

# Diabetic ketoacidosis

## What is diabetic ketoacidosis?

Diabetic Ketoacidosis (DKA) is a life-threatening complication of diabetes mellitus, marked by the presence of ketonemia, electrolyte disturbances, dehydration, metabolic acidosis and concurrent disease, make these animals emergency patients that need intensive treatment.

A study with 42 cats with DKA, showed a mortality rate of 26% (1). The prognosis is often more determined by the nature and the severity of concurrent diseases than by the ketoacidotic state (7).

## What is the working mechanism of insulin?

Insulin is a small protein, composed of two amino acids. It is synthesized in the  $\beta$ -cells of the pancreas. It has a half-life of approximately 6 minutes, being degraded mainly in the liver, to a lesser extent in the kidney, the muscles and only slightly in most other tissues (7).

The major action of insulin is the promotion of storage of nutrients, in which the liver, the muscles and the adipose tissue play a central role (5).

- 1) In the liver, insulin
  - a) promotes synthesis of glycogen, protein and fat
  - b) inhibits glycogenolysis, ketogenesis and gluconeogenesis (catabolic effects)
- 2) In muscle, insulin increases protein synthesis and storage of muscle glycogen
- 3) In adipose tissue insulin
  - a) promotes triacylglycerol (fat) storage in adipocytes
  - b) inhibits lypolysis

(7)

To initiate its effects, insulin binds with and activates membrane receptor proteins (6). It is these activated receptors, not the insulin, that causes the subsequent effects. Within seconds after the binding process, these membranes in about 80% of the body's cells markedly increase their uptake of glucose, especially in the muscle and adipose cells. The cell membranes become also more permeable for many amino acids, potassium ions (by stimulating the Na-K-ATPase, (7)) and phosphate ions. Brain cells do not need insulin, since they are permeable for glucose.

Slower effects of insulin influence among others metabolic enzyme activity and DNA transcription rates (7).

## How does diabetes mellitus lead to DKA?

For DKA to develop, a combination of events is necessary:

- an insulin deficiency
  - relative: insulin resistance
  - absolute
- presence of counter-regulatory hormones:
  - glucagon, cortisol and growth hormone: all are secreted in response to hypoglycemia
  - epinephrine and norepinephrine: increase plasma glucose concentration during periods of stress but increase fatty acid concentration at the same time
- fasting
- dehydration

In the majority of the cases, concurrent disease increases the amount of counter-regulatory hormones and contributes to the insulin resistance (7,8).

The absence of glucose and insulin in the tissues results in accelerated lipolysis and production of excess free fatty acids. Stimulated by increased levels of glucagon and lower levels of insulin, the liver increases the  $\beta$ -oxidation of these fatty acids, producing ketones (acetoacetic acid which is converted into  $\beta$ -hydroxybutyric acid and acetone).

These ketones are substrates for the extrahepatic tissues, in fact a normal process: this way the liver produces an energy source for the tissues that is easier to process than fatty acids, in which way the glucose can be spared for the central nervous system. Under the circumstances mentioned above however, the production of ketones is abnormally high, while the utilization of the ketones in the tissues is depressed.

## The DKA patient

### Symptoms:

In addition of a history of clinical signs typical of diabetes mellitus, animals with DKA frequently show

- lethargy, weakness, depression
- anorexia, vomiting, weight loss
- dehydration
- acetone odor breath
- tachypnea or slow, deep breaths (Kussmaul breathing), due to metabolic acidosis
- signs of an underlying illness (7)

These patients are usually critical metabolic emergencies, that require an aggressive therapeutic plan. To establish the diagnosis of DKA and perform an appropriate treatment, it is important to perform at least the following tests:

- urinalysis: stick and specific gravity

- hematocrit
- blood glucose
- total plasma protein, creatinine
- serum electrolytes (sodium, potassium, chloride)

After the initial emergency treatment:

- potassium and glucose regularly
- additional tests to diagnose concurrent diseases (8)
- calcium, magnesium and phosphate
- arterial or venous blood gases
- urinary culture

### **Results:**

Laboratory findings for DKA patients typically include

- ketonuria, glucosuria, signs of cystitis
- hyperglycemia
- increased PCV, TP, BUN and creatinine due to dehydration
- electrolytes variable, often low to normal
- hyperosmolality
- metabolic acidosis

The reagent in dipsticks detects only acetone and acetoacetate. The concentration of  $\beta$ -hydroxybutyrate however typically exceeds that of acetoacetate in DKA, so this reaction underestimates the degree of ketonuria. When insulin is administered and metabolism of ketones proceeds, there is a shift toward acetoacetate and the dipstick reaction transiently becomes more positive (7). Home blood glucose monitoring equipment with the capability to measure  $\beta$ -hydroxybutyrate on finger stick blood, is now available for humans (2).

When no urine is available, the urine stick can also be used on serum/ plasma to diagnose ketone bodies.

The acetone that is formed during ketosis, is a volatile substance that gives the breath the acetone smell. It does not contribute additional fixed acid (7).

### **Concurrent disease:**

Concurrent disease in DKA patients is very common. As mentioned above, these disease processes contribute to the development of DKA. One study (1) describes that 39 out of 42 cats (93%) presenting with DKA had an underlying disease.

Disorders mentioned commonly in DKA patients are

- hepatic lipidosis, cholangiohepatitis
- pancreatitis
- chronic renal failure
- urinary tract infection and other bacterial infections
- hyperadrenocorticism and diestrus (in dogs)
- heart disease
- neoplasia

### How do patients get this ill?

When plasma ketone concentrations keep increasing, they eventually surpass the renal tubular threshold for complete resorption, and spill into the urine, accompanied by their buffer, bicarbonate. This contributes to the osmotic diuresis caused by glycosuria and enhancing the excretion of solutes (e.g., sodium, potassium and magnesium) and to acidosis, through the loss of bicarbonate. Insulin deficiency per se also contributes to the excessive renal losses of water and electrolytes (insulin influences electrolyte uptake in the tissues). The result is an excessive loss of electrolytes and water, leading to volume contraction, underperfusion of tissues, prerenal azotemia and lactic acidosis. As ketones continue to accumulate in the blood, the body's buffering system becomes overwhelmed, and progressively worsening metabolic acidosis results. Further loss of water and electrolytes occurs as a result of vomiting and/or diarrhea combined with a lack of fluid intake, problems that often develop as the metabolic acidosis worsens. The rise in blood glucose concentration raises the plasma osmolality. The resulting osmotic diuresis further aggravates this by causing water losses in excess of the salt loss. The increase in plasma osmolality causes water to be shifted out of cells, leading to cellular dehydration and the eventual development of obtundation and coma (7, 8).

## Treatment

### 1. Start fluid therapy (7, 8)

The primary goal of initial fluid therapy is treating shock, if present, and dehydration, to restore intra and extra vascular fluid deficits. Restoring normal kidney function is essential, since the kidneys play the main part in correcting fluid, electrolyte and acid base disorders. Dehydration is treated aggressively over 4-6 hours, unless there is a contraindication, like concurrent heart disease or renal failure.

| *Type* : 0.9 % saline or Ringers' Lactate

| *Rate* : based on hydration status (6-10% dehydration) and ongoing losses  
(5% dehydration is hardly recognizable, 15% is fatal)

#### **60-100 ml/kg fluid deficit**

Give 50% of the estimated losses in the first 4-6 hours, the other 50% over 6-12 hours

example : cat 5 kg

10 % dehydration → =500 ml fluid deficit

50%=250 ml, in 4 h=62,5 ml/h, plus 10 ml maintenance=72 ml/h

After 6 h: 250/18=14 ml/h, plus 10 ml maintenance= 24 ml/h

| For ongoing losses (polyuria?) one has to make an estimation.

*Monitoring:* based on urine output, serial measurement of body weights, blood values, (central venous) blood pressure (when available).

## 2. Restore electrolytes

### Hypokalemia

We have learned that acidosis is accompanied by a hyperkalemia, due to the following mechanisms:

- In the distal tubules of the kidneys,  $K^+$  and  $H^+$  are exchanged against  $Na^+$ . When there is a  $H^+$  excess, more  $H^+$  will be exchanged against  $Na^+$  than  $K^+$ .
- A decrease in pH causes a shift of  $H^+$  ions into the cells, to be buffered by intracellular buffers. To keep isoelectricity, potassium ions will leave the cell.

This is mainly true for acute, mineral (anorganic) acidosis (e.g. HCl,  $NH_4Cl$ ), but not for organic acids, like ketones and lactic acid.

In ketoacidosis, the absence of insulin and the hyperosmolality are more responsible for the hyperkalemia (7):

- hyperosmolality will cause water movement from ICF to ECF and potassium follows because of solvent drag and as a result of the increased ICF potassium concentration resulting from cellular water loss
- the absence of insulin makes the cell membranes less permeable for potassium and some other electrolytes, and decreases renal tubular potassium absorption.

Why do DKA patients then still present with normo- or hypokalemia?

The chronic metabolic acidosis, combined with a lack of insulin and vomiting, leads to severe electrolyte losses, that are not compensated by oral uptake, due to anorexia. Even DKA patients presenting with hyperkalemia thus may suffer from a serious total potassium deficit.

Hypokalemia can cause muscle weakness, ECG changes and cardiac arrhythmias. As soon as the treatments starts, hypovolemia and acidosis will diminish, causing a dilution and shifting of the potassium, while urinary losses will continue. When administration of insulin is started in this phase, potassium will further shift into the cells, which can bring the serum potassium to dangerously low levels. For this reason potassium supplementation should be started before administration of insulin.

Patients with refractory hypokalemia after 24-48 hours of therapy, should be checked for hypomagnesemia. One of the functions of magnesium is being the cofactor with ATP as the driving force behind intracellular ion pumping activity, such as the Na-K-ATPase. However, total serum magnesium represents only 1% of the body's magnesium stores. Serum Mg does not correlate with the diagnosis of a suspected magnesium deficit, nor does it correlate well with serum ionized magnesium. Because clinical signs of hypomagnesemia are very rare, supplementation is seldom necessary (7,8).

### Hypophosphatemia

Phosphorus is influenced by similar processes as potassium.

Phosphorus is an important component of ATP and is therefore critical in certain energy-dependent physiologic processes (4). If serum phosphate drops below 0.32 mmol/l, a crisis may develop in body cells that are high energy users, including red blood cells, skeletal

muscle cells and brain cells. Hemolytic anemia is the most common problem and can be life-threatening, if not recognized (3).

Supplementation of phosphate is advised when serum phosphorus drops below 0.5 mmol/l:

*Amount: 0.01-0.03 mmol/kg/hr* in Ca-free fluids

It is however described that hemolytic anemia develops despite this supplementation (1). Adverse effects of overzealous phosphate administration include hypernatremia, hypotension, calcifications and hypocalcemia and its associated neuromuscular signs.

### **3. Start insulin therapy**

Insulin therapy is critical for the resolution of ketoacidosis, but overzealous insulin treatment can cause severe hypokalemia, hypophosphatemia and hypoglycemia during the first 24 hours of treatment. Initiation of fluid therapy, including potassium corrections, should always be the first step in the treatment of DKA. Delaying insulin therapy, allows the benefits of fluid therapy to begin before the effects of insulin commence. It is recommended however to start insulin therapy within 4 hours of initiation of (aggressive!) fluid therapy.

The goal of initial insulin therapy is to lower very high blood glucose concentrations slowly, preferably not more than 5 mmol/l/h. A too rapid decline in serum glucose can give large shifts in osmolality and can cause cerebral edema.

A declining blood glucose concentration ensures that lipolysis and the supply of fatty acids for ketone production have been effectively turned off. Glucose concentrations, however, decrease much more rapidly than do ketone levels. In general, hyperglycemia is corrected within 6-12 hours, but ketosis often takes 48 to 72 hours to resolve (8) (10-96 h, (1)). For this reason, glucose 5% is added to the fluid therapy, to prevent hypoglycemia, while insulin application can be proceeded. Keep the plasma glucose level between 7.5 and 15 mmol/l.

Ideally, longer acting insulin should not be administered until the dog or cat is stable, eating, maintaining fluid balance without any intravenous infusions, and is no longer acidotic, azotemic, or electrolyte deficient (8).

For insulin dosages, see separate protocol.

### **4. Restore acid-base balance**

The acidosis in DKA diminishes when fluid therapy and insulin administration start. Improvement of renal perfusion restores electrolyte balances and enhances urinary loss of ketoacids. Insulin therapy reduces the production of ketoacids and promotes their utilization in the tissues, producing bicarbonate. For these reasons, correction of the acidosis with bicarbonate is rarely indicated.

*Indication* : pH < 7.0-7.1 and no improvement after the first hour of fluid therapy  
*Amount* : Body weight (kg) x 0.4 x (12 – patients bicarbonate) x 0.5

0.4 represents the % of extracellular fluid space in which bicarbonate is distributed (40% of body weight) and 0.5 means that we start with half of the amount of bicarbonate deficit.

*Complications:* hypokalemia, cerebral edema, paradoxal cerebrospinal fluid acidosis (bicarbonate enters the CSF more slowly than CO<sub>2</sub>)

## Concurrent illness

Therapy for DKA frequently involves the management of concurrent, often serious illness. Additional diagnostic tests like ultrasound and radiographs are recommended. Disorders mentioned common in DKA patients are, as already mentioned above,

- hepatic lipidosis, cholangiohepatitis
- pancreatitis
- chronic renal failure
- urinary tract infection and other bacterial infections
- hyperadrenocorticism and diestrus (dogs)
- heart disease
- neoplasia

Modifications in therapy for DKA (e.g., fluid therapy with concurrent heart failure or renal failure) and/or additional therapy (e.g., antibiotics) may be required. Insulin therapy, however, should never be delayed or discontinued, since resolution of ketoacidosis can be obtained only through insulin therapy.

## References

### Articles:

1. Bruskiwicz KA, Nleson RW, Edward, Feldman C, Griffey SM. Diabetic ketosis and ketoacidosis in cats: 42 cases (1980-1995). *J Am Vet Med Assoc* 1997; Vol 211, No2: 188-192.
2. Kitabchi AE. Hyperglycemic crisis: improving prevention and management. *American Family Pyisician* 2005; Vol 71, No 9: 1659-1660.
3. Nichols R. Complications and concurrent disease associated with diabetes mellitus. *Seminars in Vet Med and Sur (Small Animal)* 1997; Vol 12, No 4: 263-267.
4. Conally HE. Critical care monitoring considerations for the diabetic patient. *Clin Tech in Small An Prac* 2002; Vol 17, No 2: 73-78.

### Textbooks:

5. Rijnberk A. Endocrine pancreas. In *Clinical Endocrinology of Dogs and Cats*. Kluwer Academic Publishers Dordrecht-Boston-London, 1996; 95-98.
6. Guyton AC, Hall JE. Insulin, Glucagon and Diabetes Mellitus. In *Medical Physiology*, 11<sup>th</sup> edition. Elsevier Saunders, 2006; 961-977.
7. DiBartola SP. Fluid, Electrolyte and Acid-Base Disorders in Small Animal Practice, 3<sup>rd</sup> edition. Elsevier Saunders, 2006; 111-113, 169, 198, 221, 261-262, 306, 327, 478-483.
8. Ettinger SJ, Feldman EC. *Textbook of Veterinary Internal Medicine*, 6<sup>th</sup> edition. Elsevier Saunders, 2000; 1568-1575.

## Samenvatting protocol Diabetische ketoacidose

- 1) Vloeistoftherapie (vereenvoudigd): Ringer lactaat IV: 10 ml/kg/uur (minimaal 2-4 uur)
  - a) Daarna over op geforceerde diurese (= 4 ml/kg/uur), tot plasma ureum/kreat vrijwel genormaliseerd.
  - b) Dan over op onderhoud (= 2 ml/kg/uur).
- 2) Plasmaglucose bepalen: (en ureum, kreat, kalium, natrium, bloedgasen)
  - a) <15 mmol/l geen insuline
  - b) >15 mmol/l insuline geïndiceerd, eerst kalium corrigeren, maar start insuline niet langer dan ca. 4 uur uitstellen (zie 4c).
- 3) Kalium-correctie:
  - a)  $(5 - [K]) \times LG \times 0.6 = \text{mmol/ KCl}$ . 1 mmol = 1 ml
  - b) Op maximale snelheid: 0.5 mmol/kg/uur IV
- 4) Insuline toedienen (normaal insuline = Actrapid, 100 IE/ml, 1:10 verdunnen)
  - a) 2 IE totale dosis voor katten en honden  $\leq 10$  kg IM (deze dosering is eenmalig)
  - b) 0.25 IE/kg voor honden > 10 kg IM (deze dosering is eenmalig)
  - c) Indien het kalium nog niet goed gecorrigeerd is, starten met halve dosis insuline.
- 5) Controleer plasma-glucose elk uur en herhaal gift Actrapid elk uur IM (als glucose > 13 mmol/l):
  - a) 1 IE totale dosis voor katten en honden  $\leq 10$  kg IM
  - b) 0.1 IE/kg voor honden > 10 kg IM
  - c) Dosering Actrapid evt. verlagen als het glucose sneller daalt dan 5 mmol/l/uur.
- 6) Controleer kalium na elke correctie
- 7) Tot plasmaglucose verlaagd is tot 8-13 mmol/l
  - a) 8-13 mmol/l 0.5 IE /kg SC (3-4 dd)
  - b) < 8 mmol/l Geen insuline, RL vervangen door 5 % glucose + 2 ml KCl per 100 ml
- 8) Om de 3-4 uur glucose en kalium controleren. Probeer het glucose met Actrapid en glucoseinfuus tussen de 7.5 en de 15 mmol/l te houden (Actrapid doseringen als nodig aanpassen met 10-20%) tot de patiënt stabiel is, dwz geen infuus of correcties nodig heeft en niet meer acidotisch of uremisch is.
- 9) Dan pas overstappen op Caninsulin. Hou ongeveer 5 uur aan tussen de laatste Actrapid gift en de eerste Caninsulin gift.

# Ketoacidose

## Onder de top van de ijsberg

Laura J. Ruys  
Specialist in opleiding Emergency and Critical Care



Mede dankzij  
Hill's Pet Nutrition  
Idexx Laboratories

# Diabetische ketoacidose (DKA)

Een levensbedreigende complicatie van diabetes mellitus, gekenmerkt door

Ketonemia, elektrolytstoornissen, dehydratie, metabole acidose en vaak een onderliggende ziekte

Spoedpatiënten die metabool ernstig ontregeld zijn en intensieve behandeling nodig hebben

# Hoe werkt insuline ook al weer?

Klein eiwit, geproduceerd in de  $\beta$ -cellen van de pancreas, met een halfwaardetijd van ca. 6 minuten

Bindt aan en activeert receptoren op de celmembraan

Deze receptoren veroorzaken de daarop volgende effecten

- $\uparrow$  doorlaatbaarheid voor glucose in 80% van de lichaamscellen (vnl. lever en vet)
- $\uparrow$  doorlaatbaarheid membranen voor aminozuren en elektrolyten (o.a. kalium en fosfaat)
- Lange termijn effect op metabole enzymactiviteit en DNA transcriptie snelheid

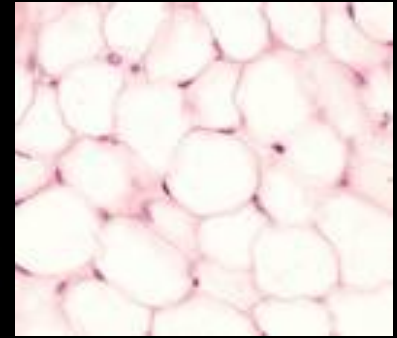
# Een veelzijdig hormoon

De belangrijkste functie van insuline is de opslag van voedingstoffen in het vetweefsel, de lever en de spieren

Insuline werkt remmend op katabole processen als ketogenese en lipolyse

In afwezigheid van insuline krijgen katabole processen de overhand

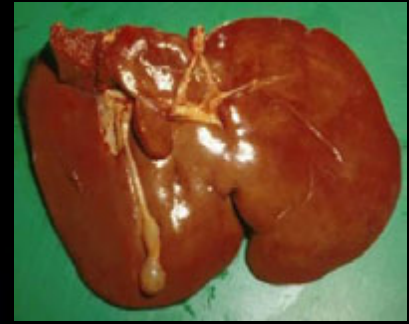
# Vetweefsel



In de afwezigheid van glucose

- neemt de vetopslag in vetcellen af
- neemt de lipolyse toe, waardoor er een verhoogde hoeveelheid vrije vetzuren als brandstof beschikbaar komt

# Lever



In de lever worden ketonlichamen geproduceerd:

- Normaal gesproken vooral bij vasten
- De toename van ketonlichamen heeft als doel de weefsels een alternatieve 'hapklare' energiebron aan te bieden
- Bij DM valt de remming op katabole processen weg
- De lever kan de ketonlichamen niet verbranden maar ook de weefsels hebben insuline nodig voor deze verbranding

# Spieren



Onder normale omstandigheden wordt onder invloed van insuline eiwit gesynthetiseerd en spierglycogeen opgeslagen

Onder katabole omstandigheden hebben spieren een grote capaciteit voor verbranding van ketonlichamen

# Wanneer wordt diabetes DKA?

Als er een combinatie is van

1. een absoluut of relatief insulinetekort (insuline resistentie)
2. vasten
3. dehydratie
4. aanwezigheid van 'counter-regulatory hormones'

# Counter-regulatory hormones

- Glucagon
- Cortisol
- Groeihormoon
- Catecholamines

Komen extra vrij bij bepaalde ziekteprocessen

Hebben o.a. als effect het verhogen van plasmagluucose  
en vetzuren

Dragen bij aan het ontstaan van insulineresistentie

# Hoe worden DKA patiënten zo ziek?

De toenemende hoeveelheid ketonlichamen wordt aanvankelijk met de buffer bicarbonaat uitgescheiden in de urine

Dit versterkt de osmotische diurese door glucosurie en veroorzaakt elektrolytverlies, dehydratie en, door bicarbonaatverlies, acidose

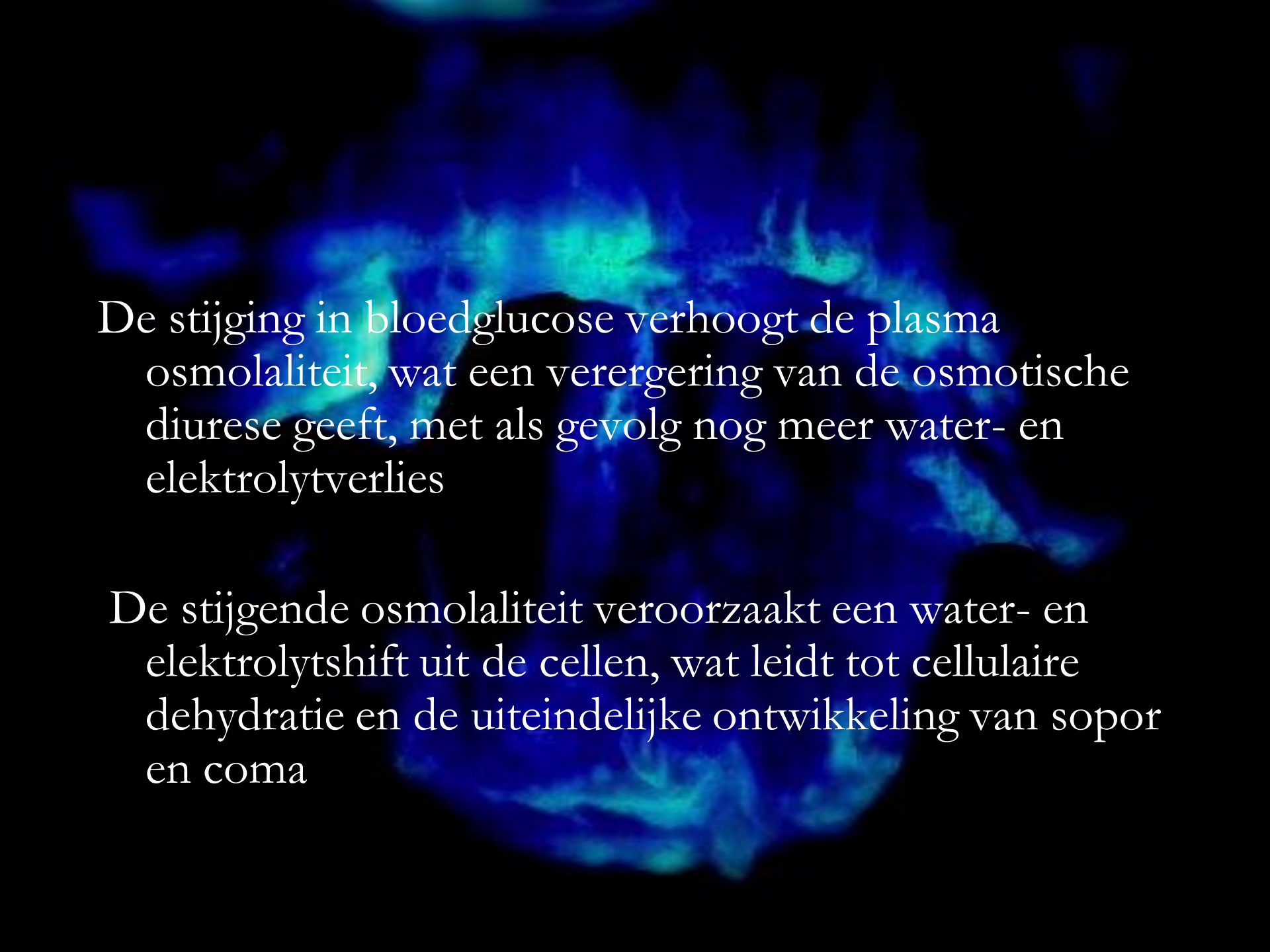
Insuline bevordert elektrolytopname in de cellen. Bij DM gaan dus extra elektrolyten en water verloren



Dit leidt tot hypovolemie, onderperfusie van de weefsels, prerenale uremie en lactaat acidose

De toenemende hoeveelheid ketonen overbelast uiteindelijk het buffersysteem, met als gevolg een toename van de acidose

Braken en diarree icm anorexie door acidose of onderliggende ziekte veroorzaken nog verdergaande dehydratie en elektrolytverlies



De stijging in bloedglucose verhoogt de plasma osmolaliteit, wat een verergering van de osmotische diurese geeft, met als gevolg nog meer water- en elektrolytverlies

De stijgende osmolaliteit veroorzaakt een water- en elektrolytshift uit de cellen, wat leidt tot cellulaire dehydratie en de uiteindelijke ontwikkeling van sopor en coma

# De DKA patiënt

Mees

Kat, MG

13 jaar



# Symptomen

- Soms symptomen van DM in anamnese
- Zeer sloom
- Vermagerd
- Anorexie, braken
- Acetongeur uit de bek
- Langzame ademhaling met diepe ademteugen
- Dehydratie en soms ook shock

# Bloedonderzoek



Kreatinine ↑

GPT ↑, icterus

TP ↑

Ht ↑

Glucose ↑↑

Kalium ↓

# Urineonderzoek:

Eiwit ↑

pH ↑

Glucose ↑↑

Ketonlichamen ↑

Bilirubine ↑

Bloed ↑

S.g. ↑



# Behandeling

Shock:

- Hond 20-30 ml/kg in 5-10 min  
evaluatie, als nodig herhalen
- Kat 10-15 ml/kg als 'bolus' in 1<sup>e</sup>  
kwartier  
evaluatie, als nodig herhalen



## Dehydratie:

- Maak een inschatting van het dehydratiepercentage (6-10%)
- 60-100 ml/kg vloeistof tekort
- Dit voor 50% toedienen in de eerste 4-6 uur
- De tweede 50% in 6-12 uur
- PLUS onderhoud, PLUS verliezen
- Hou rekening met evt. onderliggende ziekten als nier- en hartfalen

# Kalium

Hyperkaliemie door acidose en bij anurie

Hypokaliemie door elektrolytverlies,  
afgenomen elektrolytopname en  
gestoorde processen door afwezigheid  
insulinewerking

Laag kalium kan spierzwakte en aritmieën  
veroorzaken

# Het topje van de ijsberg

Gemeten kalium vaak een geflatteerd beeld door acidose bij een ernstig tekort in het lichaam

Dit wordt versterkt door het starten van

- vloeistoftherapie: verdunning acidose en kalium shift naar intracellulair, verlies via urine gaat door
- insulinetherapie: veroorzaakt een sterke kaliumshift

Bij laag kalium: start kalium correcties voordat er met insuline begonnen wordt, op maximale correctiesnelheid ( $0.5 \text{ mmol/kg/uur}$ )

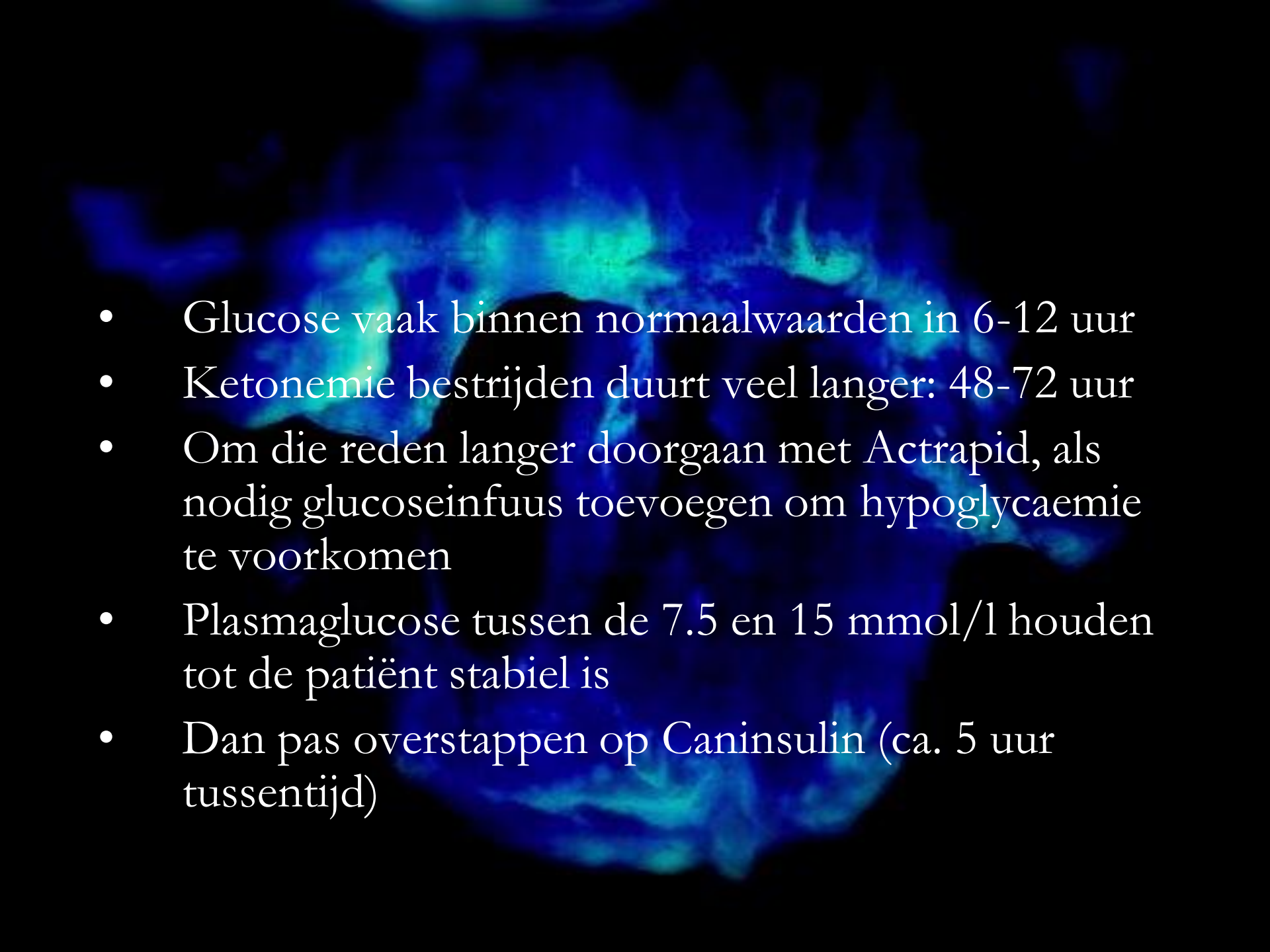
Ook als het kalium normaal is, kalium aan infuus toevoegen (hoeveelheid minder goed in te schatten, vaak ook snelle toediening noodzakelijk)

Zeer frequente controles: bij start behandeling samen met glucose elk uur

Bij voorkeur binnen ca. 4 uur beginnen met insulinetherapie

# Insulinetherapie

- Normaal insuline (Actrapid®)
- Essentieel in de bestrijding van de ketoacidose: verbranding van ketonlichamen wordt hervat, vorming van ketonlichamen en vetzuren wordt gestopt
- Kan ernstige hypokaliemie, hypofosfatemie en hypoglycaemie veroorzaken
- Daling van het plasmaglucose niet sneller laten verlopen dan 5 mmol/l/u

- 
- Glucose vaak binnen normaalwaarden in 6-12 uur
  - Ketonemie bestrijden duurt veel langer: 48-72 uur
  - Om die reden langer doorgaan met Actrapid, als nodig glucoseinfuus toevoegen om hypoglycaemie te voorkomen
  - Plasmaglucose tussen de 7.5 en 15 mmol/l houden tot de patiënt stabiel is
  - Dan pas overstappen op Caninsulin (ca. 5 uur tussentijd)



# Andere koudwaterzwemmers

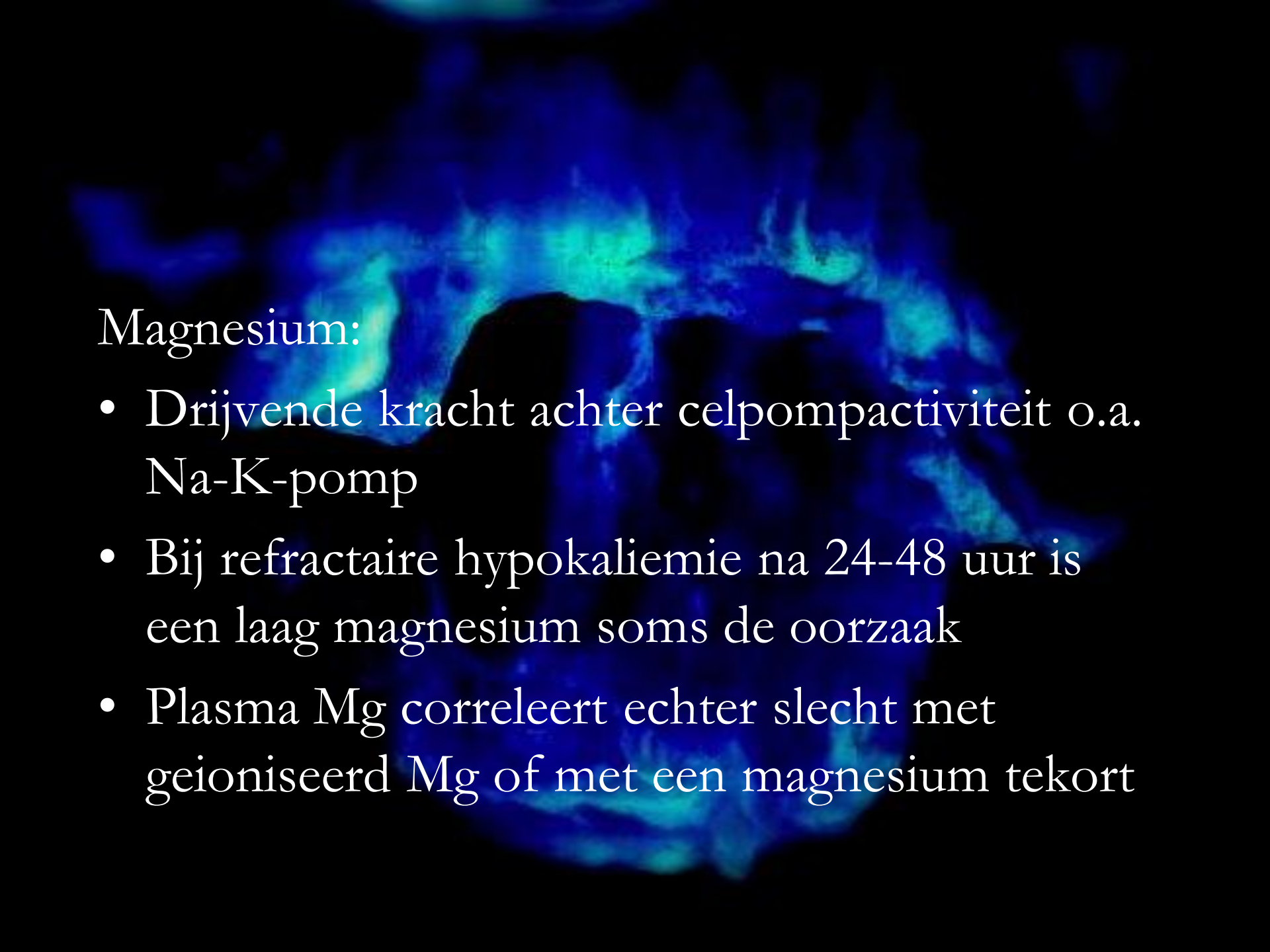
## Metabole acidose

- Bij DKA vooral op basis van ketonlichamen en vaak ook lactaat
- Vermindert al bij start vloeistoftherapie: verdunning en verbetering nierperfusie
- Insulinetherapie: afbraak van de ketonen waarbij bicarbonaat vrijkomt
- Bijwerkingen bicarbonaat: hypokalemia, hersenoedeem, paradoxe cerebrospinale acidose
- Om die reden alleen geïndiceerd bij  $\text{pH} < 7.1$



## Fosfaat:

- Wordt beïnvloed door vergelijkbare processen als kalium
- Belangrijke component van ATP essentieel voor energievreters als erythrocyten, skeletspiercellen en hersencellen
- Hypofosfatemie kan hemolyse veroorzaken



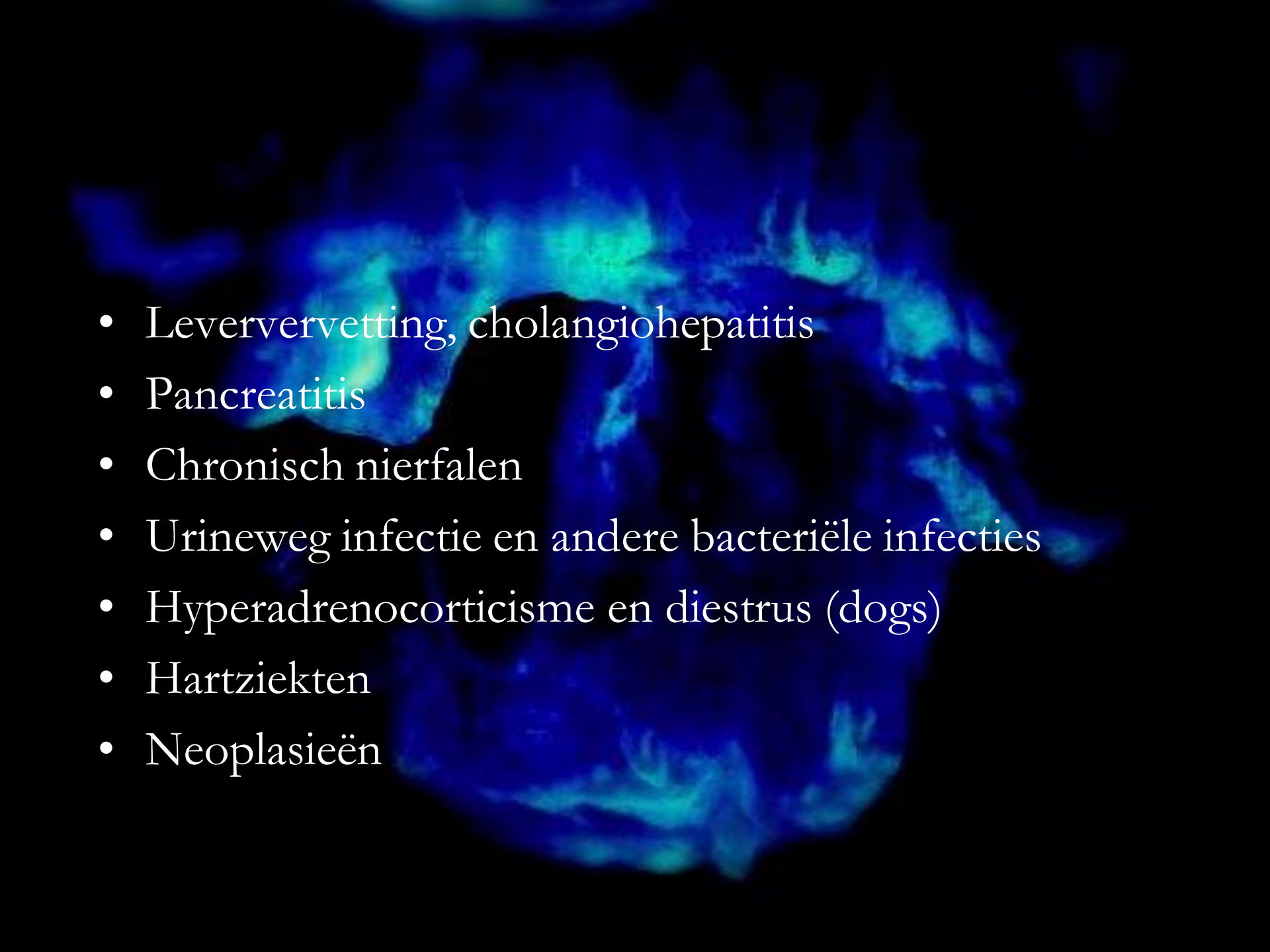
## Magnesium:

- Drijvende kracht achter celpompactiviteit o.a. Na-K-pomp
- Bij refractaire hypokaliemie na 24-48 uur is een laag magnesium soms de oorzaak
- Plasma Mg correleert echter slecht met geïoniseerd Mg of met een magnesium tekort



## Onderliggende ziekte

- Bij zeer groot deel van de DKA patiënten (80-90%?) aanwezig
- Dragen bij aan de insulineresistentie door een toename van counter regulatory hormones
- Bepalend voor overleving, veel meer dan de behandeling van de DKA
- Oorzaak/ gevolg?

- 
- Leververvetting, cholangiohepatitis
  - Pancreatitis
  - Chronisch nierfalen
  - Urineweg infectie en andere bacteriële infecties
  - Hyperadrenocorticisme en diestrus (dogs)
  - Hartziekten
  - Neoplasieën

# Herstel



Start pas met voeren als de patiënt deels gestabiliseerd is wat betreft hydratatie, elektrolyten en zuur-basen (b.v. na de eerste 12 uur)

Soms dwangvoeren noodzakelijk (voedingssondes)

Soms terugval in DKA

A stylized, glowing blue and green map of Africa is centered on a black background. The map is composed of numerous small, irregular shapes that form the outline of the continent, with some internal details like major rivers and lakes. The colors are vibrant, with shades of blue and green, giving it a digital or scientific appearance. The word "Vragen?" is written in white, serif font, centered over the map.

Vragen?