

# Diabetic ketoacidosis

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**ABSTRACT** Diabetic ketoacidosis remains the most important acute complication of diabetes mellitus, causing metabolic decompensation with an associated morbidity and mortality of 1–10%. Although levels of morbidity and mortality are falling with modern management protocols, a significant threat still remains. While DKA is most common in patients with type 1 diabetes mellitus, it should not be overlooked in patients with type 2 diabetes mellitus, especially in those who require insulin. In contrast to chronic management, acute complications often present to Acute Medicine rather than to specialist diabetes services. Prompt recognition, diagnosis, and treatment are therefore essential.

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**LIST OF ABBREVIATIONS** Diabetic ketoacidosis (DKA), urea and electrolytes (U&E), electrocardiogram (ECG), full blood count (FBC), mid-stream specimen urine (MSSU), Glasgow Coma Scale (GCS), computed tomography (CT), intensive care/therapy unit (ICU/ITU), blood pressure (BP)

**DECLARATION OF INTERESTS** No conflict of interests declared.

## INTRODUCTION

Diabetic ketoacidosis is a medical emergency, and presentations to the acute setting are increasing. The reported incidence of diabetic ketoacidosis varies: for example, EURODIAB reported that 8.6% of patients with type 1 diabetes had been admitted with a diagnosis of DKA in the previous 12 months. It occurs in patients who have either no, or reduced, insulin production with subsequent impaired uptake of glucose within tissues. This, combined with increased production of glucose within the liver, leads to the clinical situation of DKA.

## DIAGNOSIS

Diagnosis of DKA should be based on clinical history, along with the demonstration of ketonaemia, ketonuria, metabolic acidosis, and, usually, hyperglycaemia.

Hyperglycaemia is detected initially by bedside glucometer reading and/or confirmed by laboratory testing. Ketonuria is detected by urine dipstick testing. Acidosis should be confirmed initially by venous/arterial blood gas analysis or serum bicarbonate measurements. There are other clinical situations, however, that can result in ketonuria, such as starvation.

## PRECIPITATING FACTORS

Diabetic ketoacidosis often occurs after a precipitating event. In a large number of cases, infection is the underlying factor in the development of DKA. However,

Precipitant	Occurrence (%)
Infections such as pneumonia or urinary tract infection.	30
Insulin errors (including non-compliance) and faulty equipment.	15
New diagnosis of type 1 diabetes.	5–15
Other stresses such as myocardial infarction, alcohol, pancreatitis, and drugs (thiazides and corticosteroids).	5
No cause identified.	40

**TABLE 1** Common events leading to DKA.

no identifiable cause is found in 40% of cases. In younger diabetic patients in particular, non-compliance with insulin can play a major role. Other factors are listed in Table 1. It is important to obtain an accurate history with appropriate investigation to identify any precipitant.

During periods of illness, insulin requirements increase significantly despite even minimal oral intake. As part of 'Sick Day Rules', patients are educated never to omit insulin and to seek advice and help early.

## SYMPTOMS AND SIGNS

Patients normally present with thirst, polydipsia, and polyuria, although all of these need not be present to make a diagnosis. Other symptoms may include:

- Nausea and vomiting.

- Diffuse abdominal pain.
- Weakness and lethargy.
- Altered consciousness and confusion.
- Weight loss.
- Dehydration.
- Acidosis. This results in Kussmaul respiration (deep fast breathing) as the patient compensates for the acidosis.
- Acetone may be detected in the breath.

In addition, symptoms and signs of the underlying cause may be associated, such as clinical signs of infection. In children, the diagnosis can be more difficult as they may not present with a classical picture, and this may be further complicated if the existence of diabetes was not previously diagnosed.

## INVESTIGATIONS

Initial investigations are aimed at making the diagnosis. They are as follows:

- Urea and electrolytes, laboratory glucose, and venous blood gas are required initially.
- Urine should be checked for ketones.
- Laboratory blood glucose should be checked hourly. Once blood glucose is  $< 20$  mmol/L, it is reasonable to use a point-of-care meter to monitor blood glucose.
- Urea and electrolytes and bicarbonate should be closely monitored throughout treatment.
- Chest X-ray, blood cultures, ECG, FBC, MSSU and viral titres should be considered to determine any underlying cause such as infection or myocardial infarction.

Amylase is often raised in the absence of pancreatitis. A leucocytosis can also be found without any underlying infection.

## GENERAL MANAGEMENT PRINCIPLES

Treatment for DKA should be started as soon as the diagnosis is made. Owing to the significant mortality associated with DKA, monitoring within a high dependency facility is recommended. Not all hospitals will have such a facility, but the following clinical signs should still always be discussed with senior team members and consideration should be given to cardiac and central venous monitoring:

- Respiratory rate  $>20$  /minute.
- Pulse  $>90$  beats/minute.
- Systolic BP  $<100$  mmHg.
- Circulatory compromise – pale, sweaty, cool or clammy peripheries. Mottling indicates severe circulatory compromise.
- Temperature  $>38^{\circ}\text{C}$  or  $<36^{\circ}\text{C}$ .
- Glasgow Coma Scale  $<8$ .

Accurate fluid balance should be maintained in all cases. A nasogastric tube should be inserted in cases of protracted vomiting. A urinary catheter should be inserted if the patient is oliguric.

### Fluids

Once a diagnosis of DKA has been established, fluid replacement should be commenced immediately. It is recommended that 0.9% saline should be infused initially unless there is significant hypovolaemia, in which case colloid should be used to restore circulatory function. There is no evidence to suggest benefit in using 0.45% (half normal) saline and this is best avoided in management of DKA.

Dextrose should be introduced once glucose is  $\leq 14$  mmol/L and 0.9% saline can be used in combination, to continue rehydration.

While there will be significant fluid replacement requirements in treating DKA, faster rates of administration have been suggested as a possible cause in the development of cerebral oedema. Slower rates, on the other hand, have been associated with a more rapid correction of plasma bicarbonate. It is recommended that 1,000 ml be infused in the first hour.

More caution is needed with regard to fluid replacement in younger patients and children as they are particularly prone to cerebral oedema. It is important therefore that this group be managed in close collaboration with paediatric colleagues or in accordance with local guidelines; e.g. British Society of Paediatric Endocrinology and Diabetes.

### Insulin

Continuous intravenous infusion of modest doses of insulin gives the most consistent beneficial results.

While there is no specific evidence that a rate of fall in glucose level greater than 5 mmol/h should be avoided, there may be an increased risk of cerebral oedema if the glucose level drops too quickly.

Any soluble insulin may be used, although human sequence insulin (e.g. Actrapid) is often specified. It is generally administered via a syringe pump (normally 50 units in 50 ml normal saline) at a concentration of 1 unit/ml and starting at 6 ml/h. The rate should be adjusted in accordance with blood glucose monitoring.

If there is likely to be a delay in commencing intravenous insulin infusion, then the intramuscular route may be used initially, but the insulin will not be absorbed when tissue perfusion is poor.

Serum potassium level (mmol/L)	Amount of potassium administered (mmol)
> 5	None added
3.5–5	20
< 3.5	40

Continue to maintain within potassium range and monitor twice daily.

**TABLE 2** Potassium replacement, unless patient is anuric.

### Potassium

In DKA there will be a total body deficit of potassium, but because of acidosis and dehydration, the initial serum value can vary. Once the level is known, potassium should be added to the intravenous fluid infusion (see Table 2), unless the patient is anuric. Replacement should be adjusted to maintain potassium values within the normal laboratory ranges.

Under no circumstances should potassium be administered at a rate greater than 20 mmol/h.

### Bicarbonate

Studies have failed to show any positive benefit from treatment with sodium bicarbonate. It may delay correction of the metabolic defects and may be associated with more hypokalaemia, hypoxia, and paradoxical cerebrospinal fluid acidosis. Treatment with sodium bicarbonate should therefore be reserved for situations of cardiogenic shock or other lactic acid-generating conditions.

## COMPLICATIONS

Aspiration pneumonia owing to gastric stasis and sepsis from intravenous lines and catheters may occur.

Thromboembolism can occur with severe hypoperfusion and dehydration.

Cerebral oedema, which is rare but frequently fatal, is the most serious complication of DKA. It typically presents within 2–24 hours of onset of treatment, with headache and deterioration in consciousness level. The pathophysiology is poorly understood, but new-onset diabetes and longer duration of DKA give increased risk. Rapid rates of fluid administration, rapid correction of blood glucose level, and the use of bicarbonate have all been associated with onset of cerebral oedema. Children and adolescents are most susceptible. Mortality is around 70%. Full recovery with no residual impairment is only 7–14%.

- Monitoring for signs of cerebral oedema should start from the time of admission and should continue until at least 12 hours after admission.
- Administer intravenous mannitol (100 ml of 20% over 20 min) or dexamethasone 8 mg as soon as cerebral oedema is clinically suspected.
- Undertake CT scan to confirm findings.
- Consider transfer to ICU/ITU.
- If any suspicion of cerebral oedema or if the patient is not improving within 4 hours of admission, call a consultant.

**TABLE 3** Action to prevent and treat cerebral oedema.

## CONTINUING CARE

It is recommended that every patient with DKA be referred for review to some or all of the members of the diabetes team (diabetes specialist nurse, dietician, and doctor specialising in diabetes) in order to help determine the cause of DKA and to undertake diabetes education and knowledge review.

Some or all of the following aspects should be considered between practitioner and patient.

- Revision of patient knowledge and understanding of the condition.
- Review of 'Sick Day Rules'.
- Equipment: pens and insulin.
- Home blood-glucose monitoring.
- Diet.

Patients should not be discharged until they are biochemically normal, eating normally, and established on subcutaneous insulin.

Many local and national protocols have been developed for the management of DKA to emphasise the importance of careful management and close observation. Examples include the American Diabetes Association Guidelines, and a Scotland-wide DKA protocol developed for the Acute Management of Diabetic Ketoacidosis in Adults. This protocol is available from [www.diabetesinscotland.org/diabetes](http://www.diabetesinscotland.org/diabetes). Paediatric management guidance is available from [www.bsped.org.uk](http://www.bsped.org.uk).

## KEYPOINTS

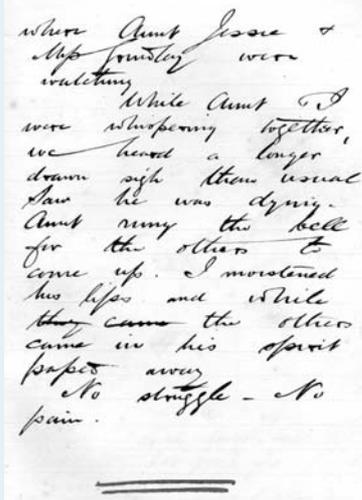
- Diabetic ketoacidosis remains the most important acute complication of diabetes mellitus, causing metabolic decompensation with an associated morbidity and mortality.
- Diabetic ketoacidosis often occurs after a precipitating event.
- Fluid replacement should be commenced immediately. More caution is needed in younger patients and

children as they are particularly prone to cerebral oedema.

- Owing to the significant mortality resulting from DKA, monitoring within a high dependency facility is recommended.
- It is recommended that every patient with DKA be referred for review to some or all of the members of the diabetes team.

## FURTHER READING

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### THE SIMPSON DIARY – THE FINAL ENTRY

#### 'No struggle – no pain': the last days of Sir James Young Simpson

A lost diary which was discovered in a charity bookshop in Edinburgh has been added to the College Library. It describes the last days of one of the most famous physicians of the nineteenth century, Sir James Young Simpson.

James Young Simpson was Professor of Midwifery at Edinburgh for over 30 years, and President of the Royal College of Physicians of Edinburgh from 1850 to 1852. Although one of the founders of modern obstetrics and gynaecology, he is most popularly known for his application of chloroform as an anaesthetic.

The diary, written by his nephew Robert Simpson, describes the great physician's illness and declining health during the two months leading up to his death in 1870. Although it was used in the preparation of a biography of Sir James published in 1873, its whereabouts had been unknown for over 130 years. It was discovered in August 2006 among a bundle of miscellaneous books handed in by an anonymous donor to the *Shelter* charity bookshop in Stockbridge, Edinburgh. The manager, recognising its possible importance, contacted the College Library, and it now forms a valuable addition to the Simpson Collection bequeathed to the College in 1916.

The diary gives a touching account of

the last two months of Simpson's life. It outlines the onset of his illness, visits from his family and friends, what books he liked read to him, and near the end, describes how his elder brother sat through the night cradling him in his arms. 'It was most touching to see the elder brother – 14 years older than the younger, and who had watched his progress with such fond affection – watching by the death bed. "Oh Sandy, Sandy," uncle repeatedly said showing he knew who was beside him.' The final entry reads: 'I moistened his lips, and while the others came in his spirit passed away. No struggle – no pain.'

Simpson's contribution to medicine made him one of the most famous men of his time, receiving honours from all over the world. The day of his funeral was declared a day of public mourning in Edinburgh. Many shops and businesses closed, and two thousand people followed his hearse through streets lined by over thirty thousand mourners.

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