Unusual Endocrine Emergencies- They Don’t Need To Be A Crisis

Presenters:

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Disclosures:

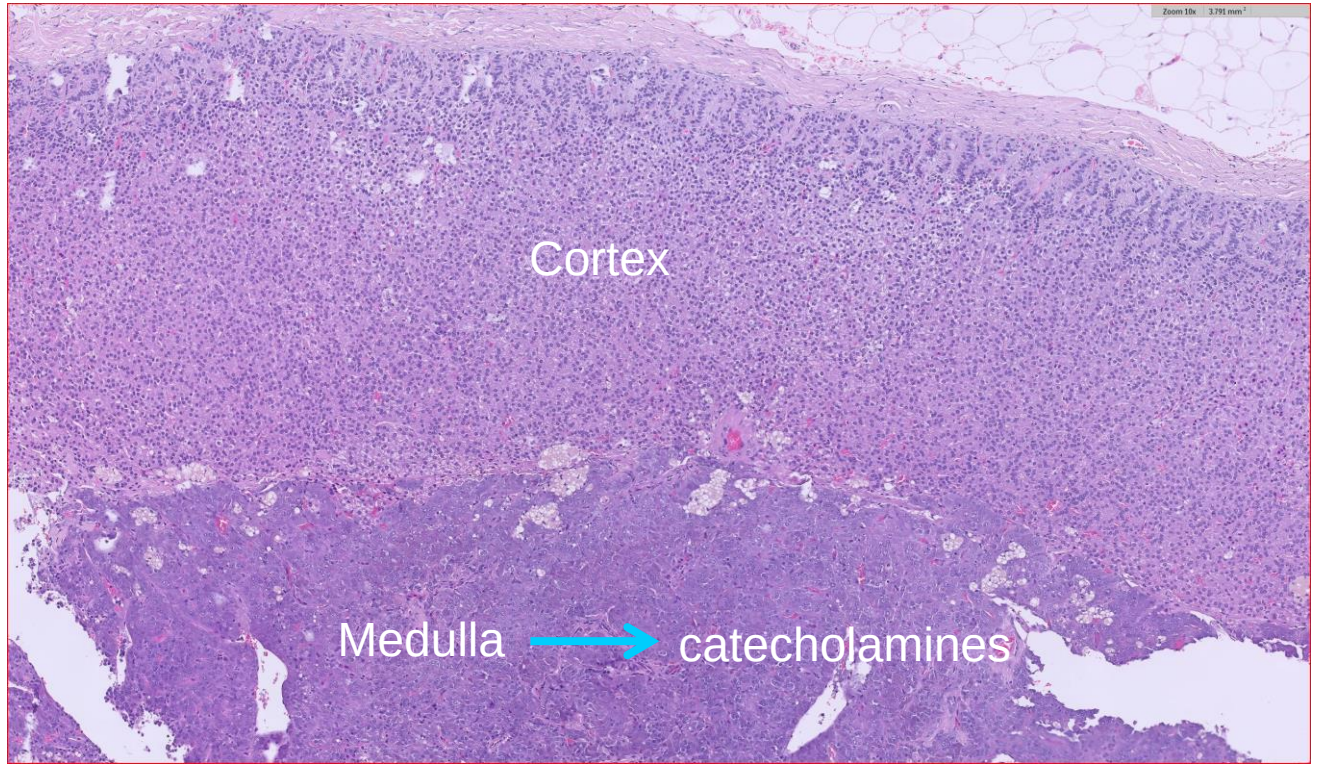
Employee of IDEXX, UK

Employee of AniCura, France

Phaeochromocytoma

Phaeochromocytoma

- Neuroendocrine tumour
  - Chromaffin cells of adrenal medulla
  - Produces catecholamines (adrenaline noradrenaline)
  - Malignant
- Rare
  - 0.01-0.1% of all tumours
- Middle aged to older dogs
  - Usually older than 7yrs
- No sex or breed predilection



Pheochromocytoma

- Tumour of adrenal medulla
  - Secretes catecholamines in response to a physiological stress
- Metastases to regional LNs, liver spleen, lungs etc
- Look for vascular invasion
  - Caudal vena cava, phrenicoabdominal art/vein, adrenal art/vein, renal art/vein
- Concurrent cortical disease can be present

Phaeochromocytoma- Clinical Signs

+ May be asymptomatic
+ Vague and non-specific findings
+ Weakness/lethargy (40%)
+ Arrhythmias (30%)
+ Tachypnoea (25%)
+ Collapse (22%)
+ PUPD (20%)
+ Seizures (8%)

+ Hypertension in only 50% of cases

Galac, S. and Korpershoek, E. (2017), Pheochromocytomas and paragangliomas in humans and dogs. Vet Comp Oncol, 15: 1158-1170. https://doi.org/10.1111/vco.12291

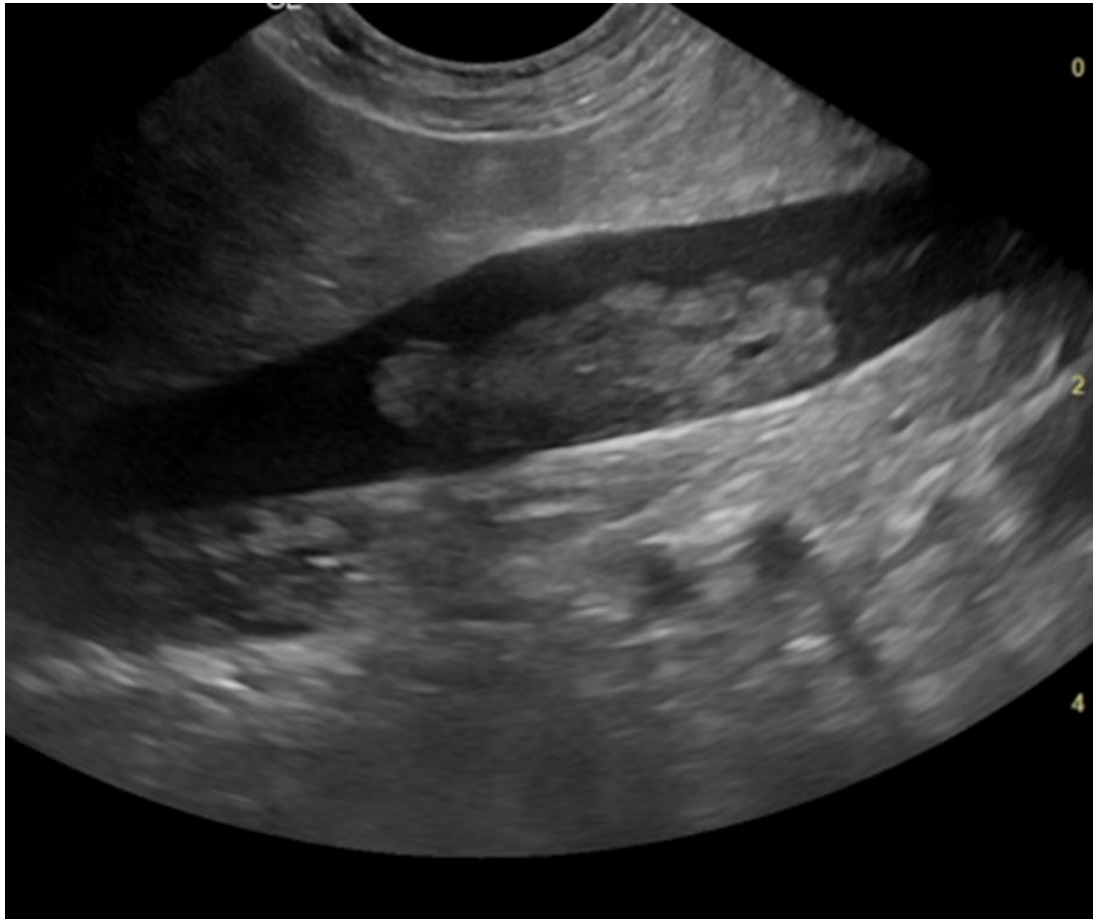
Diagnosis

+ High clinical suspicion
+ Rule out other causes
+ Adrenal mass?
    + Often incidental finding
+ Normetanephrines
+ Histology (special stains)

Baum JI, Boston SE, Case JB. Prevalence of adrenal gland masses as incidental findings during abdominal computed tomography in dogs: 270 cases (2013-2014). J Am Vet Med Assoc. 2016 Nov 15;249(10):1165-1169. doi: 10.2460/javma.249.10.1165. PMID: 27823369.

Imaging Radiography & Ultrasound

- Thoracic rads usually unremarkable
- May see a ST mass on abdo radiographs
  - Only small proportion are mineralised
- Ultrasound
  - Look for vascular invasion
- US guided FNAs possible (under GA)
  - Low complication rate (15.9%)



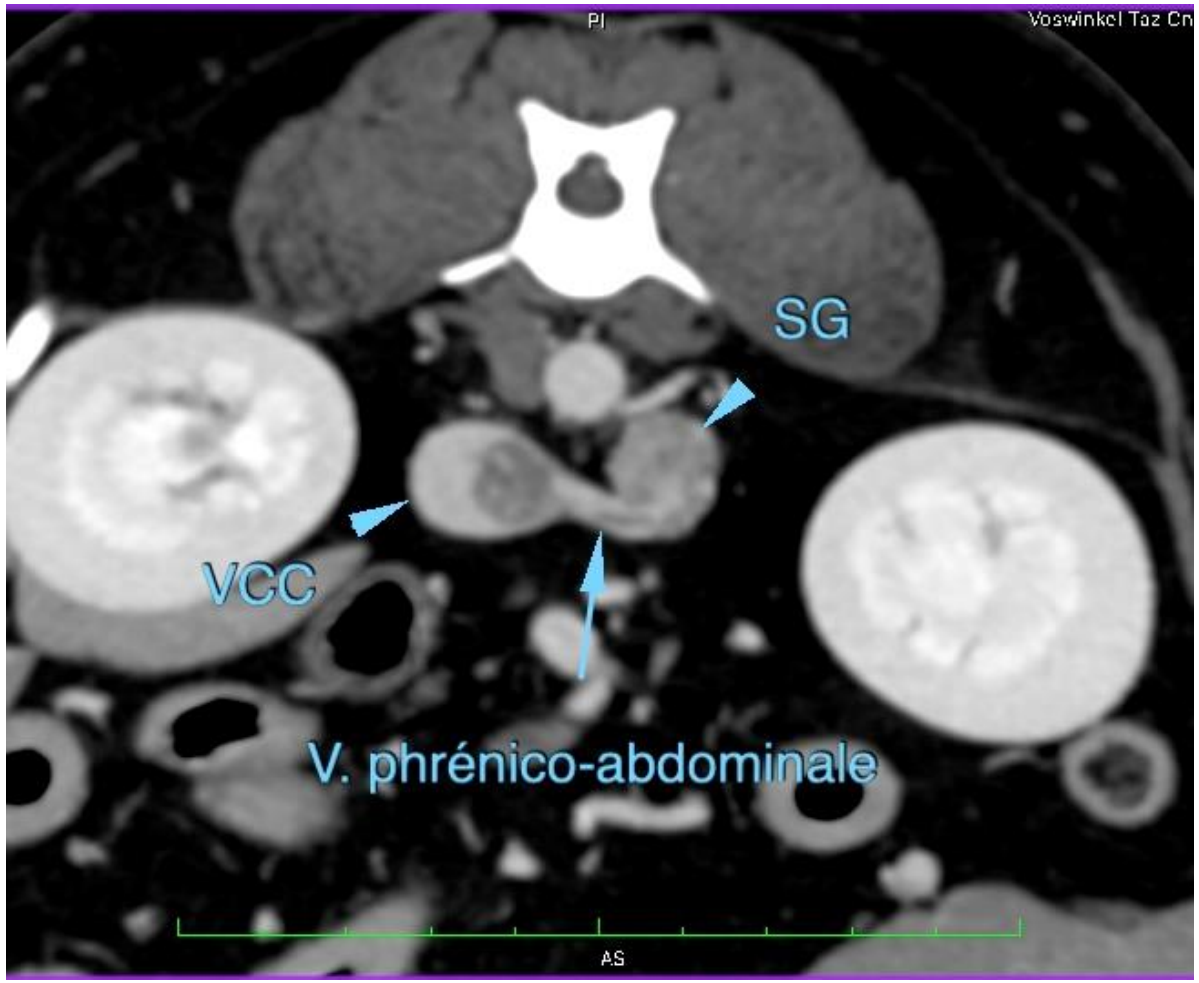
Pey P, Diana A, Rossi F, Mortier J, Kafka U, Veraa S, Groth A, MacLellan M, Marin C, Fracassi F. Safety of percutaneous ultrasound-guided fine-needle aspiration of adrenal lesions in dogs: Perception of the procedure by radiologists and presentation of 50 cases. J Vet Intern Med. 2020 Mar;34(2):626-635. doi: 10.1111/jvim.15743. Epub 2020 Mar 11. PMID: 32159260; PMCID: PMC7096638.

Piegols, H.J., Williams, R.W., Pathak, N., Selmic, L.E., Tremolada, G., Sakacs, R., Millward, L. and Lapsley, J. (2025), Cytologic Evaluation as a Diagnostic Tool to Differentiate Adrenocortical Tumors and Pheochromocytomas. J Vet Intern Med, 39: e70021. https://doi.org/10.1111/jvim.70021

Imaging- CT

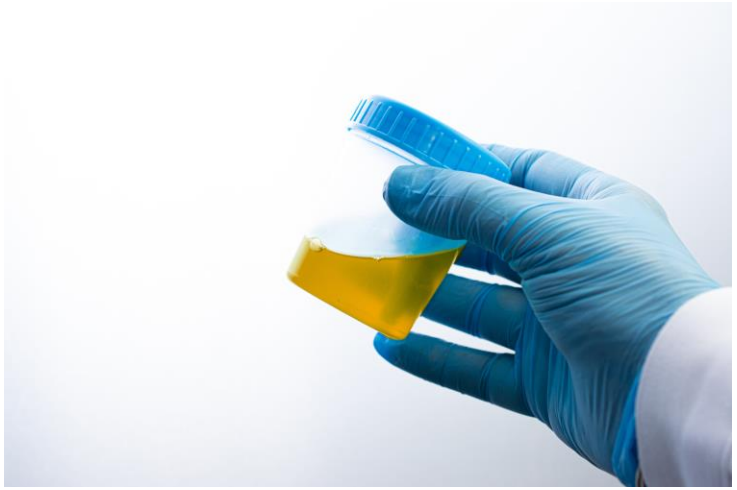
- Adrenal gland enlargement
- Contrast enhancement

- Vascular invasion frequent
  - Caudal vena cava, phrenicoabdominal art/vein, adrenal art/vein, renal art/vein
  - doesn’t preclude surgery



Urinary Normetanephrines

+ 10mls fresh urine
+ Boric Acid



Normetanephrine (Urine) a ~

a. Urine Creatinine 673 umol/l
Urine Normetanephrine 662 nmol/l
Urine Normetanephrine:Creatinine Ratio 984 x10^-6

Comment:
Samples from 5 normal dogs gave a Normetanephrine/Creatinine Ratio (NCR) of < 100.

Dogs with phaeochromocytoma have a very high NCR (> 400) compared to normal young dogs (<100) or those with hyperadrenocortism or non-adrenal disease.

Quante S, Boretti FS, Kook PH, Mueller C, Schellenberg S, Zini E, Sieber-Ruckstuhl N, Reusch CE. Urinary catecholamine and metanephrine to creatinine ratios in dogs with hyperadrenocorticism or pheochromocytoma, and in healthy dogs. J Vet Intern Med. 2010 Sep-Oct;24(5):1093-7. doi: 10.1111/j.1939-1676.2010.0578.x. Epub 2010 Aug 12. PMID: 20707840.

Treatment

- Adrenalectomy
- May require caval venotomy
- Pre-op treatment?
  - Controversial
- Difficult anaesthesia!!!!!!
  - Specialist anaesthetist recommended
  - ICU care after surgery
- Transfusions may be necessary

Pre-op Medical Treatment

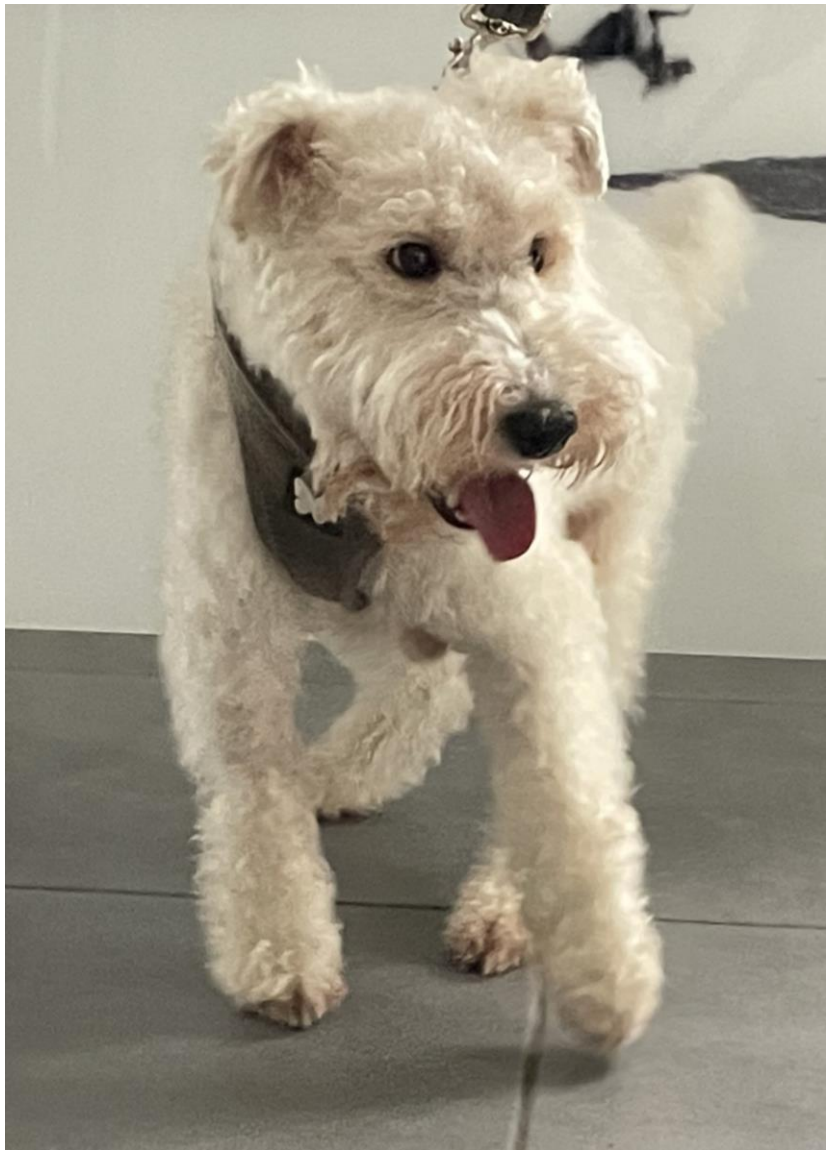
- Phenoxybenzamine?
  - Non-competitive alpha1 and alpha2 blocker
  - 0.25-1 mg/kg PO BID
  - Initially thought to reduce mortality if used for 2 weeks pre-op
  - Later studies did not concur
  - So, we don’t have an agreement!
- Prazosin?
  - Alpha1 blocker
  - Use if phenoxybenzamine not available
- Monitor blood pressure
- Add beta blocker if still tachycardic
  - But only after starting phenoxybenzamine

Intra-operative treatment

+ Magnesium
+ Alpha-blocker (Urapadil)
  + For hypertension
  + Vasodilator
+ Beta blockers if tachycardia
  + Esmolol
+ Lidocaine
  + If dysrhythmia
+ Noradrenaline

Prognosis

- High perioperative mortality?
  - Specialist anaesthetist recommended
- Better prognosis if:
  - Complete resection
  - No obvious metastases
  - Small mass (<3cm)
- Good long-term survival after surgery



If Surgery Not Possible

- Toceranib?
  - Tyrosine kinase inhibitor
- May have some benefit
  - Larger studies needed (only 5 dogs)
  - 1 dog had partial response
  - 4 dogs had stable disease
    - (11-36 weeks)

Research article | Open access | Published: 03 September 2018

Retrospective evaluation of toceranib phosphate (Palladia®) use in the treatment of inoperable, metastatic, or recurrent canine pheochromocytomas: 5 dogs (2014–2017)

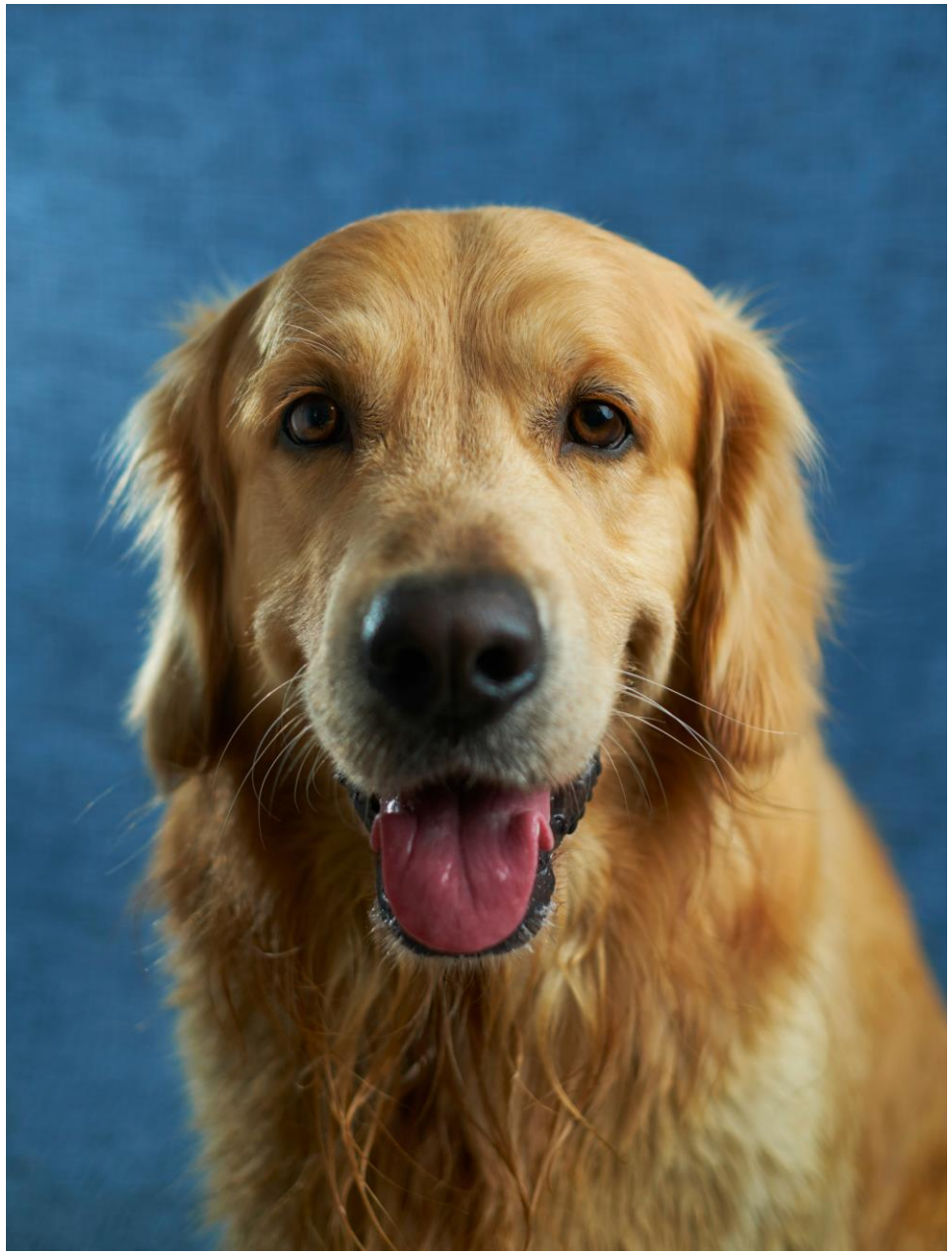
Margaret L. Musser, Kathryn L. Taikowski, Chad M. Johannes & Philip J. Bergman

BMC Veterinary Research **14**, Article number: 272 (2018) | Cite this article

Insulinoma

Insulinoma

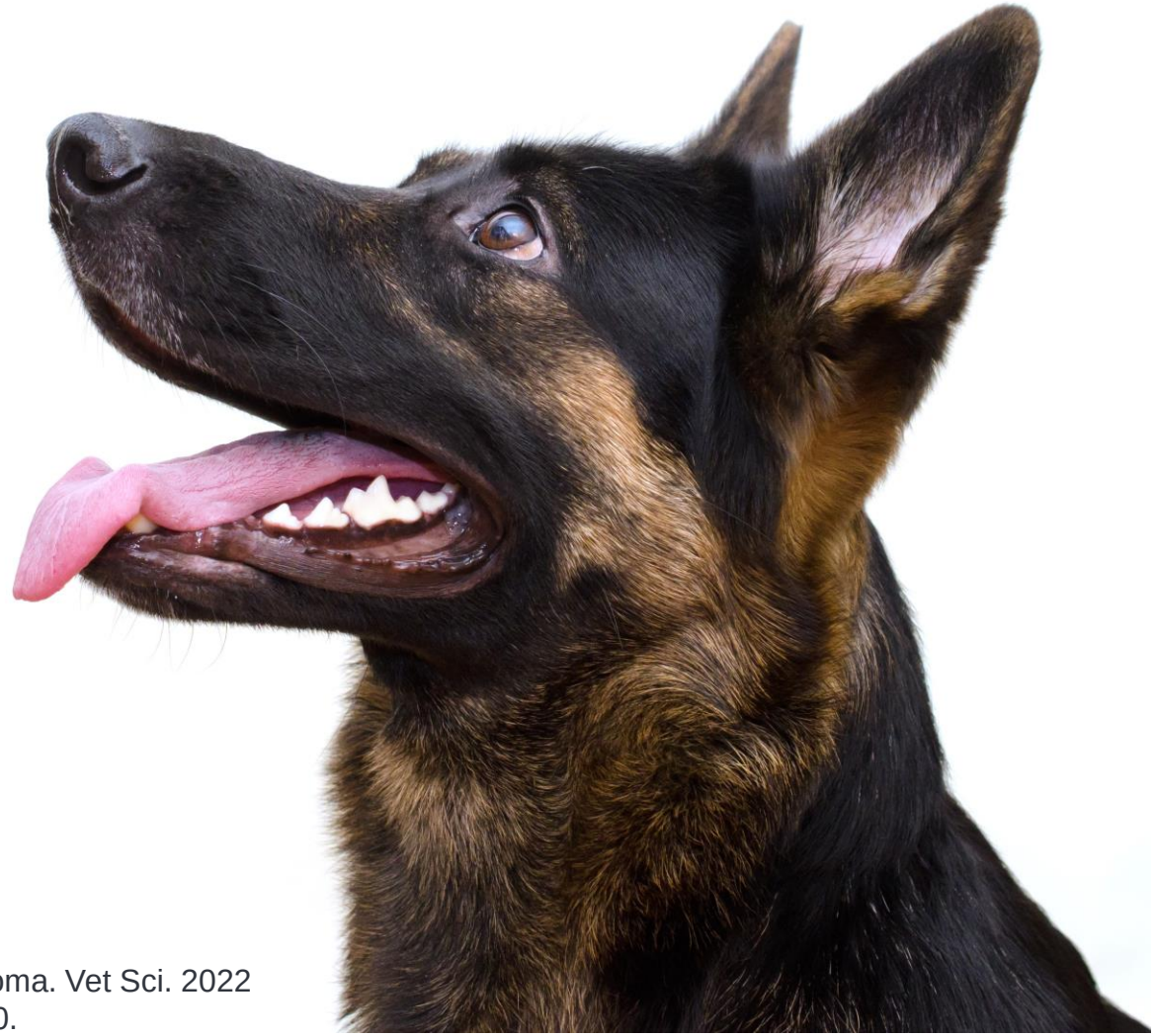
+ Insulin secreting tumour of pancreatic beta cells
+ Malignant in more than 95% cases
+ Small size (usually less than 2.5cm)
+ Left or right limb of pancreas
+ Metastasis usually present at diagnosis



Buishand FO. Current Trends in Diagnosis, Treatment and Prognosis of Canine Insulinoma. Vet Sci. 2022 Sep 29;9(10):540. doi: 10.3390/vetsci9100540. PMID: 36288153; PMCID: PMC9611890.

Signalment

- Older dogs
  - Average age 9 years
- Large breed dogs
  - Boxers, GSDs, Retrievers, Collies
- Occasionally small breed dogs
  - WHWT, Jack Russel



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Pathophysiology

- Hypersecretion of insulin
  - Suppression of hepatocyte glucose secretion
- Causes hypoglycaemia
- Neuroglycopenia
  - Brain uses glucose as its main source of fuel

Clinical Presentation- Neuroglycopenia

+ Generalised seizures (52%)
+ Weakness (42%)
+ Collapse (28%)
+ Shaking/trembling
+ Ataxia
+ Collapse

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Diagnosis

+ Hypoglycaemia!
+ Low fructosamine
  + Can support diagnosis
+ Insulin assay
+ Pancreatic mass
+ Histopathology

Insulin Assay

- Sample MUST be collected at time when sample is hypoglycaemic
  - Blood glucose <3.5mmol/l
- Fast the patient until hypoglycaemia occurs
  - Usually takes less than 24hrs
- Insulin high or normal

Insulin	221.0	5.0 - 40.0 ulU/mL	

ENDOCRINOLOGY

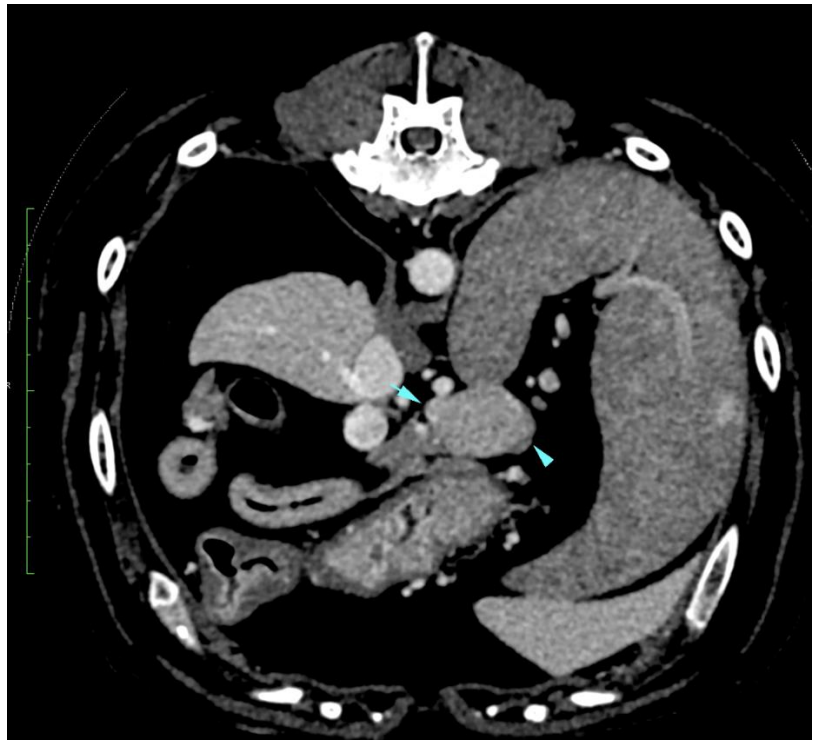
ALERT	TEST	RESULT	UNITS	REF.INTERVAL	
	*Insulin (#)	28.0	ulU/mL	5.0 - 40.0	

Hypoglycaemia- Differential Diagnoses

- Artefact
  - Delayed separation of sample
- Toy breed/juvenile hypoglycaemia
- Addison's Disease
- Hepatic insufficiency
- Portosystemic shunt
- Sepsis

- Non pancreatic neoplasia
  - Hepatocellular carcinoma
  - Leiomyosarcoma
  - Metastatic mammary carcinoma
  - Lymphoma

Insulinoma- Imaging



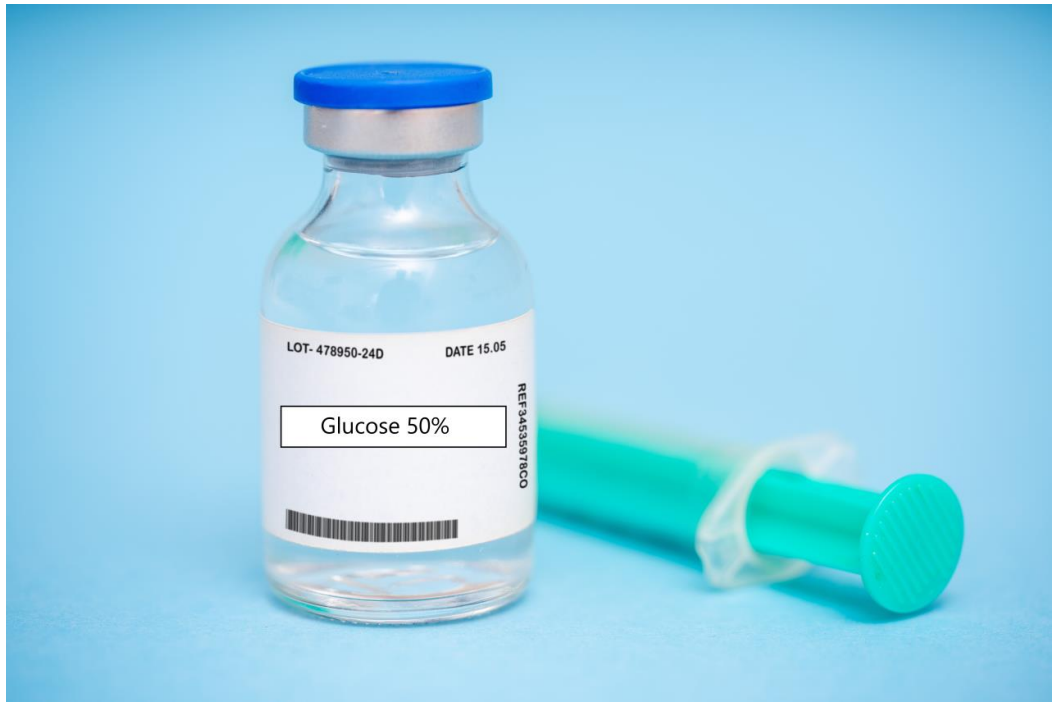
- Ultrasound
  - Low sensitivity (36%)
  - Masses often small
  - Doesn’t allow for staging
  - Does allow of FNAs of enlarged LNs
- Dual Phase CT Angiography
  - Evaluates arterial and venous phases
  - Arterial phase highly sensitive
    - Hyperattenuation
  - Guides surgery

Robben J.H., Pollak Y.W., Kirpensteijn J., Boroffka S.A.E., van den Ingh T.S.G.A.M., Teske E., Voorhout G. Comparison of ultrasonography, computed tomography, and single-photon emission computed tomography for detection and localization of canine insulinoma. J. Vet. Intern. Med. 2005;19:15–22. doi: 10.1892/0891-6640(2005)

Medical Treatment of Hypoglycaemic Crisis

+ Slow 50% glucose infusion
  + (1ml/kg diluted in saline)
+ Feed the patient when alert enough
+ 2.5-5% CRI of glucose if needed
+ Stop glucose when patient asymptomatic!
  + Avoid hyperglycaemia
+ Dexamethasone 0.5mg/kg IV
+ Glucagon bolus and CRI

+ If still seizuring
  + Benzodiazepines



Surgery

+ Treatment of choice
+ Remove mass
+ Remove any visible metastases

+ Chronic medical treatment if surgery not performed

Post-op Complications

+ Pancreatitis in around 10%
+ Failure to resolve hypoglycaemia
  + Likely due to functional metastases
+ Diabetes mellitus in 10-20%
  + Usually transient

Prognosis After Surgery

- Stage 1
  - Tumour confined to pancreas
  - MST of 14 months
- Stage 2
  - Insulinoma spread to local LNs
- Stage 3
  - Spread to distant sites e.g. liver
  - MST of 6 months
- Better prognosis if hyperglycaemic or normoglycaemic post-op

Medical Treatment Of Insulinoma

- Small frequent meals
  - 4-6 meals per day
  - High in protein, fat and complex CHO
  - Low in simple CHO (avoid soft moist dog foods)
- Limit exercise
- Prednisolone
  - Increases gluconeogenesis
  - 0.2-0.5mg/kg/day

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Other Medical Therapies For Inoperable Cases

- Toceranib
  - Tyrosine kinase inhibitor
  - Proven clinical benefit
    - 67% dogs had CR or PR or stable disease
    - MST 656 days
- Diazoxide
  - Enhances hepatic glucose production
  - Reduces insulin release by beta cells
  - 10-40mg/kg/day divided BID or TID
- Steptozocin and ocreotide
  - No longer recommended
  - Variable response

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Galac, S., Fracassi, F. (2025). Canine Endocrinology: Veterinary Internal Medicine Series. (n.p.): Edra Publishing.

Euglycaemic Ketoacidosis in Cats

EDKA Definition

Euglycaemic diabetic ketoacidosis is:

Presence of acidosis, increased plasma or urine ketones and euglycaemia

Euglycaemic DKA

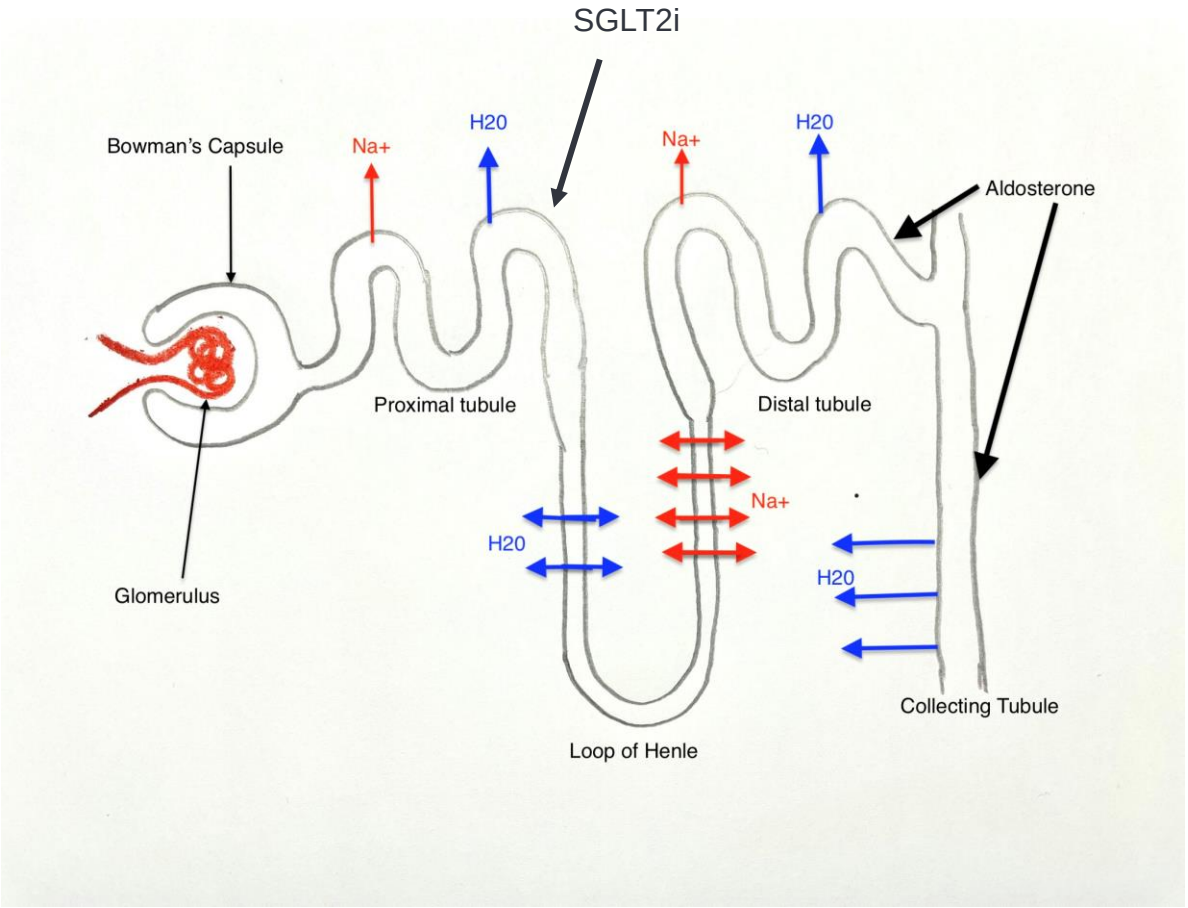
- Emerging condition
  - DKA but euglycaemic
- Can follow use of SGLT2 inhibitors (velagliflozin)
  - Usually in first 2 weeks after starting Tx
  - But can occur at any time
- Occurs in 5-7% cats receiving SGLT2i
- Higher risk if:
  - Concurrent disease
  - Prolonged period of untreated DM
  - Ketones present
  - Previous insulin treatment
- Difficult to diagnose

Pathogenesis

- Hepatic glucose production decreases when diabetic patient stops eating
  - Underlying condition often present
- Carbohydrate depletion
- Lack of insulin-induced inhibition of lipase may increase lipolysis and FA production
  - Leads to ketone production
- Lower blood glucose, carb deficit, osmotic diuresis→ fluid loss

SGLT2 Inhibitors (Velagliflozin)

- Oral hypoglycaemic
  - Once daily oral solution
- Promotes glycosuria
  - Inhibits tubular reabsorption of glucose
  - Block glucose mediated Na reabsorption in proximal convoluted tubule (SGLT2)
  - Lowers blood glucose
  - Minor inhibition of SGLT1- prevents hypoglycaemia developing
- Can be used in diabetic cats that have never received insulin or diabetics previously treated with insulin
  - Higher risk of eDKA if pre-treated with insulin or co-morbidities



SGLT Inhibitors- Contraindications

- Do not use if blood ketones or urine ketones present
- Do not use in sick/unstable diabetics
- Do not use if
  - Clinical pancreatitis
  - Cachexia
  - Diarrhoea

Treatment with Velagliflozin

- Once daily oral solution (1mg/kg)
  - Use in healthy diabetics
  - Glycaemic control often achieved within a week
- Day 0
  - Clinical exam and check for ketones
- Day 2-3
  - Owner checks for ketones
- Day 7
  - Clinical exam and check for ketones
- Day 14
  - Clinical exam and check for ketones
- Day 28 and then every 3 months
  - Clinical exam and fructosamine and check for ketones and UTI

Adverse Effects of SGLT2i

+ Vomiting and diarrhoea
  + Usually self-limiting
+ Ketosis or diabetic ketoacidosis
+ Pancreatitis
+ Hypercalcaemia
+ Hyperlipidaemia
+ Urinary tract infection
+ Rarely hypoglycaemia

+ Lack of response
  + In 10-20% of cases

When To Stop SGLT2 Inhibitors

- Anorexia or hyporexia
- Dehydration or weight loss
- Increase in ketones during treatment
- Poor response to treatment by 8 weeks
  - Poor glycaemic control
  - Increased fructosamine
- Diarrhoea unresponsive to supportive treatment

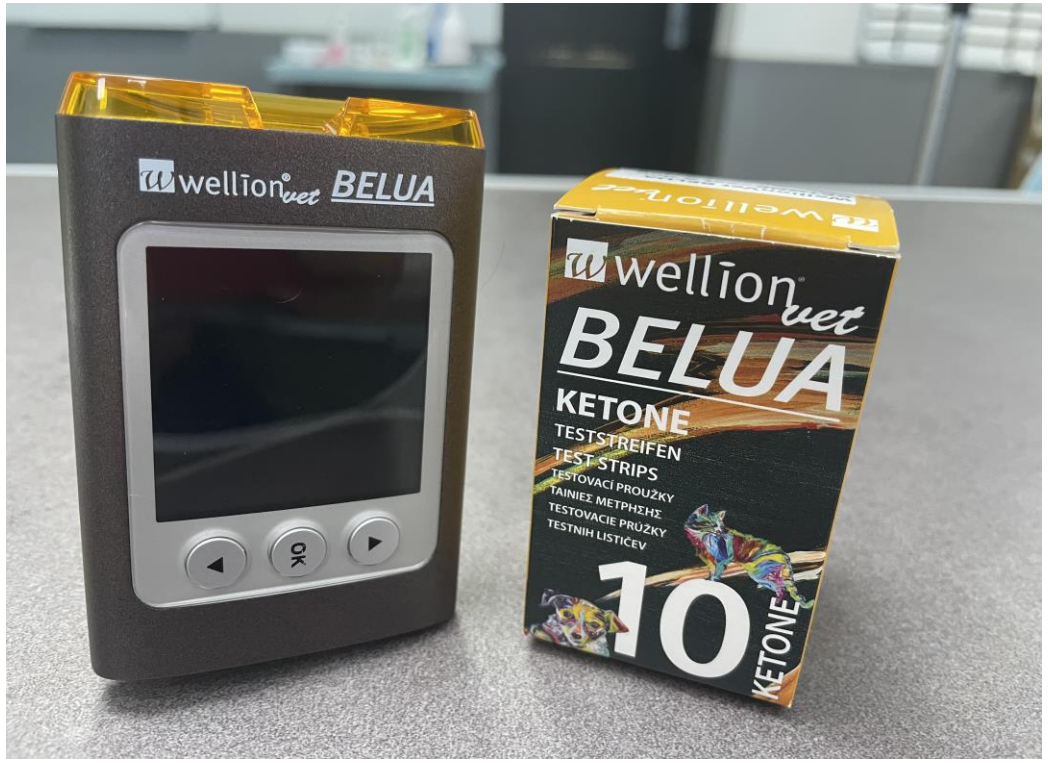
Clinical Signs of eDKA

+ Lethargy
+ PUPD
+ Reduced appetite
+ Vomiting
+ Dehydration
+ Neurological signs
+ Normoglycaemia

+ May be hypoglycaemic if anorexic

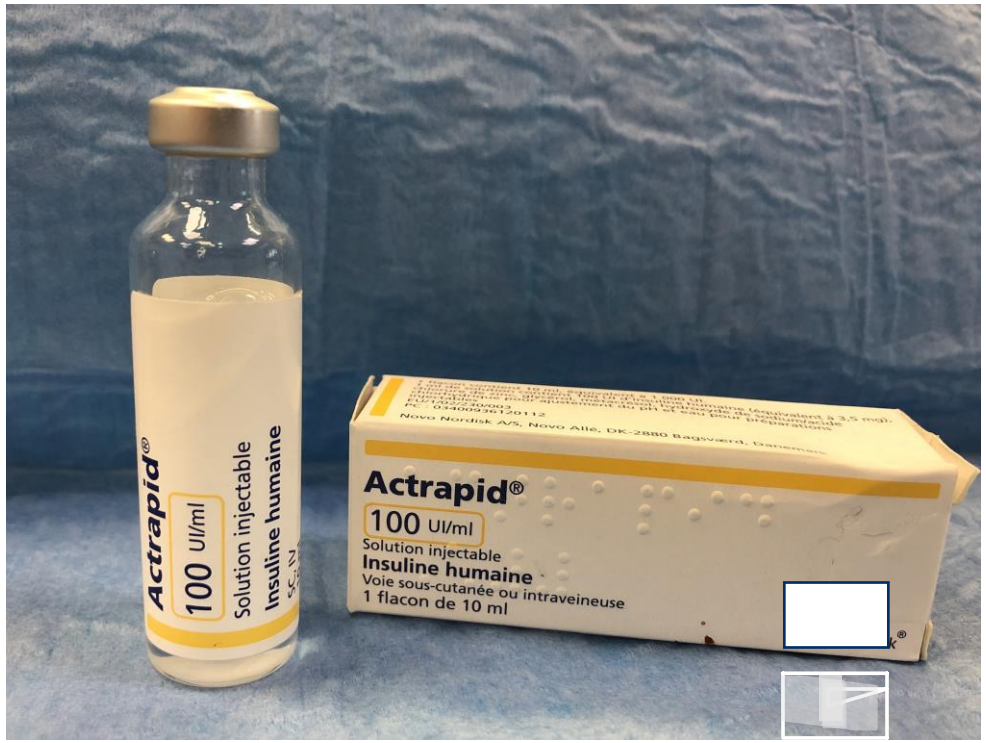
Diagnosis of eDKA

- Relative euglycaemia
  - Glucose less than 13.9mmol/l (or 250mg/dL)
- Acidosis (or sick animal in absence of blood gas analyser)
- Ketosis
  - BHB >2.4mmol/l (25mg/dl)
    - Ketone meters available
  - Ketonuria (sticks do not detect BHB)



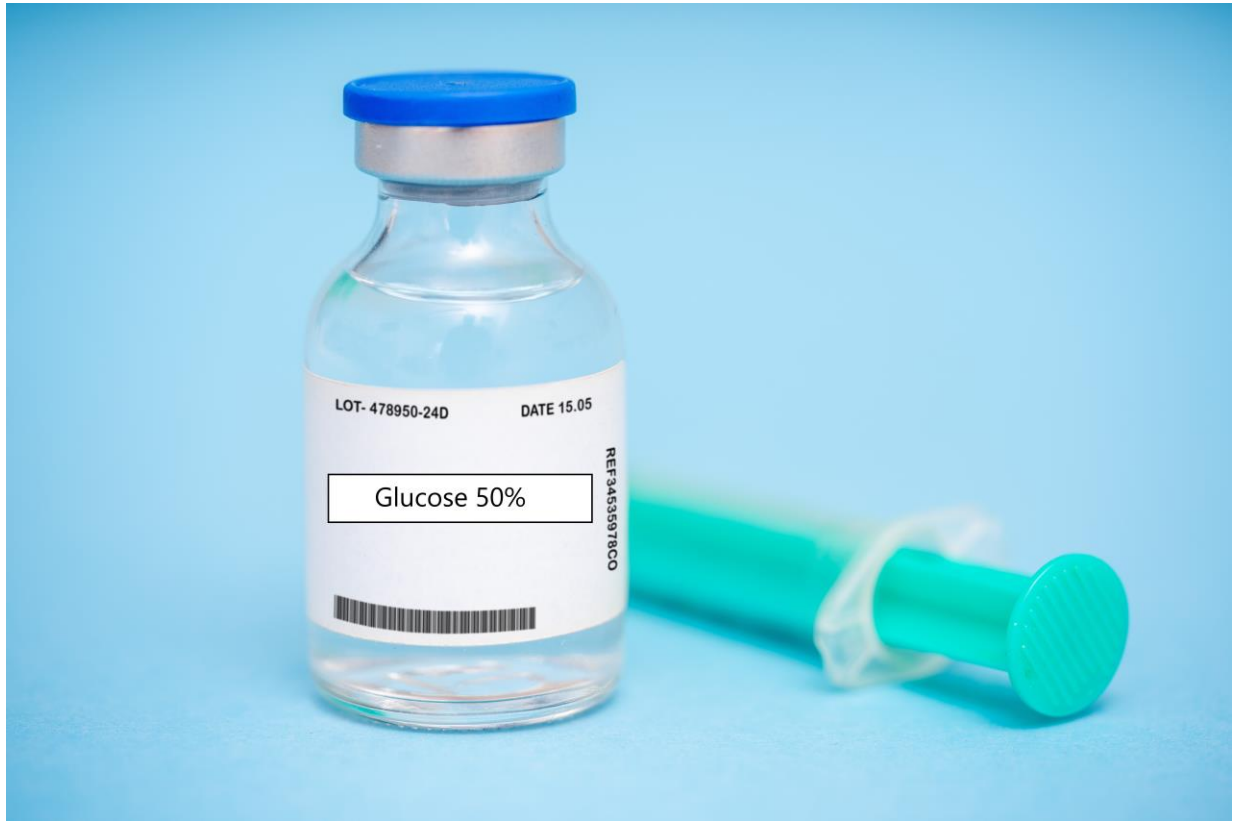
Treatment eDKA

- Stop SGLT2 inhibitors!
- Fluid therapy
- Electrolyte supplementation
  - Aggressive KCl supplementation
- Regular insulin administration
  - Once K >3.4mmol/l
- Glucose administration if BG <14mmol/l
  - Often high concentrations needed
- Nutritional support
  - Carbohydrate rich??
  - Avoid progression to hepatic lipidosis
  - Feeding tube
- Identify & treat concurrent disease



Differences from Hyperglycaemic DKA Management

- Glucose may be normal or even low
- Often requires aggressive glucose supplementation
  - Glu 5-10% solution CRI
- Higher emphasis on nutrition
- Effects of SGLT2 inhibitors can last several days after treatment has been stopped



Thanks for coming.

Notes are available at the IDEXX booth