SECTION A

Endocrinology

Canine Internal Medicine: What's Your Diagnosis? First Edition. Jon Wray.

CASE 1

Clinical presentation

An 11 year-old male-neutered Border terrier (**Figure 1.1**) weighing 10.4 kg is presented with a history of lethargy, anorexia, vomiting and progressive dullness resulting in a reluctance to walk. His owners report that he has had previous episodes of self-limiting vomiting lasting 2–3 days of which he has had four episodes over the previous 6 months. They have noticed both his water consumption and urination increased dramatically over the previous 2 weeks. No haircoat or skin abnormalities have been noted but he has lost some weight over this time. His appetite up until 48 hours ago has been excellent. He has vomited, accompanied by abdominal effort, 8 times in the last 24 hours and the vomitus has been bile-stained fluid.

Physical examination demonstrates a very depressed dog in overweight body condition (body condition score 4/5) who is reluctant to walk. The eyes are sunken and normal skin turgor is lost. Mucous membranes are very tacky to the touch but are of a normal colour with a capillary refill time of 2.5 s. Heart rate is 144/min, respiratory rate is 32/min and rectal temperature is 38.3 °C. Peripheral pulse quality is slightly poor. Auscultation of the heart and respiratory tract is normal and abdominal palpation generates reproducible cranial abdominal discomfort but no palpable structural abnormalities. The urinary bladder is moderately full and after palpation the dog spontaneously voids urine without apparent difficulty, and some is collected for analysis.

Figure 1.1 The patient at presentation.

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A blood sample is also taken and the following results were obtained:

Haematology

Parameter	Value	Units	Range
RBC	6.89	× 10^{12}/l	(5.5–8.5)
Haemoglobin	14.4	g/dl	(12.0–18.0)
Haematocrit	0.49	l/l	(0.37–0.55)
Mean cell volume	71.3	fl	(60–77)
Mean cell haemoglobin cconcentration	30	g/dl	(30.0–38.0)
Mean cell haemoglobin	20.9	pg	(19.5–25.5)
Total white cell count	**19.26**	× 10^9/l	(6.0–15.0)
Neutrophils	**16.37**	× 10^9/l	(3.0–11.5)
Lymphocytes	**0.96**	× 10^9/l	(1.0–4.8)
Monocytes	**1.96**	× 10^9/l	(0.2–1.4)
Eosinophils	**0**	× 10^9/l	(0.1–1.2)
Basophils	0	× 10^9/l	(0.0–0.1)
Platelets	223	× 10^9/l	(200–500)

Biochemistry

Parameter	Value	Units	Range
Total protein	**78**	g/l	(54–77)
Albumin	39	g/l	(25–40)
Globulin	39	g/l	(23–45)
Urea	**13.5**	mmol/l	(2.5–7.4)
Creatinine	132	μmol/l	(40–145)
Potassium	3.6	mmol/l	(3.4–5.6)
Sodium	143	mmol/l	(139–154)
Chloride	118	mmol/l	(105–122)
Calcium	2.2	mmol/l	(2.1–2.8)
Inorganic phosphate	0.9	mmol/l	(0.60–1.40)
Glucose	**34**	mmol/l	(3.3–5.8)
ALT	**385**	IU/l	(13–88)
AST	**96**	IU/l	(13–60)
ALKP	**2130**	IU/l	(14–105)
GGT	**32**	IU/l	(0–10)
Bilirubin	3	μmol/l	(0–16)
Cholesterol	**10.2**	mmol/l	(3.8–7.0)
Triglyceride	**2.4**	mmol/l	(0.56–1.14)
Creatine kinase	168	IU/l	(0–190)

Urinalysis

Parameter	Value	Units	Range
Appearance	Clear, straw		
Chemistry			
Specific gravity	1.032		
pH	8.1		
Protein	Trace		
Nitrite	–		
Blood / Hb	–		
Glucose	++++		
Ketones	++++		
Bilirubin	–		
Urobilinogen	–		
Cytology			
Red cells	2	/hpf	(0–2)
White cells	1	/hpf	(0–2)
Epithelial cells	0	/hpf	(0–5)
Casts	–		
Crystals	–		
Bacteria	–		
Other			

Questions

1. **How would you interpret these laboratory results in the context of the history and clinical examination findings, and what is this dog's clinical diagnosis?**
2. **How might this have arisen and what further information might be gained to plan appropriate treatment?**
3. **What are this dog's immediate fluid and other medical therapy needs and what problems may be anticipated/pre-empted during the initial stages of treatment?**

Answers

1. **How would you interpret these laboratory results in the context of the history and clinical examination findings, and what is this dog's clinical diagnosis?**
   - The haematology shows a mild neutrophilia, a monocytosis and concurrent lymphopenia and eosinopenia, all components of a stress leukogram. Inflammation may also account for neutrophilia and monocytosis but would not be expected to cause the concurrent lymphopenia and eosinopenia.
   - The biochemistry demonstrates:
     - A marked hyperglycaemia which, with concurrent glucosuria, is consistent with diabetes mellitus.
     - A rise in urea without a concomitant rise in creatinine, which suggests that a pre-renal azotaemia may be present and indeed the urine SG of 1.032 (i.e. > 1.030) is supportive of this.

  - Total protein is marginally elevated, though albumin and globulin are just within the upper end of their respective reference intervals. With the pre-renal azotaemia, haematocrit that is in the upper end of the reference interval and clinical examination findings, this is most likely due to dehydration.
  - A moderate rise in ALT and AST together with a more marked raise in ALKP and GGT is seen. This is likely to represent hepatopathy with a cholestatic component or response to endogenous or exogenous glucocorticoids.

The similarity in biochemistry between diabetic and Cushingoid patients

It is important to remember that such changes in hepatocellular and cholestatic markers are common in untreated diabetic patients due to the effects of hepatic lipidosis induced by insulin deficiency. Such biochemical findings are very similar to those seen in patients with hyperadrenocorticism (in which hepatic glycogen is stored in excess, not lipid) and it is common in the author's experience that veterinary surgeons commonly have suspicion aroused of concurrent hyperadrenocorticism by such findings, rather than considering them an expected effect of untreated diabetes mellitus. Improvement in these with serial biochemical monitoring after institution of insulin therapy is the key differentiator.

  - A hyperlipidaemia comprising rises in both cholesterol and triglyceride is present. This may be present in diabetes mellitus, pancreatitis, hypothyroidism, hyperadrenocorticism, protein-losing nephropathy and cholestasis (though more usually cholesterol only is elevated in these last two).
- Urinalysis demonstrates glucosuria and ketonuria.
  - Remember that urine test strips detect acetoacetate and acetone but not β-hydroxybutyrate.

The patient has been demonstrating polyuria, polydipsia, weight loss and until very recently a healthy appetite. In conjunction with the hyperglycaemia and glucosuria a diagnosis of **diabetes mellitus** can be confidently made. It is unnecessary to perform a fructosamine level to confirm this diagnosis although many clinicians advocate assessment of a fructosamine level at diagnosis for future comparison with subsequent fructosamine levels.

The patient is ketonuric and may be described as diabetic and ketotic. Diabetic ketoacidosis (DKA) has not been established at this time by measurement of blood acid-base status, but the clinical findings of depression, vomiting and recumbency strongly implicate DKA and diagnosis of DKA on clinical grounds may be confidently made.

2. How might this have arisen and what further information might be gained to plan appropriate treatment?

Diabetic ketoacidosis represents part of a continuum of severity of diabetes mellitus from uncomplicated diabetes mellitus to diabetic ketosis (animal is well but ketonuria +/– serum ketones are detectable) to diabetic ketoacidosis (animal is sick and has identifiable ketonuria and serum ketones).

The initial ketone produced is acetoacetate, which is then either converted to β-hydroxybutyrate (BHB, which accumulates and is the principle ketone body in dogs and cats with DKA) or is spontaneously decarboxylated to acetone. Most urine reagent strips only detect acetoacetate and acetone and beyond initial detection of ketonuria, serial use is limited by the fact that BHB

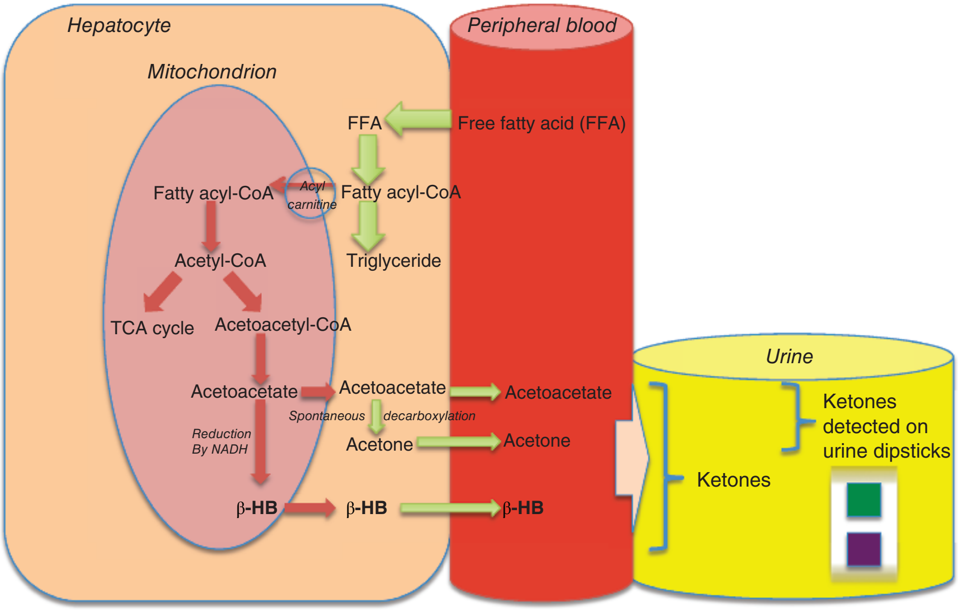

Figure 1.2 Generation of ketone bodies in diabetic ketoacidosis (DKA).

will accumulate due to conversion of acetoacetate over time. β-hydroxybutyrate may be directly measured on a serum blood sample.

Diabetic ketoacidosis develops when the extent of acetyl CoA production after beta-oxidation of free fatty acids liberated by peripheral lipolysis (in response to insulin deficiency and when storage as triglyceride is maximal) exceeds the capacity of the tricarboxylic acid (Krebs') cycle to metabolize to carbon dioxide and water (**Figure 1.2**). Frequently development of DKA is precipitated by a physiologically stressful comorbidity and it is though that development of DKA is usually seen in the setting of both hypoinsulinism and increased counter-regulatory hormone (glucagon, catecholamines, cortisol, growth hormone) production. Examples of comorbidities commonly implicated in DKA are shown in **Table 1.1.**

Table 1.1 Comorbidities commonly associated with development of DKA in dogs

- Pancreatitis
- Urinary tract infection
- Cholangiohepatitis
- Inflammatory bowel disease
- Respiratory tract infection
- Congestive heart failure
- Bacterial pyoderma
- Renal insufficiency
- Administration of insulin-antagonistic medications such as corticosteroids or progestogens
- Hyperadrenocorticism
- Hypothyroidism

In one study of 127 dogs with DKA, 65% were diagnosed at the time of initial diagnosis of diabetes mellitus and 69% of dogs with DKA had one or more comorbidities that may have contributed to the development of DKA. Of these the most common was pancreatitis (41%), urinary tract infection (20%) and hyperadrenocorticism (15%) (Hume et al. 2006).

It is therefore appropriate in patients with DKA to not only warn owners about the likelihood of complicating comorbidities but also to assess for these. Such assessment might include:

- Assessment of urinalysis and urine culture, the latter preferably by cystocentesis
- Assessment for pancreatitis, which may be by
  - Assessment of serological markers
    - Amylase, lipase
    - Pancreatic lipase immunoreactivity (PLI)
    - DGGR lipase
  - Diagnostic imaging of the pancreas, of which pancreatic ultrasound currently has the most utility and balance of cost effectiveness and sensitivity
- Consideration of hyperadrenocorticism (Cushing's syndrome) as a comorbidity

This last is complicated by the considerable overlap in clinical signs (pu/pd, polyphagia) and biochemical findings (hyperglycaemia, hyperlipidaemia, rises in ALT and ALKP due to hepatic lipidosis/glycogenosis) between diabetes mellitus and hyperadrenocorticism and the knowledge that all diagnostic tests for hyperadrenocorticism are affected by non-adrenal illness.

Diabetes mellitus is a 'non-adrenal' illness, which affects tests for Cushing's syndrome

It is important to remember that a positive ACTH stimulation test or low-dose dexamethasone suppression test (LDDST) is compatible with a diagnosis of hyperadrenocorticism *but also* with non-adrenal illness, and diabetic ketoacidosis is a *potent* inducer of false positive results in these tests. Extreme caution must therefore be undertaken with interpretation of these tests in a newly diagnosed sick diabetic dog and the author would recommend against performing tests for hyperadrenocorticism initially.

Certain features, which might lend supportive evidence to the possibility of concurrent hyperadrenocorticism (since they are not usually expected in diabetes mellitus alone), would be development of non-pruritic flank alopecia or development of calcinosis cutis. If abdominal ultrasound examination is undertaken to evaluate the pancreas the opportunity to evaluate both adrenal glands should not be missed (but bearing in mind that normal adrenal gland size does not exclude the possibility of hyperadrenocorticism and that adrenal gland 'incidentalomas' (non-functional benign tumours of the adrenal glands) are not infrequently seen in dogs. If raises in ALKP are provoking consideration of hyperadrenocorticism it is sensible to re-evaluate this after institution of insulin therapy since an improving biochemical picture suggests the waning effects of hepatic lipidosis rather than continued untreated hyperadrenocorticism.

In recognizing that development of DKA usually involves concurrent production of counter-regulatory and insulin-antagonistic hormones, one should also anticipate that with direct therapy (such as in the case of urinary tract infection) or spontaneous resolution with supportive care (such as in pancreatitis), as the source of insulin-antagonism subsides, so the relative insulin sensitivity of the patient is likely to change dramatically. This should be predicted and monitored for lest insulin overdose result due to failure to account for this.

3. **What are this dog's immediate fluid and other medical therapy needs and what problems may be anticipated/pre-empted during the initial stages of treatment?**

   The dog's initial medical needs can be summarised as:

   A. Correction of fluid deficit
   B. Provision of insulin
   C. Correction of acid–base and electrolyte disturbances
   D. Management of concurrent disease

A. Fluid needs

- Fluid loss in diabetic ketoacidosis may be prodigious because
  - Presence of glucosuria prior to onset of DKA causes osmotic diuresis and associated loss of large volumes of total body water.
  - Presence of hyperglycaemia draws fluid from the interstitial compartment to the intravascular compartment.
  - Ketoacids, primarily β-hydroxybutyrate and acetoacetate, not only act to cause further osmotic diuresis, but their strong negative charge causes substantial excretion of cations such as sodium, which in turn 'draws' further water loss with it.
  - Nausea and vomiting cause increased gastrointestinal fluid loss and diminished intake of water and moisture in food.
- An initial fluid plan should assess
  - The degree of dehydration of the patient (often referred to as *replacement requirement*).
  - The ongoing losses, which are
    - Predictable normal losses (often referred to as *maintenance requirement*).
      - Sensible losses (urine, faeces)
      - Insensible losses (respiration, metabolism)
    - Pathological losses (often referred to as *contemporary losses*)
      - Vomit
      - Diarrhoea
  - From what fluid compartments this loss is likely to have occurred/be occurring and to plan to restore this.

Fluid therapy is an 'iterative' process and an accurate prescription, not a guess!

Fluid therapy is not a 'set-up and leave-it' endeavour but an 'iterative' (constantly re-evaluated) prescription. That is, the clinician should base an initial prescription on knowledge of the above and a hands-on physical examination, plan 'way-points' at which to assess the effectiveness of the initial prescription (i.e. is it doing what was intended, at the time expected?) and to then adjust therapy accordingly. Failure to do this, or worse to fall into the unconscionably sloppy habit of considering 'multiples of maintenance' as an adequate prescription of fluids, often results in under-treatment. One of the biggest problems we see in our clinic is patients that have received inadequate fluid therapy because the initial clinician has sought to avoid making what are often perceived as 'tricky' assessments of fluid need, and have instead sought to take simplified 'short-cuts'. In reality these assessments are not tricky at all.

Table 1.2 Physical examination parameters of hydration and perfusion

Parameters that are altered in dehydration	Parameters that are altered in perfusion
Mucous membrane dryness / membrane 'slip'	Mucous membrane colour
Skin turgor	Capillary refill time
Sunken eyes	Extremity temperature
Total body weight	Peripheral pulse pressure and quality / distance
	Heart rate
	Arterial blood pressure*
	Urine output*

*Note. These fall late in the progression of intravascular volume depletion and normal blood pressure or urine output does not preclude severe intravascular volume depletion.

- An estimate of dehydration is based on the physical examination findings. Remember that dehydration is an assessment of loss of total body water. About two-thirds of total body water is intracellular and one-third is extracellular, of which about one-third is intravascular and two-thirds is interstitial. The interstitial compartment is depleted of fluid to maintain vascular fluid volume and thus perfusion and because of this and the relative amount of total body water stored here, signs of interstitial dehydration tend to occur more noticeably before alterations in perfusion. With severe interstitial dehydration, shift of fluid into the intravascular compartment cannot occur and alterations in perfusion are noted. Different physical examination parameters (**Table 1.2**) may tell the clinician about different aspects of these, which is why the hands-on physical examination, its objective and accurate interpretation, recording of this, and serial evaluation (the 'iterative' process of fluid therapy) is essential.

The degree of dehydration may be estimated by evaluating physical examination and historical findings and are listed in **Table 1.3**. Alteration in parameters of perfusion tends to occur with loss of ≥10% of total body water.

Table 1.3 Estimated level of dehydration

Estimated dehydration	History and physical examination findings
≤5%	History of increased gastrointestinal fluid loss but normal physical examination findings
5–7%	Dry mucous membranes, mild loss of skin turgor, normal heart rate and pulse quality, normal mucous membrane colour and capillary refill
7–10%	Dry mucous membranes, loss of skin turgor, sunken eyes, mild increase in heart rate, normal mucous membrane colour and capillary refill, normal pulse quality, normal extremity temperature, normal arterial blood pressure
10–12%	Dry mucous membranes, loss of skin turgor, sunken eyes, tachycardia, pale mucous membranes and extended capillary refill, poor peripheral pulse quality peripherally, clammy extremities, normal arterial blood pressure, depressed habitus
12–15%	Dry mucous membranes, loss of skin turgor, sunken eyes, tachy-or bradycardia, very pale mucous membranes and difficult to discern capillary refill, weak pulses, cool extremities, subnormal arterial blood pressure, altered level of consciousness
>15%	Death

Replacement requirement. In this patient the history and physical examination findings would suggest both interstitial dehydration (dry mucous membranes, sunken eyes, loss of skin turgor) and reduced perfusion (extended capillary refill, raised heart rate, poor peripheral pulse quality, depressed mental habitus) and a 10–12% total body water deficit can be comfortably estimated

- In this patient: (0.12 × 10.4 × 1000) = **1248** ml

Ongoing ***maintenance requirement*** may be estimated as a function of resting energy expenditure (REE) with 1 ml of body water being metabolized for each kcal of REE, calculated by 30 × body weight (kg) + 70

- In this patient being: (30 × 10.4) + 70 = **382** ml/24 hours

This patient is vomiting currently 8 times/24 hours and if we estimate 50–100 ml of fluid/vomit we may predict a further ***contemporary loss*** of

- In this patient: **800** ml/24 hours

Thus, unless the vomiting ceases immediately the overall replacement deficit is 1248 ml and the predicted ongoing losses in the next 24 hours (maintenance + contemporary losses) is a further 1182 ml. This does not, of course, take account of the fact that the underlying pathology leading to such prodigious loss of fluid is unlikely to be corrected immediately, so this total fluid requirement of 2430 ml is likely to represent, if anything, an underestimation of fluid need. This is why it is essential to re-evaluate *by hands-on physical examination*, at frequent way-points whether the physical exam parameters are changing in a way that denotes a positive impact of fluid therapy. Laboratory tools such as blood gas analysis and serum lactate may have their place in offering objective measurements of the success of fluid resuscitation but it behoves clinicians not to be seduced by the frequent performance of these in neglect of more important, cost-effective and physiologically appropriate parameters of goal-led fluid resuscitation such as physical examination parameters. As an instructive exercise, try calculating what the likely deficiency between fluid need and amount of fluid actually given if this animal was simply placed on 'three times maintenance fluid rate' in the first 24 hours of therapy.

- Crystalloid fluid therapy is principally indicated and 0.9% NaCl is usually the fluid of choice since whole-body sodium depletion is frequently present. Potassium supplementation is usually required (see below). Occasionally patients with hypernatraemia may be encountered in which use of a lower sodium fluid such as Hartmann's may be preferred.
- One common strategy is to replace 25% of the total deficit over the first 1–2 hours of therapy, 25% over the next 4–5 hours and then the remaining 50% over the rest of the first 24 hour period.
- The intravenous route is preferred and because of the fluid volume required a securely placed short length, wide bore peripheral intravenous cannula or a central venous line may be considered. Because of the frequently debilitated state of these patients, strict attention to an aseptic technique should be adhered to. Advocates of central venous line placement cite the ability to frequently measure central venous pressure and a limitation of the need for repeat venepunctures for blood glucose assessments, especially with

multi-port central venous lines. This must be weighed up against the risk of complications including thrombosis and sepsis, the need for increased nursing vigilance and the expense associated with these. Ultimately choice depends on appropriateness in the clinical circumstances.

B. Provision of insulin

- Insulin is necessary to
  - Correct hyperglycaemia and provide cellular metabolism with carbohydrate substrate.
  - Reverse the effects of massive lipolysis.
  - Reverse the metabolic effects of ketonemia, ketonuria and glucosuria causing dehydration and metabolic acidosis.
- Short-acting soluble/neutral insulin is preferred initially because
  - Its dosage can be rapidly adjusted dependent on need, allowing the clinician a great deal of control in correction of hyperglycaemia.
  - It may be delivered by the intravenous or intramuscular route and absorption of longer-acting insulins from subcutaneous depot injections may be unpredictable in severely dehydrated patients.
  - It is sensible to initially provide fluid therapy to re-expand the extracellular fluid compartment for 1 to 2 hours prior to instituting insulin therapy to prevent glucose and water shifting from the vascular space intracellularly. Provision of fluid therapy will immediately start to decrease blood glucose levels and start to reverse acidosis.
  - There are two tried-and-tested strategies in neutral insulin administration, the continuous intravenous method and the intermittent intramuscular method.
  - For intravenous method (**Table 1.4**)
    - 2.2 units/kg of neutral insulin is diluted in 250 ml of normal saline and 50 ml of this is run through the giving set.
    - Using an accurate infusion pump, this insulin solution is infused at a rate dependent on the previous blood glucose level. The timing of blood glucose assessment is initially every 1–2 hours with gradual lengthening of this as the rate of insulin administration is decreased.
    - In the original report of this method, once blood glucose decreased below 14 mmol/l, the principle fluid replacement was changed to 0.45% NaCl with dextrose added at 2.5% (blood glucose 8–14 mmol/l) or 5% (blood glucose <8 mmol/l) to prevent hypoglycaemia.

Table 1.4 Intravenous insulin infusion method

Previous blood glucose measurement	Infusion rate of neutral insulin 2.2 units/kg in 250 ml 0.9% NaCl	Reassess blood glucose
>14 mmol/l	10 ml/h	Every 2 h
11–14 mmol/l	7 ml/h	Every 4 h
8–11 mmol/l	5 ml/h	Every 4 h
5.5–8 mmol/l	2 ml/h	Every 2 h
<5.5 mmol/l	Discontinue	Every 2 h

  - For the intramuscular method
    - 0.2 units/kg neutral insulin is administered intramuscularly once then 0.1 units/kg neutral insulin is repeated i.m. every 1–2 hours after measurement of blood glucose.
    - Once blood glucose is <14 mmol/l but >5 mmol/l, a dose of 0.1 units/kg is administered i.m. every 4–6 hours
  - With either method, during this interval fluid deficit correction should be well underway and patients will usually be feeling very much better. Once this occurs, consideration should be given to administration of a longer-acting insulin, such as lente, given subcutaneously twice daily.

C. Correction of acid–base and electrolyte disturbances

- On presentation severe metabolic acidosis (due to both cellular dehydration and the accumulation of ketoacids), severe dehydration and whole-body depletion of potassium and sodium can be anticipated.
- Regular assessment of venous pH, base excess and serum electrolytes is useful to gauge correction and need for supplementation but should be performed at a frequency that is commensurate with the patient's needs and with sensitivity to the likely time-frame of changes in these analytes, not based on overzealous/defensive or protocol-driven recommendations.
- The serum potassium levels may initially appear normal but this may be due to translocation of intracellular potassium into the extracellular compartment as buffering for hydrogen ions, accumulating during metabolic acidosis, in exchange for intracellular potassium.
- With the introduction of both fluid therapy (correction of acidosis) and of insulin (which will drive both glucose and potassium intracellularly), a profound drop in circulating potassium can be anticipated within the first 24 hours of therapy, and should be pre-empted by supplemental potassium administration.
- Potassium in the form of potassium chloride may be added to fluids, but it should be borne in mind that initial fluid resuscitation rates may be necessarily very high and the clinician should take time to calculate the likely rate of potassium administration at any concentration – a dose exceeding 0.5 mmol/kg/h of potassium chloride may be fatal and recommendations include both the amount to be added to fluid and the maximal rate of administration. It is often preferable that this is either given via a separate fluid delivery line/pump or that initiation of potassium supplementation is deferred for the first 1–2 hours of fluid therapy when fluid rates are likely to be at their highest. One recommendation for rate of fluid administration is given in **Table 1.5**.
- Phosphate may also fall rapidly in DKA patients during the initial phases of treatment due to a combination of prior depletion, correction of metabolic acidosis and transcellular shifts. Decreases in serum phosphate <0.5 mmol/l may be associated with haemolytic anaemia,

Table 1.5 Potassium supplementation rate

Serum potassium	Amount added to fluids (mmol/l)	Maximum fluid administration rate (ml/kg/h)
3.6–5.0 mmol/l	20	25
2.6–3.5 mmol/l	40	12
2.1–2.5 mmol/l	60	10
≤2.0 mmol/l	80	7

especially in smaller patients. Decreases in phosphate are less predictable and less common than those in potassium and are frequently delayed 24–72 hours after the onset of treatment. Daily monitoring for phosphate decreases <0.5 mmol/l is recommended during this period and supplementation instituted with potassium phosphate given at 0.02–0.05 mmol/kg/h in normal saline considered if levels fall below this threshold. Great care needs to be taken with phosphate supplementation since hypocalcaemia and tetany may develop from overzealous application.

- The use of bicarbonate in an attempt to hasten correction of metabolic acidosis is controversial and in most circumstances judicious use of fluid therapy and institution of insulin treatment will correct this. Potential detrimental effects of bicarbonate administration include hypotension, decreased oxygen tissue delivery due to the Bohr effect, paradoxical CNS acidosis and so-called 'overshoot' metabolic alkalosis due to coinciding iatrogenic delivery of bicarbonate and metabolism of lactic acid and ketones, which result in endogenous bicarbonate elaboration. Nonetheless, in severely acidotic states (venous pH <7.1, HCO_3 <12 mmol/l), then bicarbonate administration may be considered. Recommendations vary but a dose of 0.1–0.2 × body weight × base excess over 20–30 minutes has been proposed.

D. Management of concurrent disease

- If urinary tract infection is identified, appropriate antimicrobial treatment of this should be initiated, but it should be borne in mind that the insulin-antagonism so resulting from the infection will be reversed. In animals that are already receiving treatment for diabetes mellitus this may result in a lower insulin requirement subsequently than before recognition of the infection.
- This dog has been vomiting frequently and antiemetics such as maropitant, metoclopramide or ondansetron would be helpful in modifying this.
- Management of pancreatitis is essentially supportive and is discussed further in **Case 14.**

Discussion

Diabetic ketoacidosis is a common emergency presentation and such patients challenge many aspects of medical emergency decision making. However, this challenge equally makes such cases extremely rewarding to treat and with appropriate therapy ≥70% of such patients survive to discharge from the hospital. The single factor most closely correlated with outcome is the severity of metabolic acidosis at presentation. Initial fluid therapy and close attention to pre-empting the metabolic consequences of correction of DKA are the keys to a successful outcome and fluid therapy planning and re-evaluation needs to be undertaken carefully.

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