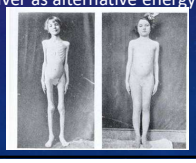
MANAGEMENT OF FELINE DKA: A STEP-BASED APPROACH

Yaiza Forcada DVM PhD DECVIM PGCertVetEd FHEA MRCVS

1

DKA

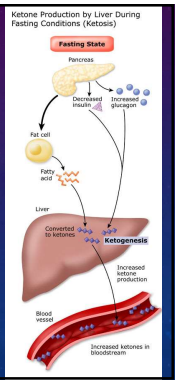
- Lethal prior to discovery of insulin (1920)
- Current mortality rate in humans 5-10%!
- Glucose deficiency: oxidation NEFA by liver as alternative energy source



2

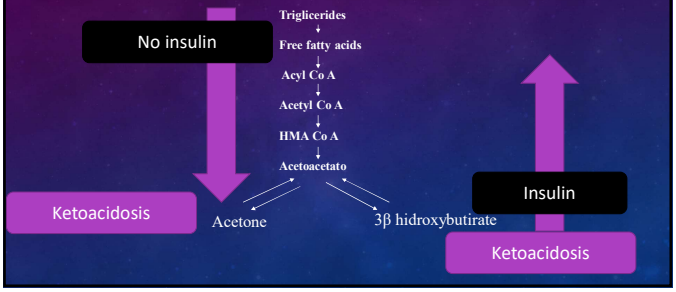
DKA: PATOPHYSIOLOGY

- Relative/absolute Insulin deficiency:
  - Glucose cannot enter cells
  - Survival mechanisms activated
    - Glucose is made from aminoacids
    - Fat deposits get used to feed cells: Fatty acid oxidation
  - Favourable conditions for ketogenesis
    - Fatty acids get mobilised
    - Liver: metabolic changes from fatty accumulation to usage
    - Insulin inhibits lipolysis and fatty acid oxidation



3

BIOCHEMISTRY OF KETONES



4

ESSENTIAL QUESTION

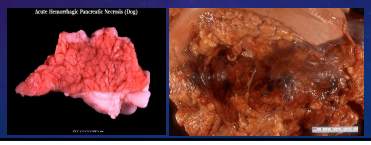
- Is this cat clinically ill and ketotic?
  - YES: DKA: needs intensive care (aggressive treatment, insulin, electrolytes, test, etc.)

  - NO: DIABETIC KETOSIS treat like a normal diabetic

5

ANOTHER ESSENTIAL QUESTION

- Why is this happening now?
  - Which was the factor that pushed this cat in to DKA? (undiagnosed DM, pancreatitis, problems with insulin, others?)
- Can we do anything to eliminate this factor?



6

7

DIAGNOSIS OF DKA

- Ketonuria and ketonemia
  - False negatives are possible with urine sticks
  - Human urine sticks: measure acetoacetate, no BH-butyrate
  - Care in patients with circulatory collapse
- Acidosis
- Diabetes mellitus

8

DKA: ADDITIONAL DIAGNOSTIC ASPECTS

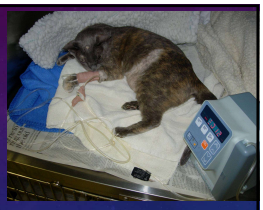
- Initial bloods (minimum database):
  - Urinalysis
  - PCV-TS
  - Glucose
  - Venous blood gas
  - BUN/Crea, electrolytes, Ca, Phos
- Additional tests depending on clinical signs/concurrent diseases
  - Radiographs, abdominal US, fPLI, etc.

9

Case: Poppy

10

"POPPY" 12YO FN DSH



- Long term diabetic
- 2 iu BID Glargine
- Diabetic diet
- Variable appetite for a while
- Now: 2 days anorexic, lethargic, vomiting
- Examn: depressed, FC 240/min, RR 40, T:37.2C, rest: no obvious findings

11

URGENT BLOODS

	Result	Reference
Total solids	85 ***	61-80 g/l
Albumin	3.8 ***	2.3-3.1 mg/dl
Globulins	4.0	2.5-4.6 mg/dl
Urea	46 ***	10-32 mg/dl
Creatinine	2.0 ***	0.6-1.4 mg/dl
Bilirubin	1.2 ***	0-0.3 mg/dl
Sodium	148	142-150 mmol/l
Potassium	3.9	3.8-5.3 mmol/l
Chloride	111	110-124 mmol/l
ALP	680 ***	1-114 U/l
ALT	210 ***	10-109 U/l
Glucose	504 ***	60-110 mg/dl
pH	7.26 *	7.30-7.40
pCO2	20 **	33-52
pO2	37	28-61
Urine	Glucose +, ketones+++	

12

POPPY

	Result	Reference
Total proteins	85	61-80 g/l
Albumin	3.8	2.3-3.1 mg/dl
Globulins	4.0	2.5-4.6 mg/dl
Urea	46	10-32 mg/dl
Creatinine	2.0	6-1.4 mg/dl
Bilirubin	1	3 mg/dl
Sodium		50 mmol/l
Potassium		mmol/l
Chl		110-124 mmol/l
		1-114 U/l
		10-109 U/l
	56	60-110 mg/dl
	7.26	7.30-7.40
	20	33-52
pO2	37	28-61
Urine	Glucose +++ ketones+++	

Poppy: DKA

13

WHICH IS THE MOST IMPORTANT INITIAL STEP IN MANAGING DKA?

1. Fluid-therapy
2. Insulin
3. Supportive treatment
4. Bicarbonate
5. Monitoring

14

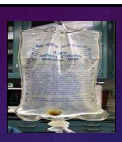
MANAGEMENT OF DKA

1. Fluid-therapy
2. Insulin
3. Supportive treatment
4. Bicarbonate
5. Monitoring

It is more than just insulin!!!

15

1. FLUID-THERAPY



- As or more important than insulin
  - Rehydration
  - Stops tissue lipolysis
  - Improves elimination of ketones through diuresis
- Type: NaCl 0.9% initially (care with fluids low in Na)
- Infusion rate: 60-100 ml/kg/24hrs
  - Hydration status
  - Urine production
  - Additional losses (vomit, diarrhoea, etc.)

16

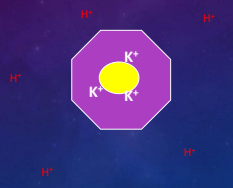
1. FLUID-THERAPY

- K supplementation: based on initial measurement and regular monitoring: if unknown, add 40 mmol KCl/l
- Phos supplementation: if PO_4 < 0.5 mmol/l or if signs of hemolytic anemia
- Phos: CRI 0.01-0.03 mmol/kg/hr in fluids without Ca (0.9% saline)
- Another option: 20 mmol/l KCl + 20 mmol/l KPO_4
- Dextrose: not until Gluc <15 mmol/l, then 2.5% dextrose in the fluids

17

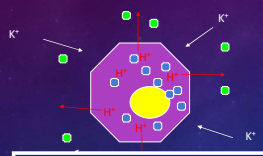
1. FLUID-THERAPY

- In acidosis



18

1. Fluid-Therapy

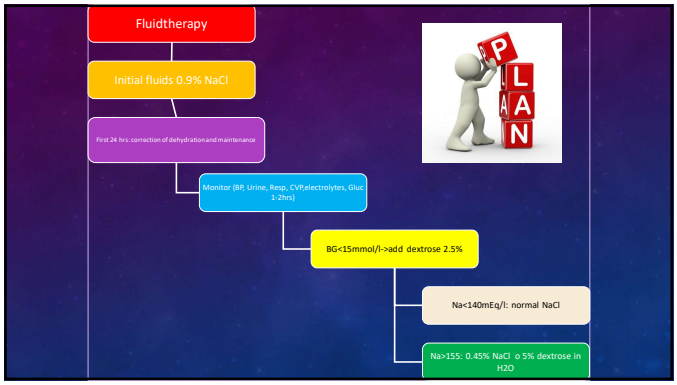


Main reasons:

- 1. Improvement of acidosis
- 2. Insulin

The K will always go down!!!

19



20

MANAGEMENT OF DKA

1. **F**luid-Therapy
2. **I**nsulin
3. **S**upportive treatment
4. **B**icarbonate
5. **M**onitoring

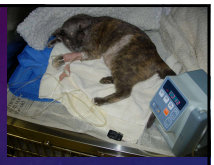
21

2. INSULIN

- Type: regular/neutral/soluble
- IM insulin protocols
  - Initial dose 0.2 iu/kg IM
  - After this: 0.1 iu/kg IM q 1h
  - Until glucose 10-15 mmol/l, then
    - IM 0.1-0.4 iu/kg q 6-8hrs (If well hydrated: SC)
    - We start dextrose IV @ 1-2x mantenance
    - If Gluc >15 mmol/l, adjust insulin/dextrose
    - If Gluc <10 mmol/l, adjust insulin/dextrose
  - If the cat improves and starts eating: change to routine insulin protocols of SC insulin q12h

22

2. INSULIN



- IV Insulin protocol (using infusion pump)
- Advantages:
  - Beter control of insulin blood concentration than with IM protocol
  - Bioavailability is more predictable
  - We can correct quickly if the glucose drops quickly
  - Less labour intensive
  - Less stressful?

23

2. INSULIN (IV PROTOCOL)

- Initial dose 0.05-0.1 iu/kg/hr
- Prepare solution: 25 ui in 500ml NaCl=25/500=0.05 iu/ml
  - ->1ml/kg/hr=0.05 iu/kg/hr
- Separate giving set (or with T-connector)+ allow solution to run 30 seconds/50ml to attach to plastic.
- Goal is to reduce glucose around 2 mmol/l/hr (NOT MORE)
- When glucose 10-15 mmol/l: halve insulin infusion rate + start 0.9% NaCL + 2.5% dextrose at 2x maintenance to keep glucose stable.

24

WHY DO WE NEED TO ADD DEXTROSE WHEN THE GLUCOSE STARTS TO GO DOWN?

A. Because insulin is working and we want to prevent hypoglycemia
B. Because the cells need extra energy in cases of DKA
C. Because dextrose promotes ketolysis

25

2. INSULIN

Revert ketogenesis

↓

Patient feels better

↓

Starts eating

↓

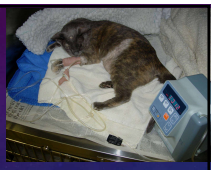
Insulin SQ 0.1-0.4 ui/kg q 6-8h

↓

Traditional protocols become possible

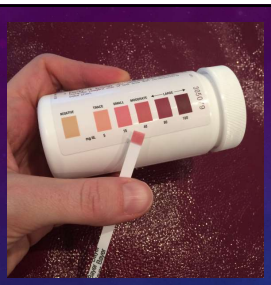
26

POPPY: WE START TREATMENT



- Fluid-Therapy NaCl 0.9%
- Supplementation with KCl & KPhos total 40 mEq/l K
- Start insulin IV (5Kg)
  - 5 IU insulin in de 500 ml NaCl 0.9%
  - Empezamos a 5 ml/hr (1 ml/Kg/hr: 0.05 ui/Kg/Hr)

27



Ketones at admission

Ketones 2h after treatment started

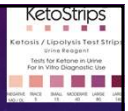
28

WHAT IS HAPPENING???

A. We got the diagnosis wrong
B. We need to give more insulin
C. Sign that the treatment is working
D. We need to start giving dextrose

29

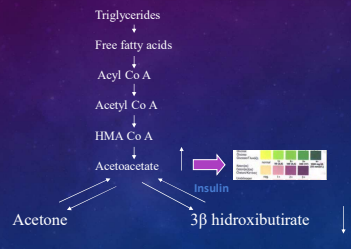
DIAGNOSIS DKA



- Diagnosis DM + Acidosis
- Ketonuria/Ketonemia
- Urine nitroprusside strips measure acetoacetate +acetone
- The don't measure B-OH-Butyrate!
  - Clinical implications:
    - In cases of circulatory collapse→→lactic acid ↑ →→redox potential Δ →→BOH-But ↑ + Acetoacetate ↓
    - Initial increase of ketone bodies in urine means: B-OH-But→→ Acetoacetate

30

PHYSIOLOGY OF DKA



31

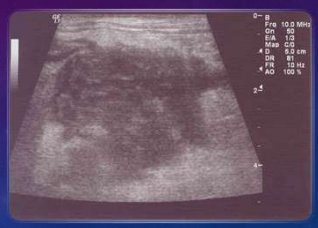
MANAGEMENT OF DKA

1. Fluidtherapy
2. Insulin
3. Supportive treatment
4. Bicarbonate
5. Monitoring

32

POPPY: ADDITIONAL TESTS

ABDOMINAL US



fPLI: >30 umol/l (0-3)

33

3. SUPPORTIVE TREATMENT

- Management of concurrent disease: pancreatitis!
  - FT, analgesia
    - 0.02 mg/kg Buprenorphine SC/IV
  - Anti-emetics
  - Antacids
  - UTI: Broad spectrum antibiotics

34

- Mortality of cats and dogs with DKA is 30 - 40%
- This high mortality rate partly due to the presence of concurrent disease
  - Important to investigate these!!!

35

MANAGEMENT OF DKA

1. **F**luid-therapy
2. **I**nsulin
3. **S**upportive treatment
4. **B**icarbonate
5. **M**onitoring

36

4. BICARBONATE THERAPY

- Not necessary in most cases
  - Fluids and insulin correct acidosis
  - 1 mEq of HCO_3 generated per each mEq of ketoacid
- It can cause problems!
  - Adverse effects HCO_3^-: worsening hypoK, cause paradoxical CNS acidosis, delaying lactate and ketones elimination

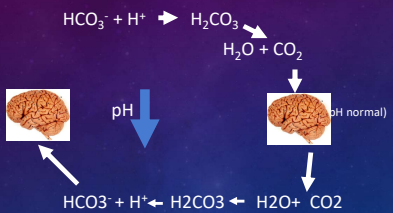
ONLY if HCO_3^-<12 mEq/l o venous CO_2 <12mmol/l

37

WHAT IS PARADOXICAL CNS ACIDOSIS IN DKA?

A. Comatous state in which ph in CNS is really low
B. Neuronal destruction due to excess of protons induced by lipolysis
C. Proton migration through the blood brain barrier
D. Excess CO2 production after administering of bicarbonate, which crosses the blood brain barrier

38



39

4. BICARBONATE

- If in doubt: DO NOT administer unless cat is critical and even so, only give one dose and focus on other treatment aspects.
- Dose: HCO_3^-(mEq): Weight(kg)x0.4x(12-HCO_3^- pacient)x0.5
- If we do not know HCO3 concentration: HCO_3^-(mEq): Weight(kg)x2
- Add to Fluid-therapy and give over 6h, NEVER bolus
- Repeat only if HCO_3^-<12 mEq/l after de 6h

40

MANAGEMENT OF DKA

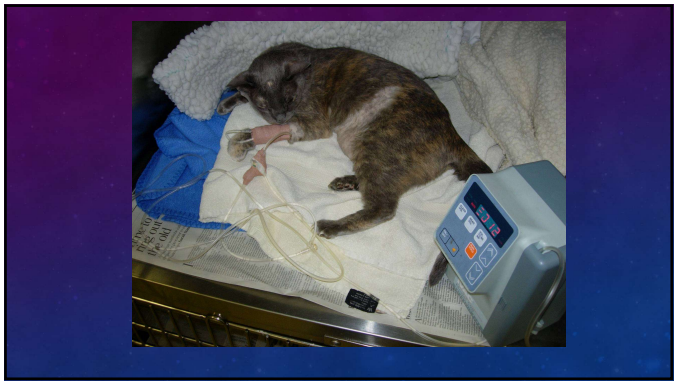
1. **F**luid-therapy
2. **I**nsulin
3. **S**upportive treatment
4. **B**icarbonate
5. **M**onitoring

41

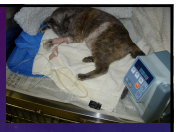
5. PATIENT MONITORING

- Glucose initially q 1-2h
- Adjust insulin+ Start dextrose when <12-15 mmol/l
- Hydration, respiration, pulse q2-4 hrs
- Electrolytes (K+PO4!) + CO_2/pH q 4-12 hrs
- Urine production, glucosuria, ketonuria q 2-4 hrs
- Weight (Fluid overload!), Hematocrit (haemolysis), temperature (sepsis, shock, infection), Blood pressure q12-24h
- Additional monitoring depending on concurrent pathology
- **Monitoring is the key to the success of DKA!!!**

42



43



"POPPY"

	2am	6am	Normal
pH	7.28	7.36	7.36-7.47
pCO2	25	35	33-52
Hct	41	37	37-55
Na	145	148	140-153
K	3.8	3.4	3.6-4.6
Cl	118	115	106-120
BG	504	180	4-6
Urea	15	9	3-10
Creat	185	145	50-140
Plasma Ketones	+++	++	-ve

rsens……

44

WHAT IS HAPPENING?

A. We were not quick enough treating the acidosis

B. The ketone bodies haven't disappeared quickly enough

C. She may have CNS disease

D. She may have renal failure

E. Other

45

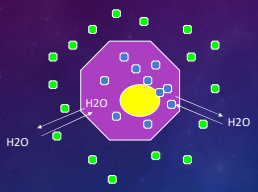
"POPPY"

- Complications
  - Lowering the BG too quickly leads to brain edema

Maximum drop 30-50 mg/dl/hr or 2-3 mmol/l/hr

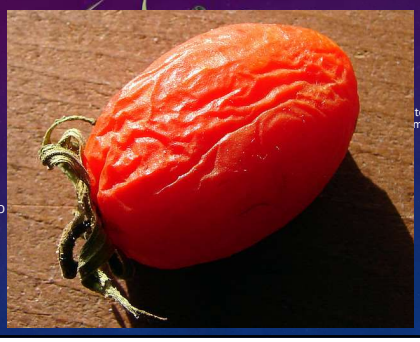
	2am	6am	Noraal
pH	7.28	7.36	7.36-7.47
pCO2	25	35	33-52
Hct	41	37	37-55
Na	145	148	140-153
K	3.8	3.4	3.6-4.6
Cl	118	115	106-120
BG	504	180	4-6
Urea	15	9	3-10
Creat	185	145	50-140
Plasma Ketonen	+++	++	-ve

46



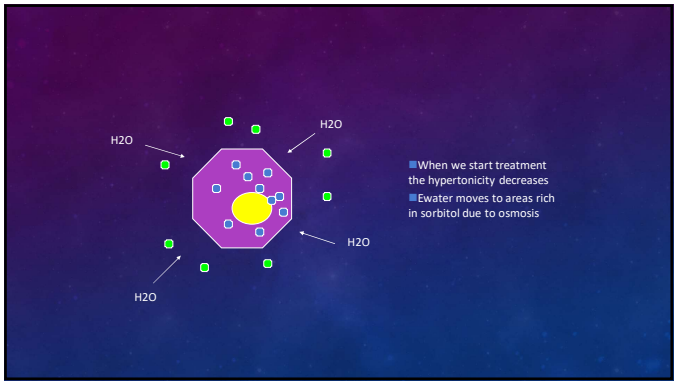
During hyperglycemia the brain makes sorbitol to protect itself from osmotic changes

47

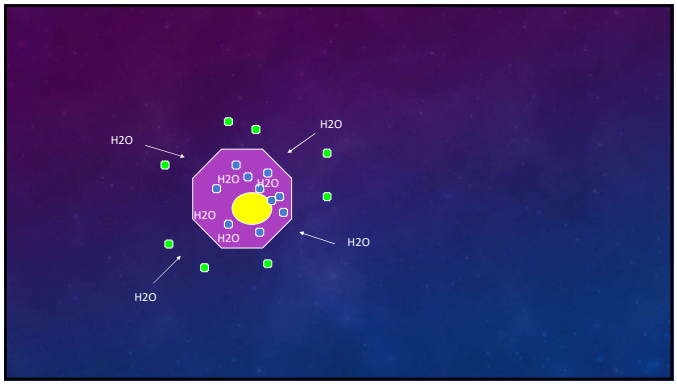


to prevent motic effects

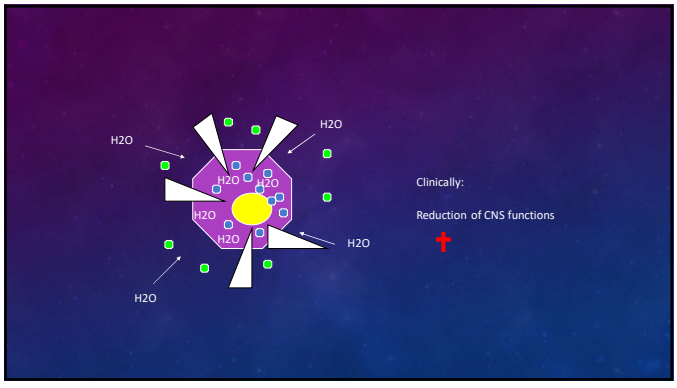
48


H2O
H2O
H2O
H2O
When we start treatment the hypertonicity decreases
Ewater moves to areas rich in sorbitol due to osmosis

49


H2O
H2O
H2O
H2O
H2O
H2O
H2O
H2O

50


H2O
H2O
H2O
H2O
H2O
H2O
H2O
H2O
Clinically:
Reduction of CNS functions
†

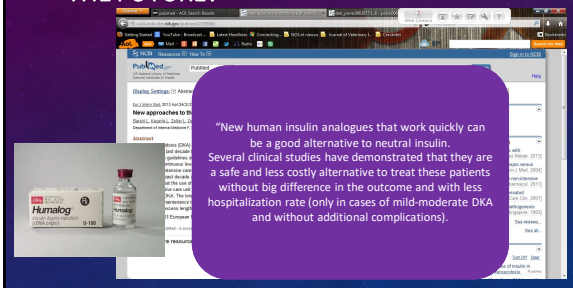
51

52

- Prevention:
  - Do not reduce glucose
  - **> 2-3/mmol/l/hr**
  - Do not reduce osmolality 0.5-1 osmol/hr (2x(Na+K)+BUN+BG)

53

THE FUTURE?



"New human insulin analogues that work quickly can be a good alternative to neutral insulin. Several clinical studies have demonstrated that they are a safe and less costly alternative to treat these patients without big difference in the outcome and with less hospitalization rate (only in cases of mild-moderate DKA and without additional complications).

54

MANAGEMENT OF DKA

DKA? Pánic!?

No:

A chance to excel in teamwork!

55