cyanide, beta-agonists, methanol, nitroprusside infusion, ethanol intoxication in chronic alcoholics, anti-retroviral drugs)
- **type B3**: Assoc with inborn errors of metabolism (eg congenital forms of lactic acidosis with various enzyme defects eg pyruvate dehydrogenase deficiency)

Note: This list does not include all causes of lactic acidosis

8.1.6 Diagnosis

The condition is often suspected on the history and examination (eg shock, heart failure) and is easily confirmed and quantified by measuring the blood lactate level. A particular problem is the diagnosis of the condition when present as part of a mixed acid-base disorder. It may be associated with other causes of a high anion gap acidosis (eg ketoacidosis, uraemic acidosis) and not be suspected. Coexistent lactic acidosis and metabolic alkalosis may result in minimally altered plasma bicarbonate level. A high anion gap may be a clue in this later situation but the anion gap is not invariably elevated out of the reference range.

Why do clinicians have difficulty diagnosing lactic acidosis?

The main reason is that traditionally a lactate level was an uncommon investigation and the diagnosis of lactic acidosis was by exclusion in patients with a high anion gap metabolic acidosis and some evidence of impaired perfusion. Other factors were a low index of clinical suspicion and a tendency to not appreciate the significance of an elevated lactate result.

The basic investigations needed to supplement the history, examination and electrolyte results in differentiating the causes of a high anion gap acidosis are:

- blood glucose level
- urinary ketones
- urea & creatinine
- urine output
- blood lactate level
- calculation of osmolar gap

8.1.7 Management

The principles of management of patients with lactic acidosis are:

- Diagnose and correct the underlying condition (if possible)
- Restore adequate tissue oxygen delivery (esp restore adequate perfusion)
- Avoid sodium bicarbonate (except possibly for treatment of associated severe hyperkalaemia)

When the circulation is restored, the liver can metabolise the circulating lactate. If lactic acidosis is severe and the cause cannot be corrected, the mortality can be quite high.

What is the role of IV bicarbonate?

Quite large doses of bicarbonate (eg 1,000 to 3,000 mmols/day!) have traditionally been administered to severe cases but the success rate is low. Interestingly, metabolic alkalosis induced by administration of sodium bicarbonate can lead to a substantial increase in the production of lactate. This may be because the intracellular acidosis strongly inhibits phosphofructokinase which is the rate-limiting enzyme in glycolysis. This suggests that bicarbonate therapy could result in induction of alkalosis intracellularly which could release this inhibition and increase pyruvate and lactate production (& thus a vicious cycle). No wonder massive doses of bicarbonate seem necessary and why the outcome is so poor.

[See also: **Use of Bicarbonate in Metabolic Acidosis**]

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Metabolic acid–base disorders

Metabolic acid–base disorders are reflected in changes in the ECF bicarbonate concentration that commonly occur because of a build-up or loss of hydrogen ions. Direct loss or gain of bicarbonate will also cause metabolic acid–base disorders. Primary metabolic acid–base disorders are recognized by inspecting the bicarbonate concentration (Fig. 1). Respiratory compensation takes place quickly so patients with metabolic acid–base disorders will usually show some change in blood PCO_2 because of hyperventilation or hypoventilation (Fig. 2).

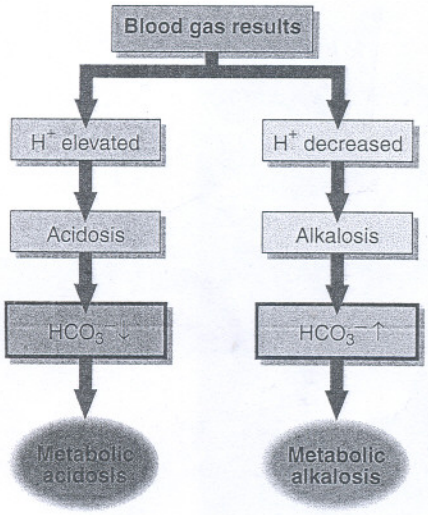

Fig. 1 **Recognizing primary metabolic acid–base disorders by inspecting the HCO_3^- concentration.**

Metabolic acidosis

In a metabolic acidosis the primary problem is a reduction in the bicarbonate concentration of the extracellular fluid. The main causes of a metabolic acidosis are shown in Figure 3. These are:

- increased production of hydrogen ions
- ingestion of hydrogen ions, or of drugs that are metabolized to acids
- impaired excretion of hydrogen ions by the kidneys
- loss of bicarbonate from the gastrointestinal tract or in the urine.

The anion gap

The cause of a metabolic acidosis will nearly always be apparent from the clinical history of the patient, but occasionally knowledge of the anion gap may be helpful. This can be assessed by looking at the serum electrolyte results and calculating the difference between the sum of the two main cations, sodium and potassium, and the sum of the two main anions, chloride and bicarbonate. There is no real gap, of course, as plasma proteins are negatively charged at normal $[H^+]$. These negatively charged amino acid side chains on the proteins account for most of the apparent discrepancy when the measured electrolytes are compared. *The anion gap is thus a biochemical tool that is sometimes of help in assessing acid–base problems. It is not a physiological reality.*

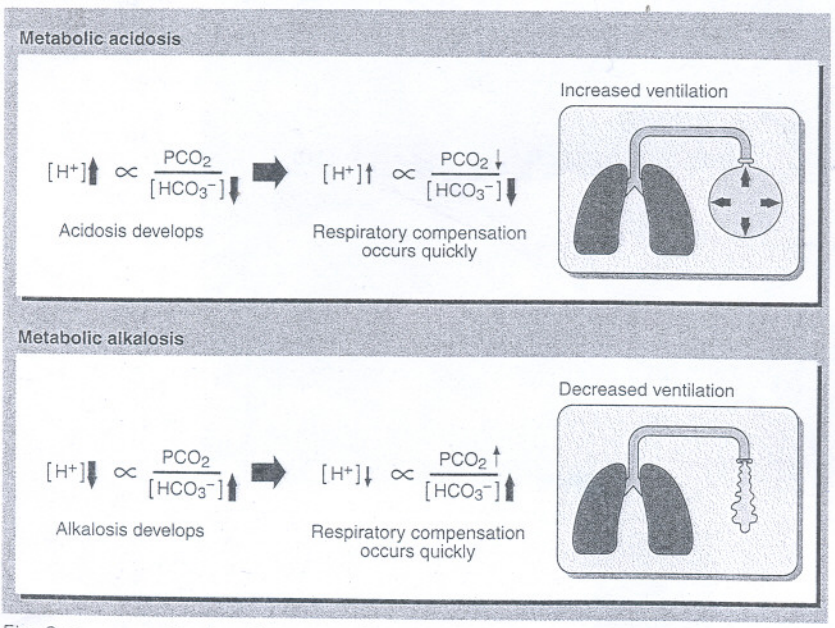

Fig. 2 **Compensation in primary metabolic disorders.**

In practice, because the potassium concentration is so small and will vary by so little, it is generally excluded when calculating the anion gap. Thus:

$$\text{Anion gap} = [Na^+] - [(Cl^-) + (HCO_3^-)]$$

In a healthy person, the anion gap has a value of between 6 and 18 mmol/L. When the bicarbonate concentration rises or falls, other ions must take its place to maintain electrochemical neutrality. If chloride substitutes for bicarbonate, the anion gap does not change. However, the anion gap value will increase in metabolic conditions in which acids, such as sulphuric, lactic or acetoacetic, are produced, or when salicylate is present.

Causes of metabolic acidosis

Metabolic acidosis with an elevated anion gap occurs in:

- *Renal disease.* Hydrogen ions are retained along with anions such as sulphate and phosphate.
- *Diabetic ketoacidosis.* Altered metabolism of fatty acids, as a consequence of the lack of insulin, causes endogenous production of acetoacetic and β-hydroxybutyric acids.
- *Lactic acidosis.* This results from a number of causes, particularly tissue anoxia. *In acute hypoxic states such as respiratory failure or cardiac arrest lactic acidosis develops within minutes and is life-threatening.* Lactic acidosis may also be caused by liver disease. The presence of a lactic acidosis can be confirmed, if necessary, by the measurement of plasma lactate concentration.
- *Certain cases of overdosage or poisoning.* The mechanism common to all of these is the production of acid metabolites. Examples include salicylate overdose where build-up of lactate occurs, methanol poisoning when formate accumulates, or ethylene glycol poisoning where oxalate is formed.

Metabolic acidosis with a *normal* anion gap is sometimes referred to as a 'hyperchloraemic acidosis' because a reduced HCO_3^- concentration is balanced by increased Cl^- concentration. It is seen in:

- *Chronic diarrhoea or intestinal fistula.* Fluids containing bicarbonate are lost from the body.

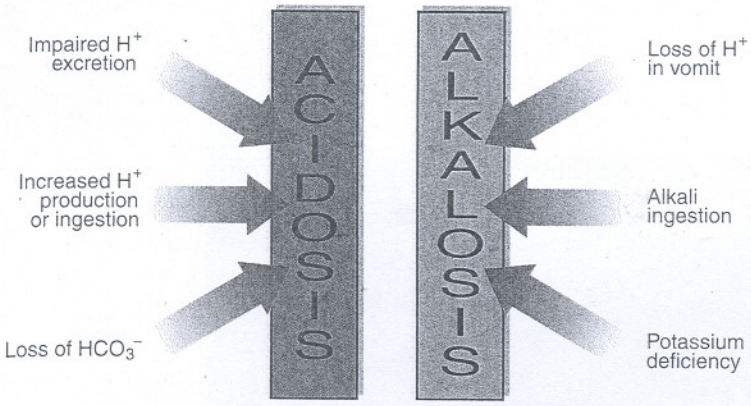

Fig. 3 **Reasons for metabolic acidosis and alkalosis.**

- *Renal tubular acidosis.* Renal tubular cells are unable to excrete hydrogen ions efficiently, and bicarbonate is lost in the urine.

Clinical effects of acidosis

The compensatory response to metabolic acidosis is hyperventilation, since the increased $[H^+]$ acts as a powerful stimulant of the respiratory centre. The deep, rapid and gasping respiratory pattern is known as Kussmaul breathing. Hyperventilation is the appropriate physiological response to acidosis and it occurs rapidly.

A raised $[H^+]$ leads to increased neuromuscular irritability. There is a hazard of arrhythmias progressing to cardiac arrest, and this is made more likely by the presence of hyperkalaemia, which will accompany the acidosis (pp. 22–23). Depression of consciousness can progress to coma and death.

Metabolic alkalosis

The causes of a metabolic alkalosis are shown in Figure 3. The condition may be due to:

- *Loss of hydrogen ion in gastric fluid during vomiting.* This is especially seen when there is pyloric stenosis preventing parallel loss of bicarbonate-rich secretions from the duodenum.
- *Ingestion of an absorbable alkali such as sodium bicarbonate.* Very large doses are required to cause a metabolic alkalosis unless there is renal impairment.
- *Potassium deficiency.* In severe potassium depletion, often a consequence of diuretic therapy, hydrogen ions are retained inside cells to replace the missing potassium ions. In the renal tubule more hydrogen ions, rather than potassium, are exchanged for reabsorbed sodium. So, despite there being an alkalosis, the patient passes an acid urine. This is often referred to as a 'paradoxical' acid urine, because in other causes of metabolic alkalosis urinary $[H^+]$ usually falls.

Clinical effects of alkalosis

The clinical effects of alkalosis include hypoventilation, confusion and eventually coma. Muscle cramps, tetany and paraesthesia may be a consequence of a decrease in the unbound plasma calcium concentration, which is a consequence of the alkalosis.

Clinical note

A patient who has had prolonged nasogastric suction following surgery will lose gastric fluid in large quantities and may develop a metabolic alkalosis.

Case history 14

A 28-year-old man is admitted to hospital with a week-long history of severe vomiting. He confessed to self-medication of his chronic dyspepsia. He was clinically severely dehydrated and had shallow respiration. Initial biochemical results were:

Arterial blood gases:

H^+	PCO_2	HCO_3^-	PO_2
nmol/L	*kPa*	*mmol/L*	*kPa*
28	7.2	43	15

Serum:

Na^+	K^+	Cl^-	HCO_3^-	Urea	Creatinine
		mmol/L			*μmol/L*
146	2.8	83	41	31	126

A random urine sample was obtained, and had the following biochemical results: osmolality 630 mmol/kg, Na^+ <20 mmol/L, K^+ 35 mmol/L, pH 5.

- What is the acid–base disorder and how has it arisen?
- How might the urine results help in the diagnosis?

Comment on page 163.

Metabolic acid–base disorders

- In metabolic acidosis, the blood $[H^+]$ may be high or normal, but the $[HCO_3^-]$ is always low. In compensated conditions, PCO_2 is lowered.
- The commonest causes of metabolic acidosis are renal disease, diabetic ketoacidosis and lactic acidosis.
- Consideration of the anion gap may sometimes be helpful in establishing the cause of a metabolic acidosis.
- In metabolic alkalosis, the $[H^+]$ is depressed and the $[HCO_3^-]$ is always raised. Respiratory compensation results in an elevated PCO_2.
- The commonest cause of a metabolic alkalosis is prolonged vomiting.

Diabetic ketoacidosis

How diabetic ketoacidosis develops

Diabetic ketoacidosis (DKA) is a medical emergency. All metabolic disturbances seen in DKA are the indirect or direct consequences of the lack of insulin (Fig. 1). Decreased glucose transport into tissues leads to hyperglycaemia, which gives rise to glycosuria. Increased lipolysis causes overproduction of fatty acids, some of which are converted into ketones, giving ketonaemia, metabolic acidosis and ketonuria. Glycosuria causes an osmotic diuresis, which leads to the loss of water and electrolytes – sodium, potassium, calcium, magnesium, phosphate and chloride. Dehydration, if severe, produces pre-renal uraemia and may lead to hypovolaemic shock. The severe metabolic acidosis is partially compensated by an increased ventilation rate (Kussmaul breathing). Frequent vomiting is also usually present and accentuates the loss of water and electrolytes. Thus the development of DKA is a series of interlocking vicious circles all of which must be broken to aid the restoration of normal carbohydrate and lipid metabolism.

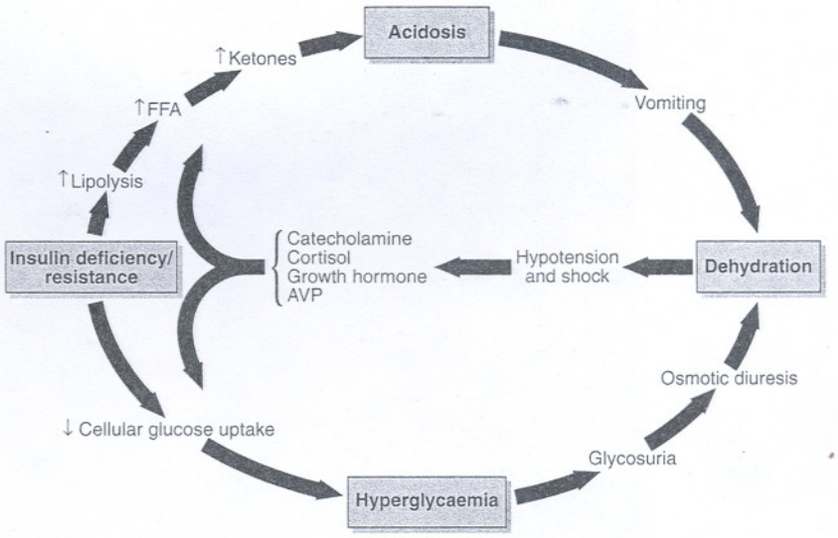

Fig. 1 **The development of diabetic ketoacidosis.**

The most common precipitating factors in the development of DKA are infection, myocardial infarction, trauma or omission of insulin.

Treatment

The management of DKA requires the administration of three agents:

- *Insulin.* Intravenous insulin is most commonly used. Intramuscular insulin is an alternative when an infusion pump is not available or where venous access is difficult, e.g. in small children.
- *Fluids.* Patients with DKA are usually severely fluid depleted and it is essential to expand their ECF with saline to restore their circulation.
- *Potassium.* Despite apparently normal serum potassium levels, all patients with DKA have whole body potassium depletion that may be severe.

In most cases, rehydration and insulin therapy will correct the metabolic acidosis, and no further therapy is indicated. However, in the most severe cases when the hydrogen ion concentration is greater than 100 nmol/L, IV sodium bicarbonate may be indicated.

The detailed management of diabetic ketoacidosis is shown in Figure 2. The importance of good fluid charts, as in any serious fluid and electrolyte disorder, cannot be over-emphasized. The initial high input of physiological (0.9%) saline is cut back as the patient's fluid and electrolyte deficit improves. Intravenous insulin is given by continuous infusion using an automated pump, and potassium supplements are added to the fluid regimen. The hallmark of good management of a patient with DKA is close clinical and biochemical monitoring.

Laboratory investigations

Initially, urine (if available) should be tested for glucose and ketones, and blood checked for glucose using a test strip. Venous blood should be sent to the laboratory for plasma glucose and serum sodium, potassium, chloride, bicarbonate,

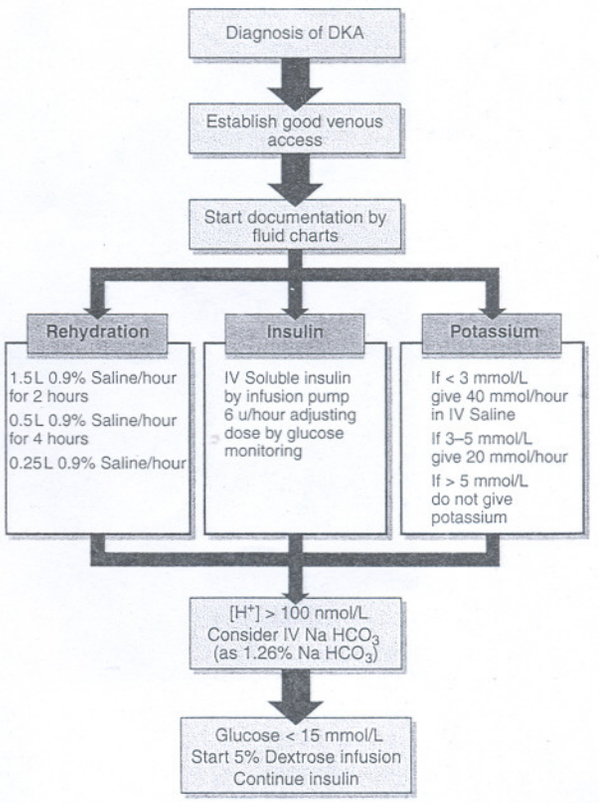

Fig. 2 **A treatment regimen for diabetic ketoacidosis.**

urea and creatinine. An arterial blood sample should also be sent for measurement of blood gases.

It is important to highlight a clinically important consequence of laboratory methodology here. The presence of ketone bodies in serum interferes with creatinine measurement; therefore serum creatinine can be falsely elevated in the acute stage. Reliable creatinine values are obtained only after ketonaemia subsides.

Amylase activity in serum is also increased in diabetic ketoacidosis. Pancreatitis should be considered as a precipitating factor only if there is persistent abdominal pain.

Blood glucose should be monitored hourly at the bedside until less than 15 mmol/L. Thereafter checks may continue 2-hourly. The plasma glucose should be confirmed in the laboratory every 2–4 hours. The frequency of monitoring of blood gases depends on the severity of DKA. In severe cases it should be performed 2-hourly at least for the first 4 hours. The serum potassium level should be checked every 2 hours for the first 6 hours, while urea and electrolytes should be measured at 4-hourly intervals (Fig. 3).

Two other forms of severe metabolic decompensation may occur in diabetics. These are hyperosmolar non-ketotic (HONK) coma and lactic acidosis. Table 1 shows the principal features of these conditions in comparison with DKA.

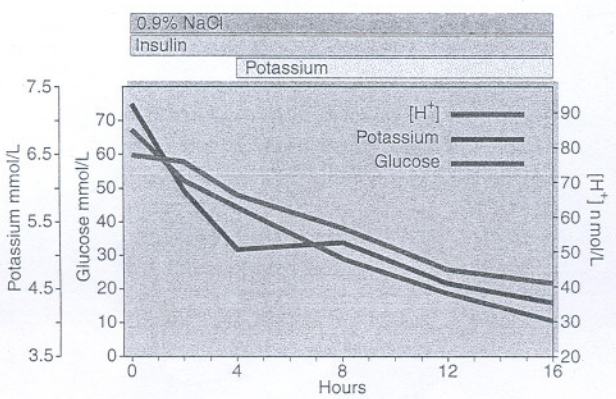

Fig. 3 **Effective treatment of a severe case of diabetic ketoacidosis.**

Table 1 **Principal features of three forms of metabolic decompensation in diabetes**

Features	Diabetic keto-acidosis (DKA)	Hyperosmolar non-ketotic coma (HONK)	Lactic acidosis
Plasma glucose	High	Very high	Variable
Ketones	Present	None	Variable
Acidosis	Moderate/Severe	None	Severe
Dehydration	Prominent	Prominent	Variable
Hyperventilation	Present	None	Present

Case history 25

A 22-year-old patient with diabetes comes to the Accident and Emergency department. She gives a 2-day history of vomiting and abdominal pain. She is drowsy and her breathing is deep and rapid. There is a distinctive smell from her breath.

- What is the most likely diagnosis?
- Which bedside tests could you do to help you to confirm this diagnosis?
- Which laboratory tests would you request?

Comment on page 164.

Hyperosmolar non-ketotic (HONK) coma

Diagnosis

HONK coma occurs mostly in elderly, non-insulin-dependent diabetics, and develops relatively slowly over days or weeks. The level of insulin is sufficient to prevent ketosis but does not prevent hyperglycaemia and osmotic diuresis. Precipitating factors include severe illness, dehydration, glucocorticoids, diuretics, parenteral nutrition, dialysis and surgery. Extremely high blood glucose levels (above 35 mmol/L, and usually above 50 mmol/L) accompany severe dehydration resulting in impaired consciousness.

Treatment

Treatment is similar to that of DKA, with the following modifications. Rehydration should be slower to avoid neurological damage. Dilute (0.45%) saline has been used where the serum sodium level is above 160 mmol/L. However, recent data indicate that in most cases the use of physiological (0.9%) saline is sufficient. The insulin dose requirements are usually lower than in DKA. There is also an increased risk of thromboembolism and prophylactic heparin is recommended.

Lactic acidosis

Diagnosis

Type I lactic acidosis occurs in hypoxic subjects and is due to an excessive production of lactate by peripheral tissues. Hypoxia is not a feature of type II lactic acidosis, which is probably caused by the impaired metabolism of lactate in the liver. Both are characterized by an extreme metabolic acidosis ($[H^+]$ above 100 nmol/L). There is a high anion gap with low or absent ketones, and high blood lactate concentrations.

Treatment

Large amounts of intravenous sodium bicarbonate may be required to correct the acidosis. Alternatively the patient may be dialysed against a bicarbonate-containing solution.

Clinical note

Always screen for infections in the diabetic patient presenting with DKA, as this is a common precipitating factor. Blood, urine, sputum and any wound fluids should be sent for culture at the earliest opportunity and certainly before antibiotics are introduced.

Diabetic ketoacidosis

- Diabetic ketoacidosis arises from a number of metabolic problems caused by insulin lack.
- Treatment is by intravenous fluids, insulin and potassium.
- Only in the most severe cases of DKA should sodium bicarbonate be used.
- Close clinical and biochemical monitoring are required to tailor the management protocol to the individual patient.
- Other, much less common, severe metabolic disturbances of carbohydrate metabolism are hyperosmolar non-ketotic coma and lactic acidosis.