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ACUTE KIDNEY FAILURE

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- Acute kidney failure (AKI) is

  a syndrome resulting from the sudden inability

  of the kidney to perform its functions:

- Rapid evolution (a few hours to a few days).
- Frequently reversible (if treated in a timely

  manner).

It results in:

A pathological state, often fatal, characterized by a decrease in glomerular filtration clinically manifesting as oliguria and causing a disruption of homeostasis (water, electrolyte, acid-base, and nitrogen balance). 3

Its clinical expression is similar to that

observed in the terminal phase of CKD.

IMPORTANCE

Less frequent than AKI, ARI is more quickly fatal.

Can lead to death in a few days without treatment; it is often a medical emergency.

PATHOGENESIS - CLASSIFICATION

3 mechanisms can lead to the onset of ARI:

1. Renal hypoperfusion, referred to as PRE-RENAL or functional ARI,

2. Organ failure, RENAL, referred to as ARI

3. Impairment in urinary flow: this is referred to as POST-RENAL AKI (obstructive).

These mechanisms are the basis for the classification of AKI.

This distinction is crucial as it conditions the treatment and allows for a prognostic evaluation.

NB:

- Most pre-renal and post-renal causes evolve towards renal injuries.

ETIOLOGY

A. PRE-RENAL AKI

Any decrease in renal blood flow can

trigger a prerenal IRA.

Due to a disturbance in hemodynamics.

Hypovolemia:

- losses: dehydration (vomiting, diarrhea, burns...) or hemorrhages.

- sequestration: shock, edema...

Drop in cardiac output:

- decompensated left heart failure (valvulopathies, cardiomyopathies...).
- Anemia.
- rhythm disorders...

Renal vascular thrombosis (rare):

- presence of hemoglobin in large quantities during hemolysis (piroplasmosis).
- disseminated intravascular coagulation (DIC).
- thrombosis of the renal artery by a clot (e.g.: nephrotic syndrome).

iatrogenic causes:

- excessive use of diuretics.
- NSAIDs (vasodilatory action),

- vasodilators, particularly the ACE inhibitors (Angiotensin-Converting Enzyme inhibitors) in the treatment of hypertension for example.
- Surgery: anesthetics are hypotensive, hemorrhages are possible.

Note:

- It is essentially in shocks that an acute renal failure of pre-renal origin is observed.

that one

- Most other situations manifest

  as sub-acute renal failure:

➢ The most classic example is that of renal failure developing gradually during left heart failure.

B. ACUTE RENAL FAILURE

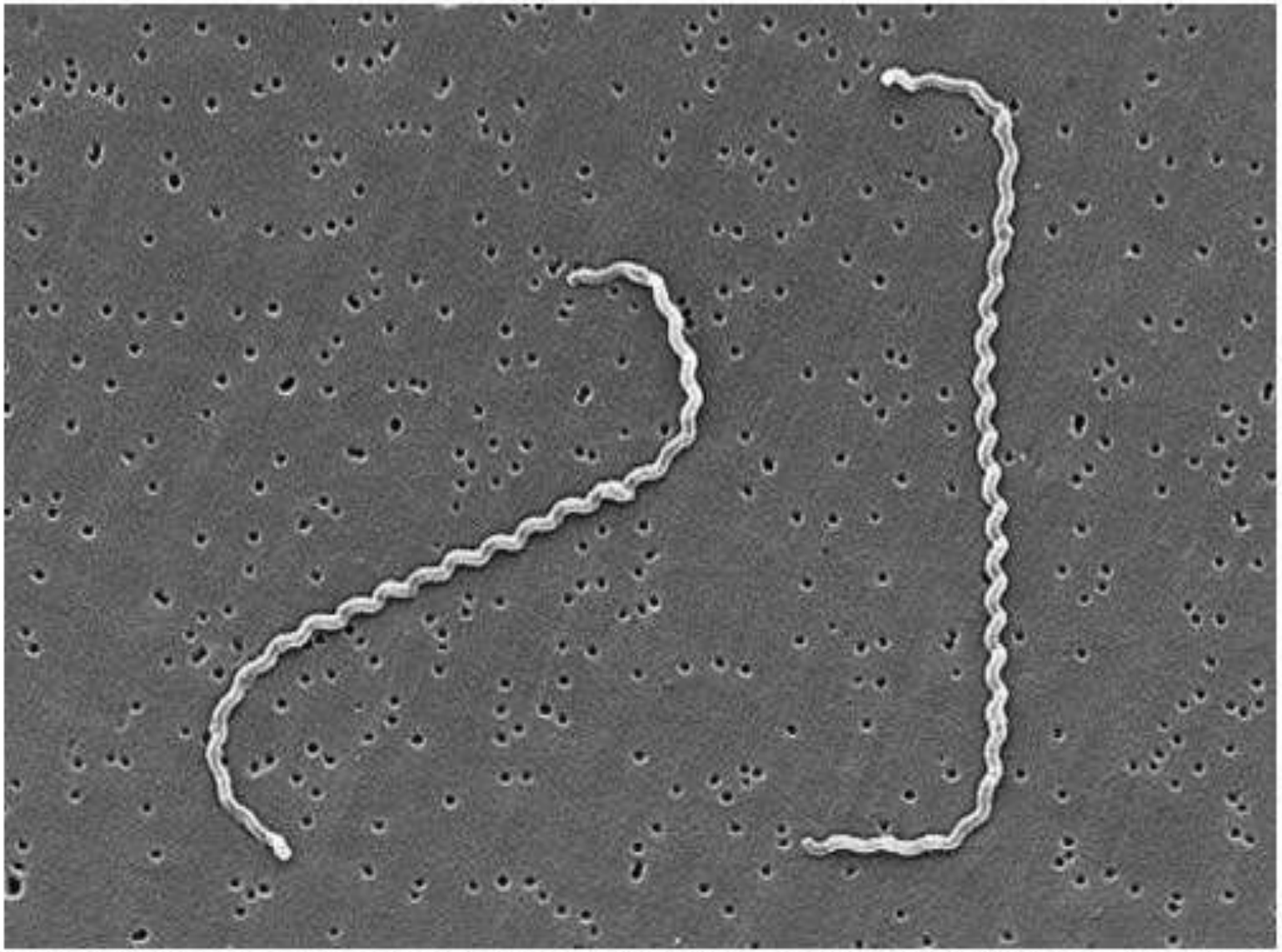
Consequence of an extensive and sudden injury to the renal parenchyma.

It may be:

- Nephrosis or glomerulopathy (degeneration).
- Nephritis (inflammation; example: acute infectious or toxic tubulo-interstitial nephritis).

Causes are distinguished as follows:

- infectious: leptospirosis, metritis, prostatitis, leishmaniasis, piroplasmosis, FIP ...
- immune: systemic lupus, immune complex deposits ...
- ischemic: untreated prerenal acute renal failure (development of heart failure)



Leptospira interrogans, au microscope électronique à balayage. Image credit : CDC/NCID/HIP/Janice Carr.

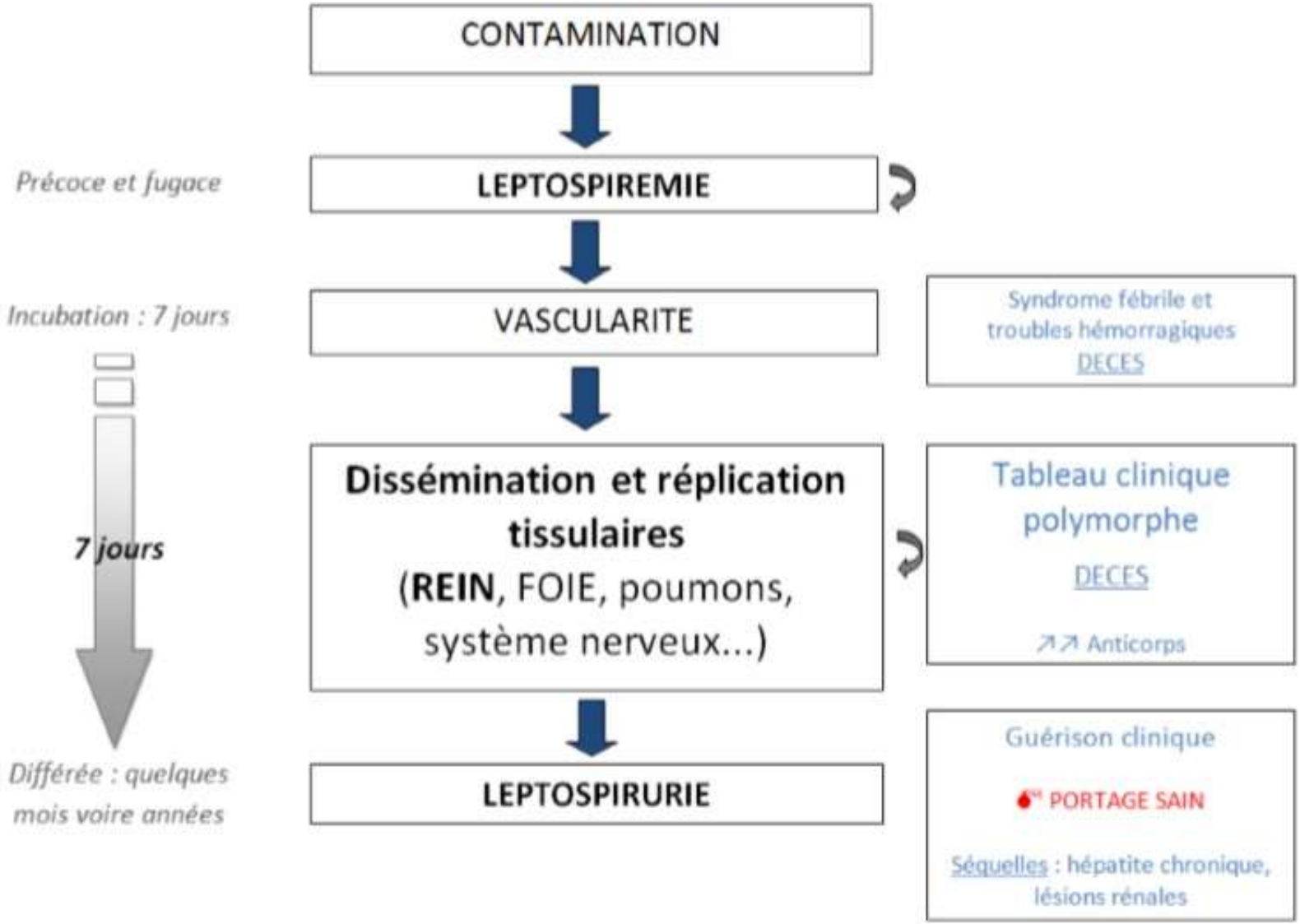
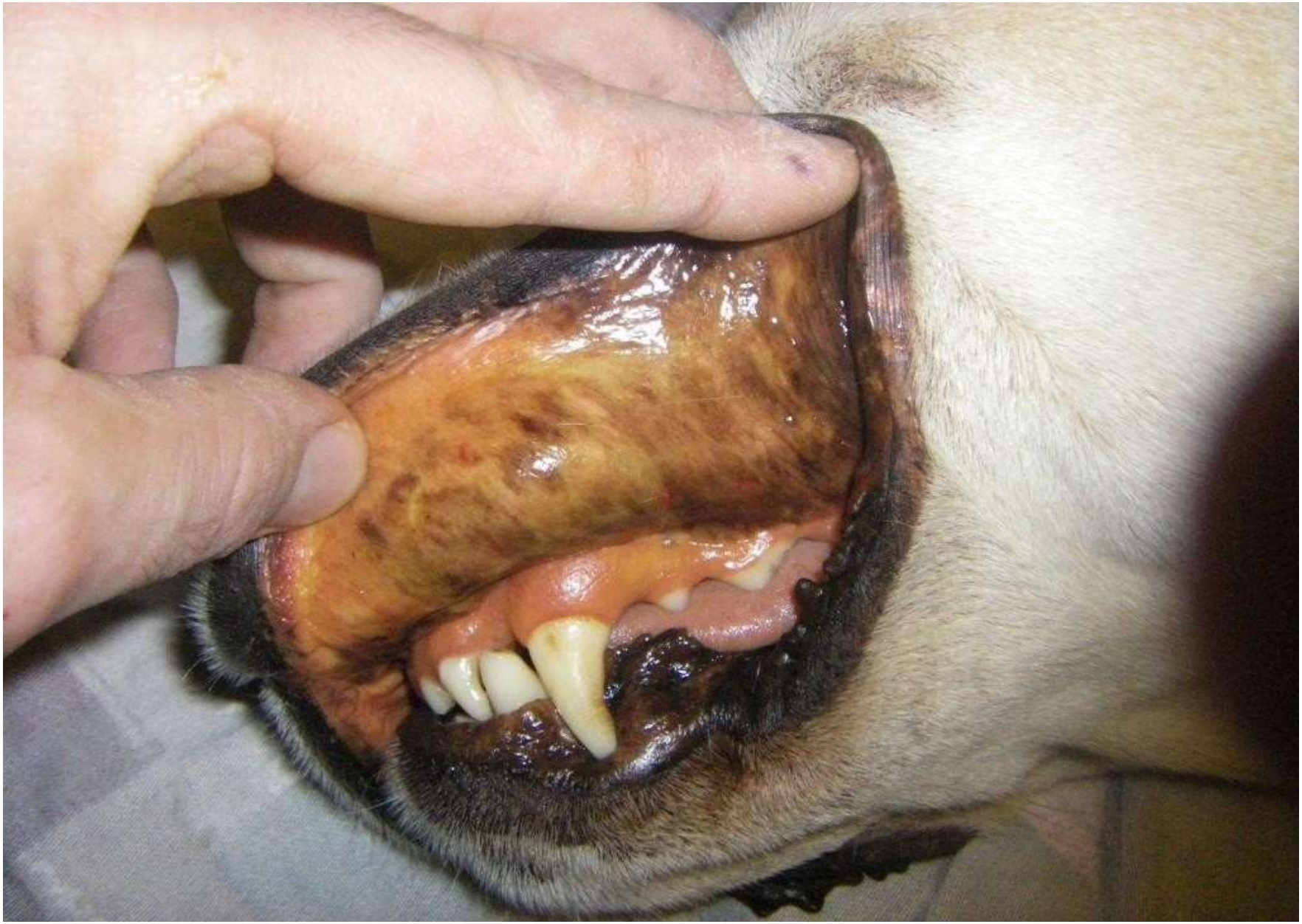


Figure 4 : Pathogénie de l'infection leptospirosique (d'après cours Marine Hugonnard, VetAgro Sup 2013)



- mechanical: untreated postrenal acute renal failure

- metabolic: hypercalcemia,
- toxics: ethylene glycol, venoms ...

- iatrogenic: aminoglycosides (gentamicin, ...), cisplatin (chemotherapy), ...

Potentially Nephrotoxic Medications

Antimicrobials

- Aminoglycosides
- Amphotericin B
- Carbapenems
- Cephalosporins
- Fluoroquinolones
- Penicillins
- Rifampin
- Sulfonamides
- Tetracyclines
- Vancomycin

Cancer chemotherapy

- Bisphosphonates
- Carboplatin
- Cisplatin
- Doxorubicin
- Methotrexate

Immunosuppressants

- Azathioprine
- Cyclosporine

Other medications

- Allopurinol
- Angiotensin-converting enzyme inhibitors
- Apomorphine
- Cimetidine
- Dextran-40
- Mannitol
- NSAIDs
- Streptokinase
- Penicillamine

Note:

- During infection, it is generally secondary immune phenomena that are responsible for kidney lesions.

- LEPTOSPIROSIS is the most

  frequent cause of acute kidney injury (AKI) in dogs.

Remember to wear gloves during urine

collection: it is a zoonosis.

- AMINOGLYCOSIDES (gentamicin): common

  cause of iatrogenic acute kidney injury (AKI).

Contraindicated in case of renal insufficiency.

If their use is necessary, it is preferable to space out the doses rather than reduce them.

- PRE and POST-RENAL AKI

  always complicate with a renal AKI if not

  treated.

C. POST-RENAL AKI

Consequence of an impediment to urine flow caused by:

A mechanical obstruction, either intrinsic or extrinsic, on the excretory pathways.

- by an obstruction:

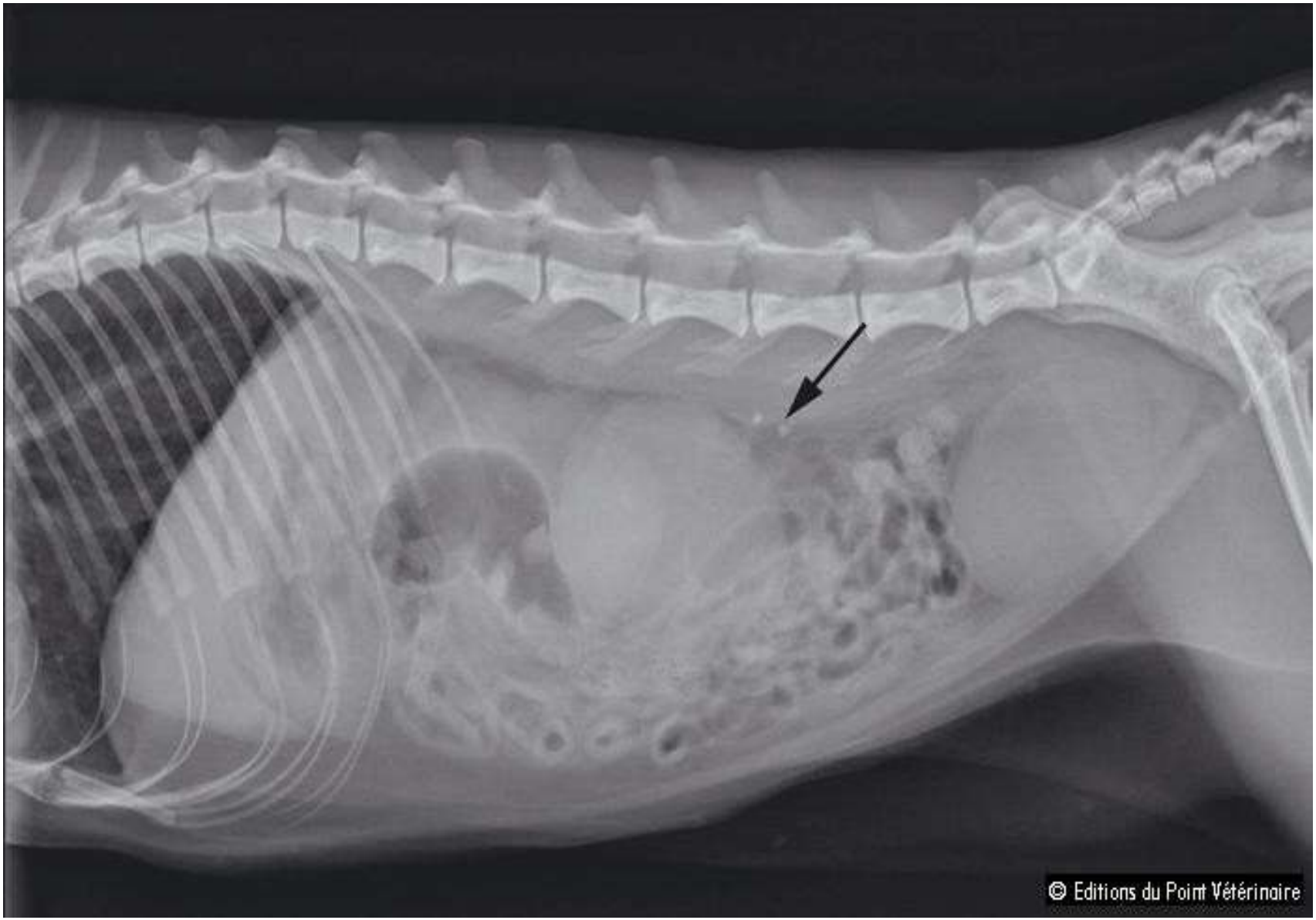
➢ ureteral stones or urethral plugs

➢ perineal hernia (with bladder retroflexion)

from the

➢ prostate tumor,

➢ vaginal tumor, ...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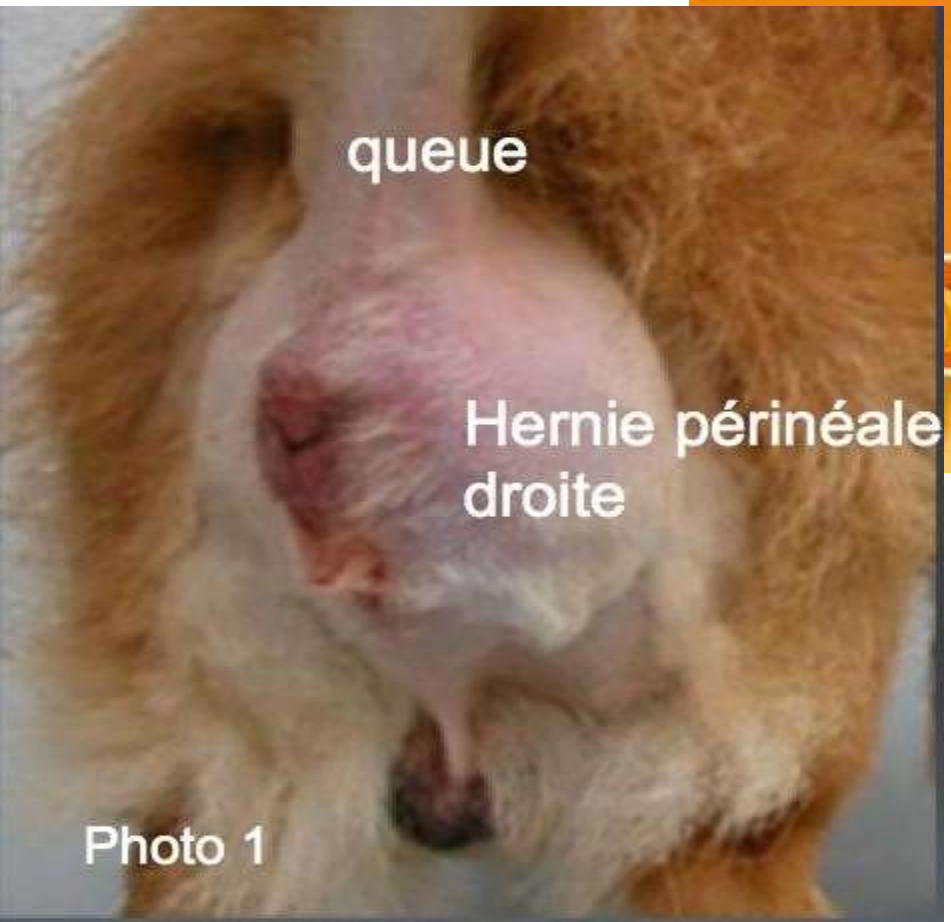
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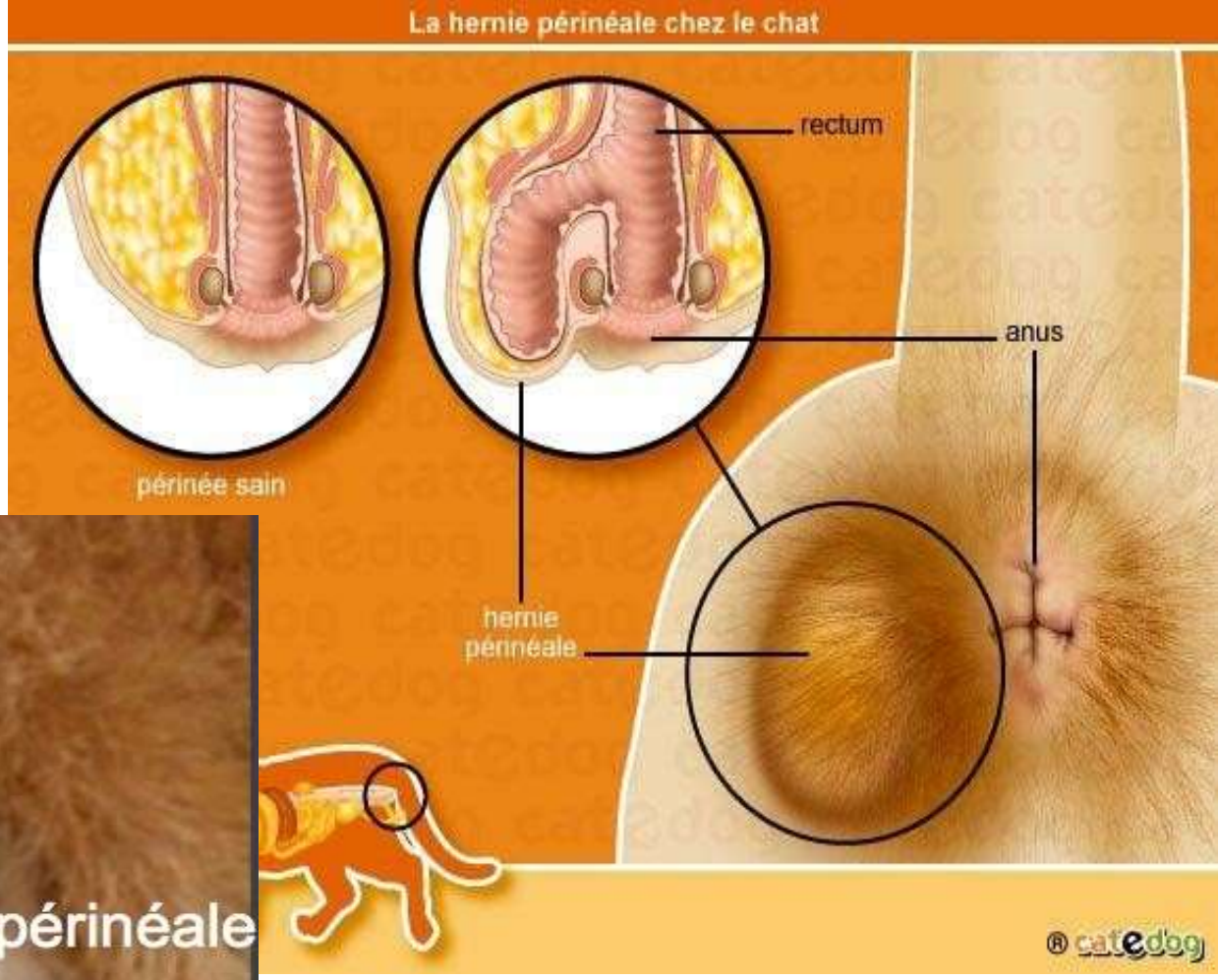
Hernie périnéale droite
Photo 1


La hernie périnéale chez le chat
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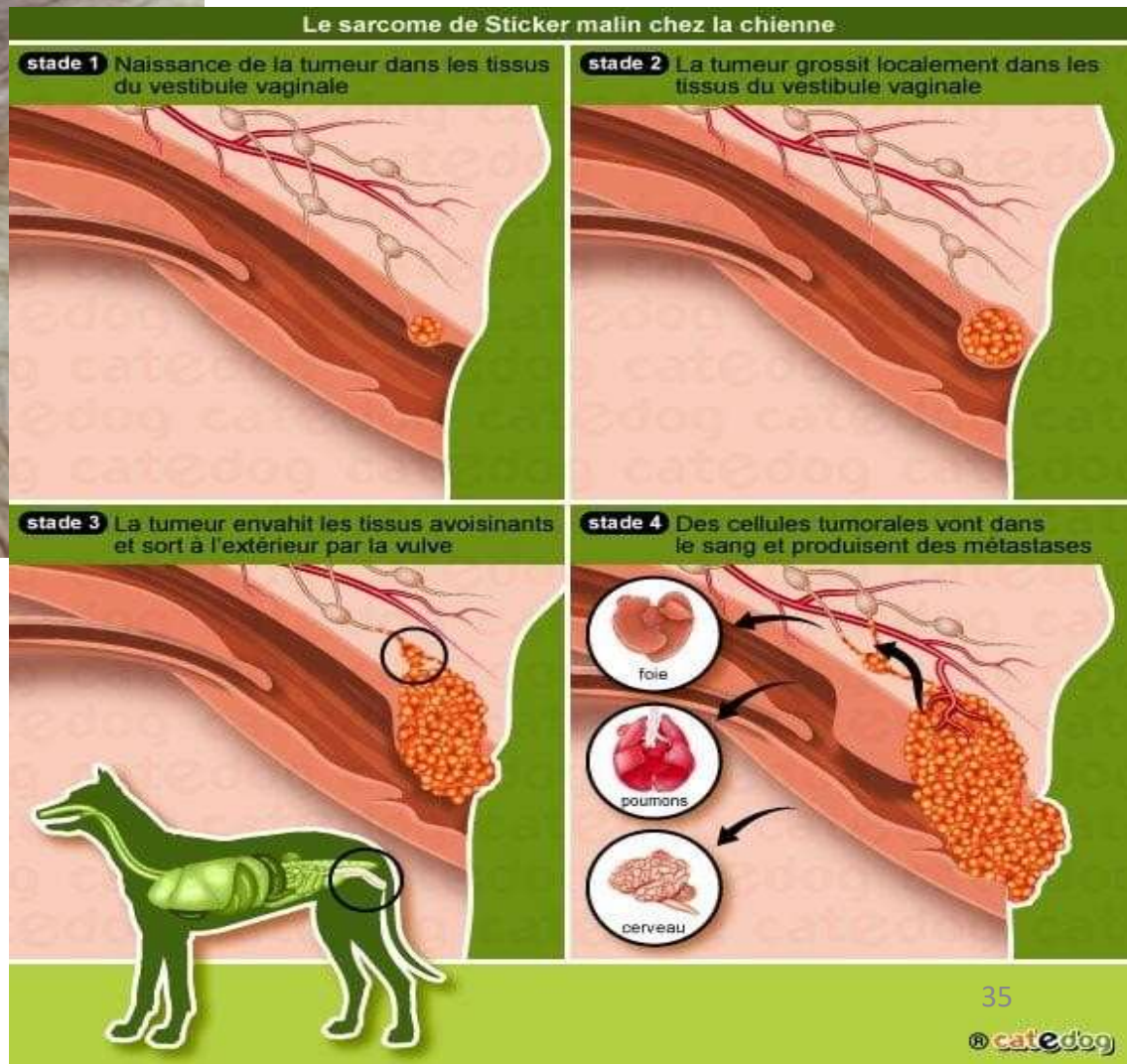

Le sarcome de Sticker malin chez la chienne
stade 1 Naissance de la tumeur dans les tissus du vestibule vaginale
stade 2 La tumeur grossit localement dans les tissus du vestibule vaginale
stade 3 La tumeur envahit les tissus avoisinants et sort à l'extérieur par la vulve
stade 4 Des cellules tumorales vont dans le sang et produisent des métastases
foie
poumons
cerveau
® catedog

- due to a rupture of the urinary tract:

➢ bladder rupture,

➢ urethral or ureteral tear.

Diagnostic approach

In practice, the history and clinical examination should aim to eliminate pre-renal causes (anemia, heart failure, cardiovascular shock) and post-renal causes (sounding, abdominal and transrectal palpation, X-ray, ultrasound), before considering a parenchymal origin.

SYMPTOMS

Extremely diverse.

The clinical signs of AKI depend on the underlying cause, the severity of azotemia, and electrolyte imbalances.

A careful history may lead to the suspicion of AKI.

However, the issues reported by the owner are not typical except for possible anuria and lumbar swelling.

- The decrease in urine production and renal filtration leads to an accumulation of toxins in the blood, known as uremic poisoning = uremic syndrome.
- It is this poisoning that causes anorexia, oral ulcers, uveitis, lethargy, and vomiting/diarrhea, a foul ammoniac smell in the mouth, and gastrointestinal bleeding.

Uremic uveitis

- Other clinical signs include pain on abdominal palpation (kidneys), oliguria, and anemia (sometimes).
- Fluid and electrolyte imbalances are observed due to the decline in kidney function.

➢ Oliguria (or anuria)

In case of AKI, there is a decrease in the amount
of urine
produced.

of AKI. of call for
Oliguria is the

symptom

In case of oliguric episodes, repeated palpations reveal that the bladder retains the same volume (particularly after a transfusion).

Pre-renal AKI:

Due to low blood flow in the kidney;

activation of the renin-angiotensin-aldosterone system; retention of Na+ and water:

- leading to decreased diuresis;
- the urinary density is then high, >1040.

Acute Renal Failure (ARF):

The kidney no longer ensures glomerular filtration.

Post-renal ARF:

Mechanical impossibility to evacuate urine

(anuria).

- **Uremic syndrome**

Uremic syndrome is only observed in cases of poisoning by nitrogenous waste.

It is never present in pre-renal ARF.

Anorexia, lethargy, vomiting, diarrhea, dehydration, then tremors, epilepsy, respiratory disorders (acidosis), coma and death.

Anemia does not have time to set in; however, oral ulcers and hypothermia may be observed.

- Rare and troubled urination, high urinary density (>1030),

proteinuria,

+/- cylindruria,

+/- crystals.

Uremia > 2 g/l

creatinemia > 50 mg/l.

The clinical picture and the biochemical modifications

(urinary and blood) of the uremic syndrome are comparable to what is observed in the terminal phase of CKD in the absence of:

- Anemia.
- Polydipsia-polyuria.
- Renal atrophy

- **Associated symptoms**

Other symptoms are added = those caused by

the etiological agent:

- Pre-renal AKI: Dehydration, heart failure,

  etc.

- Renal AKI: Jaundice (leptospirosis), use of aminoglycosides,.

Hypothermia can be observed in toxic acute renal failure (ARF).

Hyperthermia can be observed in inflammatory acute renal

failure (ARF).

Post-renal ARF: bladder distension, dysuria, rupture of the bladder.

- Low back or abdominal pain

  is sometimes observed in: nephrotoxic ARF, traumatic post-renal ARF.

- Certain renal toxins like gentamicin immediately cause polyuria and proteinuria.

- In dogs: Ethylene glycol is an alcohol that only becomes toxic once metabolized by the liver. The first clinical signs are due to the effect of alcohol on the central nervous system (CNS) and include ataxia, sensory deficits, muscle tremors, nausea, vomiting, and seizures. Polyuria and polydipsia are common as ethylene glycol and its metabolites have a diuretic effect.

DIAGNOSTIC

1. RECOGNIZE RENAL FAILURE

Look for warning signs: oliguria, dehydration, severe and sudden lethargy, etc.

A young animal, previously healthy, that suddenly presents these symptoms must be suspected of ARF.

If it is a hunting dog, leptospirosis must be suspected.

NB:

Urine analysis must be systematic in case of suspected RF, even before blood analysis.

2. CONFIRM RENAL FAILURE

The confirmation of RF involves measuring the products of nitrogen metabolism, which are then elevated (in urine and blood).

3. DATE RENAL FAILURE

Is it an IRA or an IRC?

Look for previous episodes of PUPD.

Note:

Pre-renal insufficiency can evolve in a subacute manner, as is the case, for example, in heart failure.

4. TYPE THE IRA: PRE, POST, or RENAL?

5. IDENTIFY THE CAUSE

- Complete urine analysis with ECBU (Examination Cytobacteriological Examination of Urine).
- Biopsy and histology of the kidney if renal IRA is identified.
- Search for associated signs (e.g., bilirubinuria or hyperbilirubinemia in certain leptospiroses).
- Leptospirosis serology (kinetics) ...

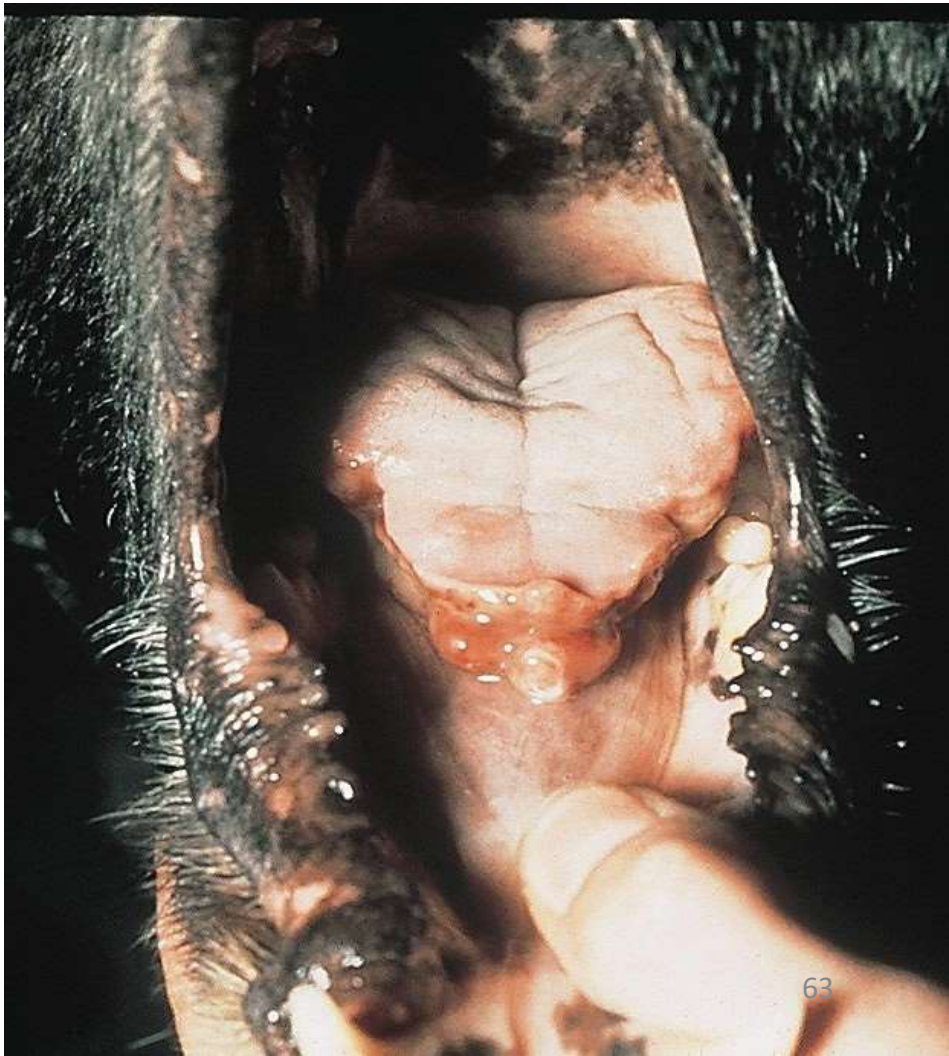
❑ Clinical data

Clinical data for the affected area. can guide toward

Search:

Dehydration, obstruction of urine flow, predisposing factors for kidney damage (e.g., heart failure), signs of urinary infection, etc.

Tongue necrosis in a dog suffering from acute renal failure.



❑ Paraclinical diagnosis

Urine analysis

- **Urinary density**

1007-1018 in general = Isosthenuria is typical of ARF.

A urinary density > 1.025 in dogs and > 1.035 in cats is generally associated with pre-renal azotemia.

❖ **Proteinuri**
a

Mild.

The presence of massive proteinuria of a sign

kidney impairment in particular:

- Glomerulonephritis
.

- Acute nephritis.

In renal IRA, we note:

- An albuminuria.
- A cylindruria (microscopic analysis of the sediment).

The discovery of proteins, in the absence of bacteria, red blood cells, white blood cells or cylinders can be indicative of a glomerular disease (Protein-losing nephropathy).

The urinary protein/creatinine ratio

(UPC) can provide an evaluation

of the exact quantitative concentration of urinary proteins; recommended for every proteinuric patient.

UPC < 0.2 = Normal.

❖ Glycosuria

Sometimes observed, for example, in ethylene glycol poisoning.

The presence of glucosuria in the absence of hyperglycemia is indicative of acute proximal tubular dysfunction but is also observed in Fanconi syndrome.

❖ Hematuria

Observed in most acute renal failure cases.

The strips allow for easy detection of

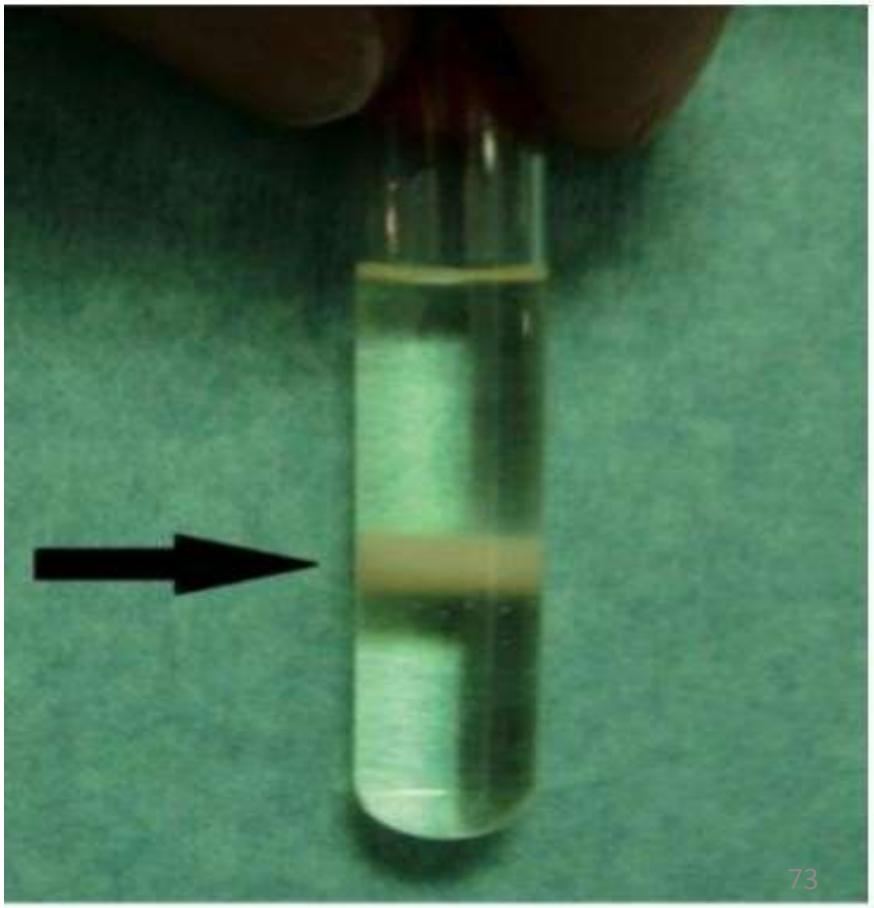
the mentioned parameters

Heller test

Allows for the detection of the presence of proteins:

- Deposit a few milliliters of concentrated nitric acid at the bottom of a test tube.
- Gently pour an equal amount of urine so that the two liquids overlap.

- In the case of proteinuria, a grayish-white halo appears at the contact zone.
- The intensity of proteinuria is proportional to the thickness of the ring.



❖ **Analysis of urinary sediment (and the examination**

cytobacteriological exam of urine = ECBU)

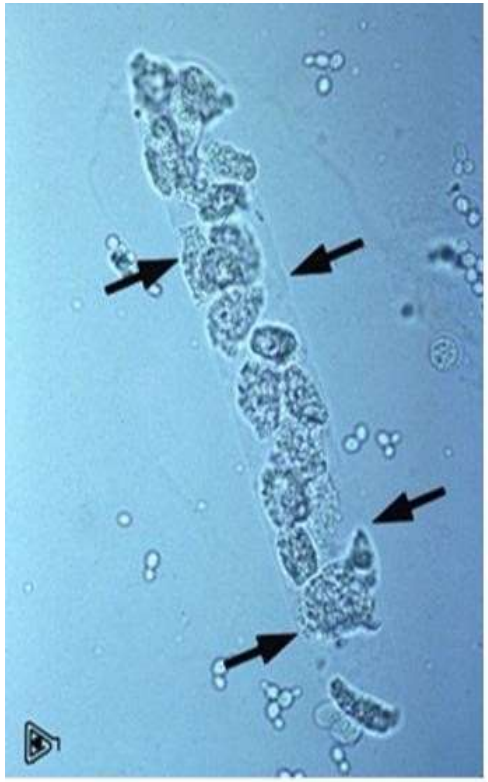
➢ ***Cast***

The presence of casts in the urinary centrifugation

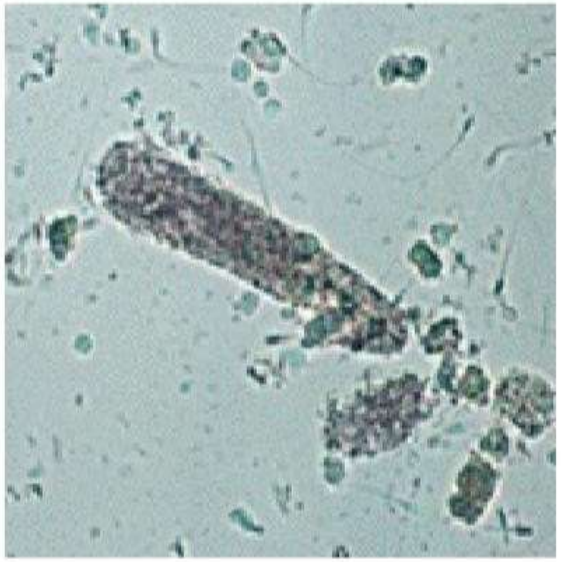
pellet indicates kidney damage.

Acute kidney injury is accompanied by cylindruria.

Cast (cat and dog)



Cylindre cellulaire
(dégénérescence cellulaire, nécrose, inflammation)



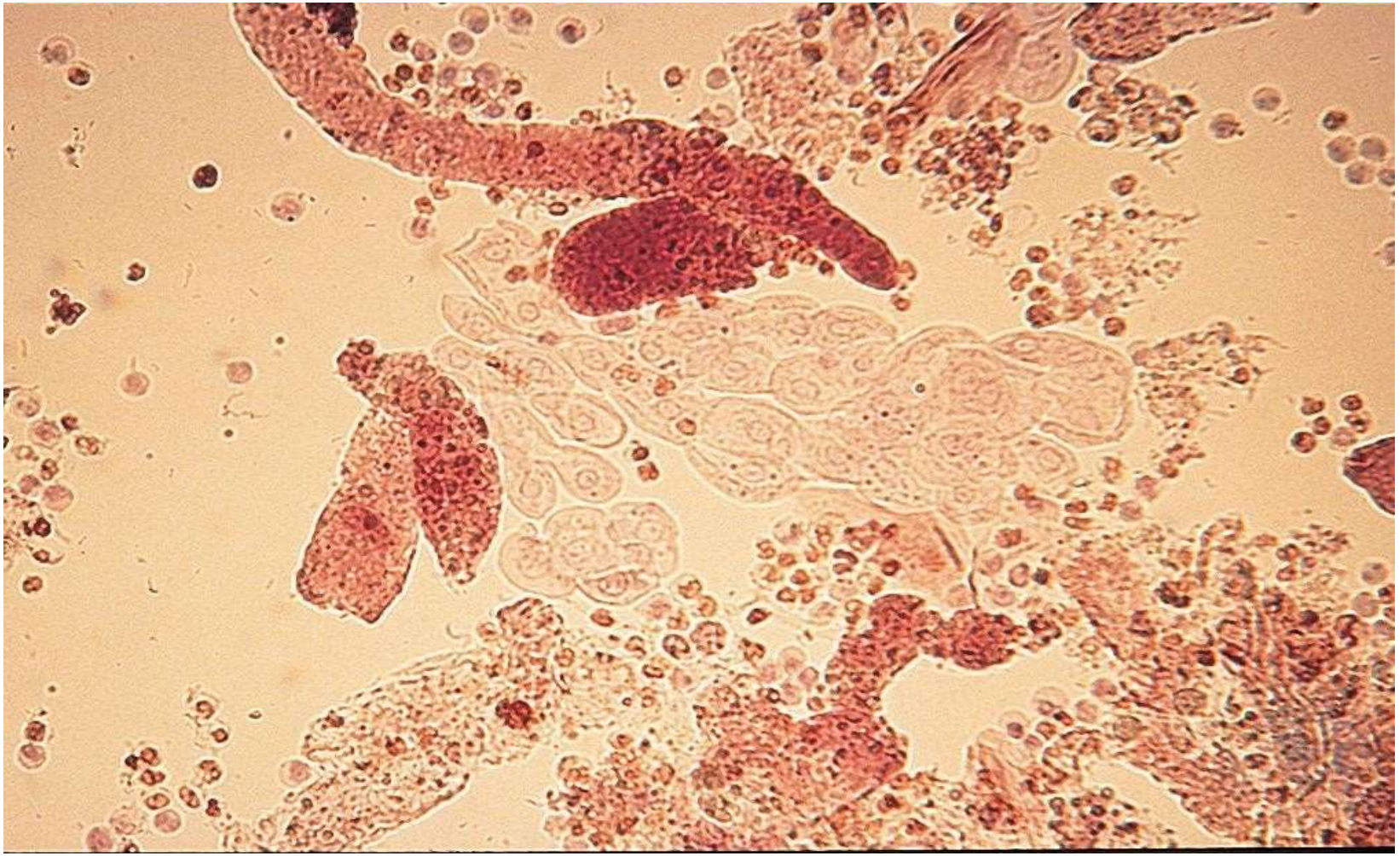
Cylindre granulaire
(dégénérescence cellulaire, nécrose, inflammation)

Cylindre hyalin
(Normal ou protéinurie ++)

Types of casts (Types of casts and associated conditions).

Hyaline casts	Proteinuria: glomerulonephritis and amyloidosis
Granular casts	Degeneration of cells or precipitation of proteins Ischemic or toxic tubular injury
Fatty casts	Granular casts containing lipid Nephrotic syndrome & diabetes
White cell casts	Pyelonephritis
Waxy casts	Final degeneration of granular casts Intrarenal stasis

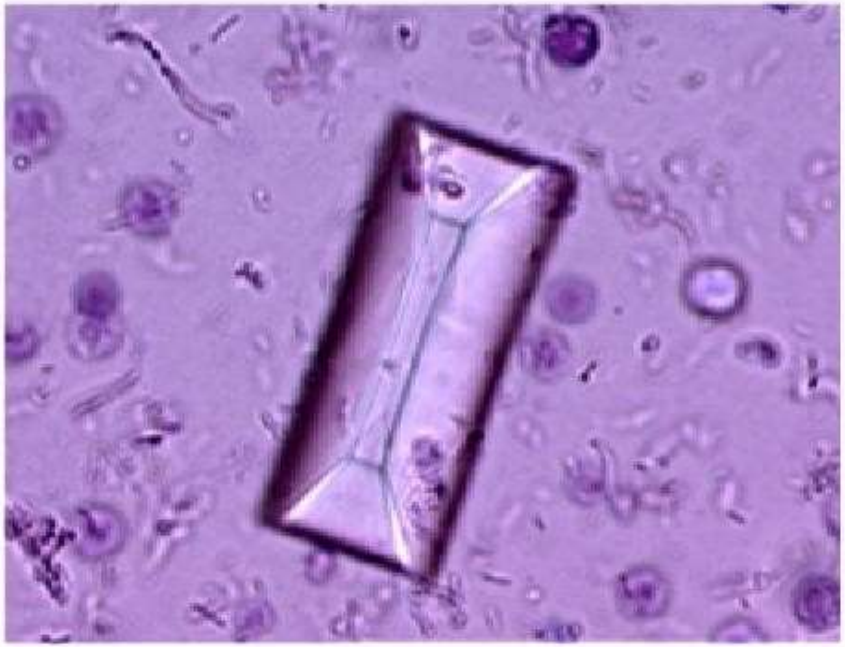
Granular casts (Granular casts in the urine sediment of a dog with acute kidney injury).



➢ *Crystals*

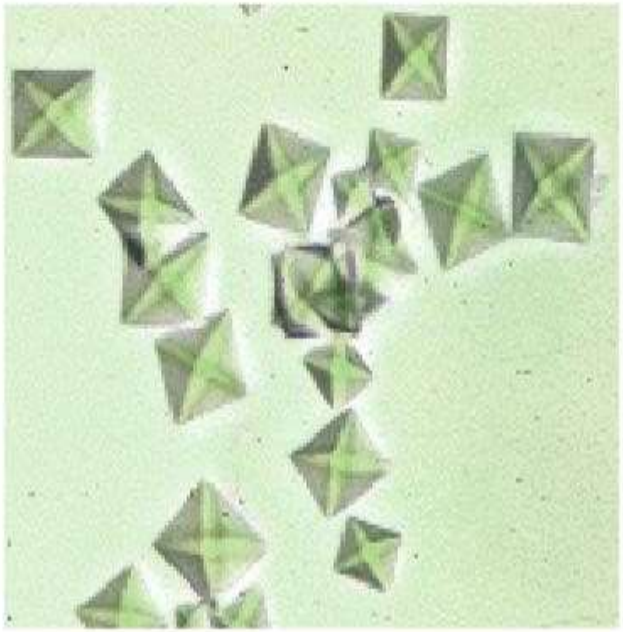
Struvites

- Présents chez les chiens et les chats surtout avec une urine **alcaline**
- Chez le chien ⇨présence de nombreux struvites ⇨ vérifier pour la possibilité d'une infection urinaire

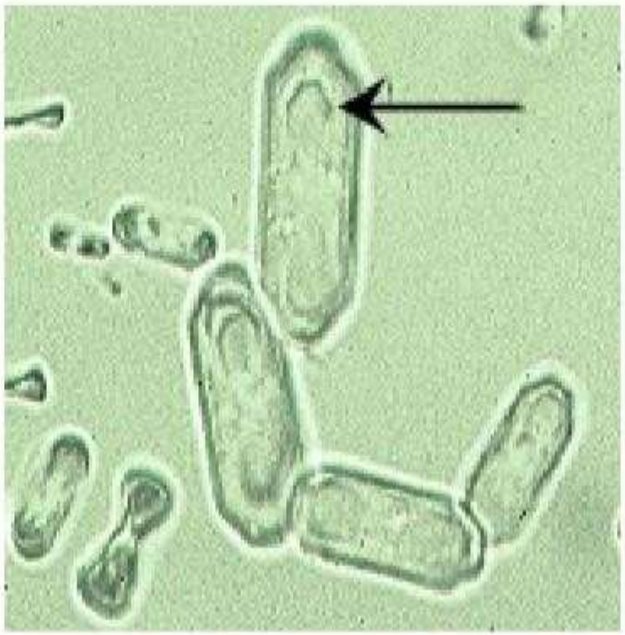


Oxalate de calcium

- Surtout en urine **acide**
- Diète acidifiante
- Chiens et chats: **hypercalcémie, intoxication à l'éthylène glycol*** (forme monohydratée ++)



Oxalates **dihydratés**



* Oxalates **monohydratés**

- ***Bacteria***

Bacteria can be observed in the case of pyelonephritis.

However, the absence of bacteria and/or inflammatory cells does not rule out pyelonephritis as a cause of AKI.

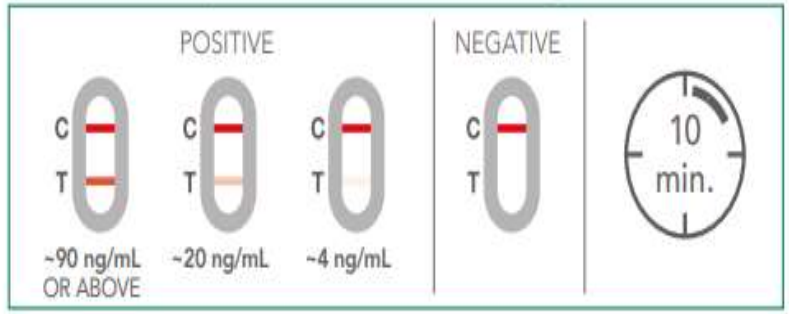
➢ *Urine culture*

- The urine culture should be performed regardless of the appearance of the urinary sediment.
- Microscopic examination of urinary sediments is not very sensitive for the detection of bacteria.
- Microorganisms may go unnoticed during the examination of diluted urine.

KI SCREENING TEST
Canine NGAL Detection

The first and only rapid test for semi-quantitative detection of NGAL in urine for early screening of kidney damage in dogs

For professional in-vitro diagnostic use only



Blood tests

❖ Complete blood count

- Changes in the complete blood count are often nonspecific.
- Elevations in the number of white blood cells may be associated with pyelonephritis and systemic infectious diseases.

❖ Blood biochemical analyses

➢ *Urea and creatinine*

- Elevation of urea and creatinine.
- The simultaneous measurement of urea and creatinine is a good way to assess whether renal insufficiency is pre-renal or not.
- Their levels can be significantly increased in acute renal insufficiency (ARI) renal and post-renal; they are moderately increased in pre-renal ARI.

- Low urea (>0.8 g/l) and creatinine

  normal: pre-renal ARI.

- High urea and slightly elevated creatinine: pre-

  renal ARI complicating with renal ARI.

- High urea (>2g/l) and very high creatinine

  (>50 mg/l): renal or post-renal ARI.

Classification of AKI - According

AKI grade	Blood creatinine	Clinical description
Grade I	<1.6 mg/dl (<140 µmol/l)	Nonazotaemic AKI: a. Documented AKI: (historical, clinical, laboratory or imaging evidence of AKI, clinical oliguria/ anuria, volume responsiveness‡) and/or b. Progressive nonazotaemic increase in blood creatinine: ≥0.3 mg/dl (≥ 26.4 µmol/l) within 48 hours c. Measured oliguria (<1 ml/kg/hour)# or anuria over 6 hours
Grade II	1.7–2.5 mg/dl (141–220 µmol/l)	Mild AKI: a. Documented AKI and static or progressive azotaemia b. Progressive azotaemic: increase in blood creatinine: ≥0.3 mg/dl (≥ 26.4 µmol/l) within 48 hours or volume responsiveness‡ c. Measured oliguria (<1 ml/kg/hour)# or anuria over 6 hours
Grade III	2.6–5.0 mg/dl (221–439 µmol/l)	Moderate to severe AKI: a. Documented AKI and increasing severities of azotaemia and functional renal failure
Grade IV	5.1–10.0 mg/dl (440–880 µmol/l)	
Grade V	>10.0 mg/dl (>880 µmol/l)	

‡ Volume responsive is an increase in urine production to >1 ml/kg/h over 6 hours; and/or decrease in serum creatinine to baseline over 48 hours. IRIS, International renal interest society; AKI, acute kidney injury

Generally, we observe:

- ***Kalemia***

Hyperkalemia in AKI (anuria). Renal and post-renal

Generally normal in pre-renal AKI.

- ***Natremia***

May be increased in renal AKI.

Sometimes decreased in post-renal AKI

- ***Metabolic acidosis = Decrease of ions bicarbonates (HC03-)***

Can be implicated in renal ARF.

It can be masked by vomiting.

Serum bicarbonates decrease while potassium increases with the degree of renal dysfunction.

➢ Anion gap

- Anion gap = ([Na+ + K+] – [Cl- + HCO3 -]).
- Normal canine anion gaps range from 12 to 24 mEq/l, while normal feline values are from 13 to 27 mEq/l.
- Increases may be associated with ketone bodies, lactate, or uremia.
- Significant increases in a patient with ARF suggest ingestion of a toxin.

- ***Phosphoremia (Inorganic phosphorus in serum):***

  Often increased, particularly in renal AKI; sometimes normal in pre-renal AKI.

- ***Calcium: Often slightly to moderately elevated, but dramatic decreases are associated with***

  ethylene glycol toxicity.

❖Hematocrit

Generally normal.

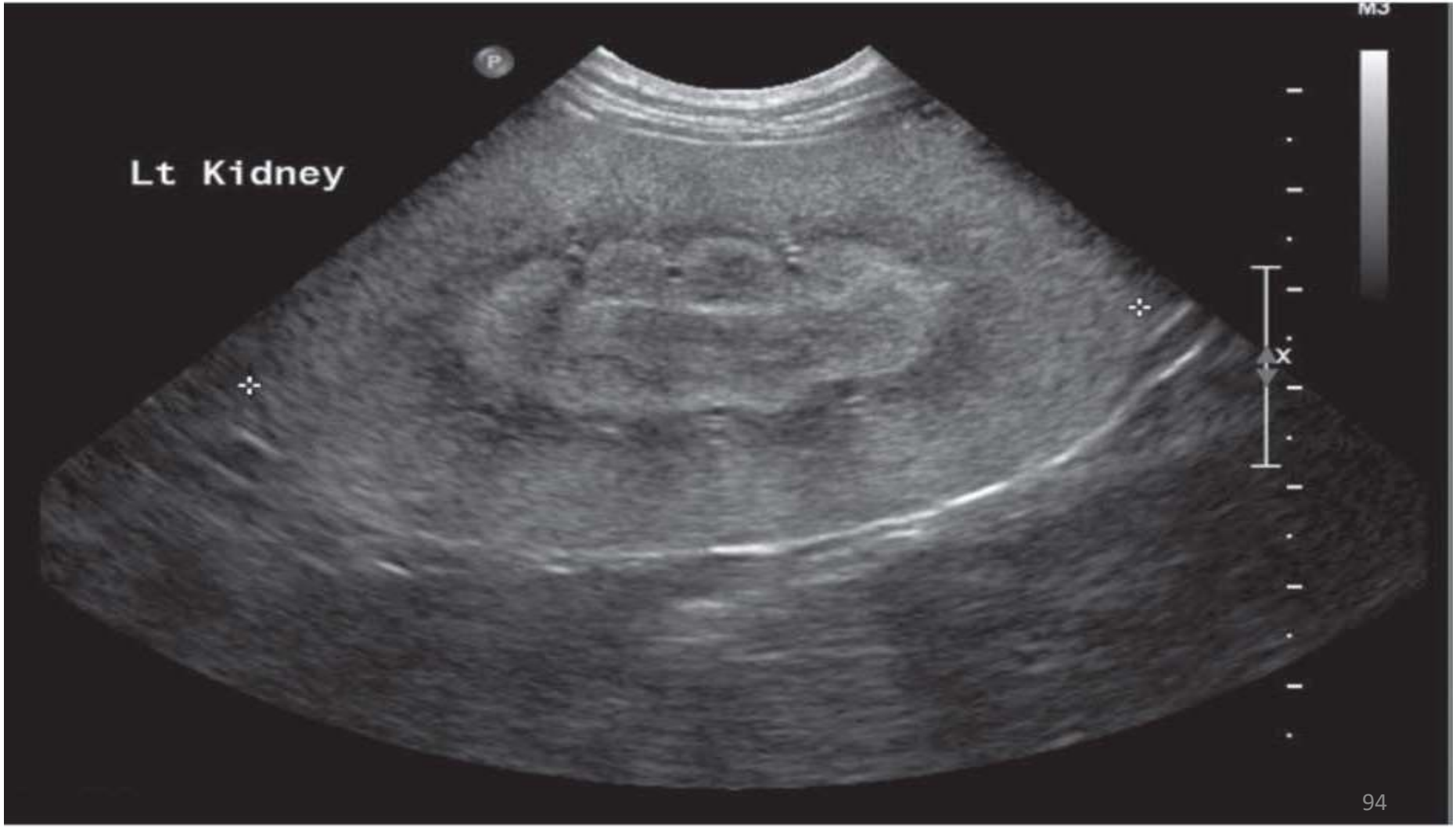
Increased due to dehydration = In pre-renal and post-renal AKI (Ht>50 l/l).

(Hematocrit norms: CT=24-45; CH=37-55).

X-ray and ultrasound

- Ultrasound can provide information on renal architecture, excretion pathways, and renal blood flow.
- Patients with acute renal failure generally some kidneys present normal to enlarged size, while of small irregularly shaped kidneys suggest chronic disease (e.g. CRF).

Ultrasound of a kidney in a dog poisoned with ethylene glycol. Note the significantly increased echogenicity of the renal cortex.



Serology for infectious diseases

- In regions where leptospirosis is endemic, antibody titers for prevalent serovars should be conducted when acute renal failure is suspected.
- There are PCR tests for leptospirosis.
- Other serological tests (e.g. leishmaniasis, rickettsiosis, babesiosis) should be considered based on the patient's location and relevant travel history.

Blood test for ethylene glycol

- Any patient presenting with severe metabolic acidosis + increased anion gap + calcium oxalate crystalluria + hypocalcemia + clinical signs = must be tested for exposure to ethylene glycol.
- There are test kits to detect exposure to ethylene glycol (sensitive in dogs, unreliable in cats).

PROGNOSIS The AKI (especially renal AKI)

Serious condition, rapidly fatal in absence of treatment.

Survival can only be hoped for at the cost of intensive care requiring significant skills and human commitment which implies a high cost.

Several parameters will influence the prognosis:

- Type of AKI,
- Etiological agent,
- Early treatment,
- Importance of azotemia,
- Response to treatment,
- Existence of another organ damage (heart, liver, etc.).

Etiologies	Taux de survie (%)
Infectieuses	**58 - 86**
• Leptospirose	56 - 85
Toxiques	**18 - 69**
• Ethylène glycol	5 - 20
• Raisin	50 - 75
• Gentamicine	20
Métaboliques / hémodynamiques	**56**

- PRERENAL AKI

Good prognosis if it is possible to quickly restore correct renal hemodynamics (correction of dehydration, treatment of heart failure, etc.).

The prognosis is less favorable in the case of shock

severe hypovolemia or already treated heart

failure.

Mild but prolonged prerenal AKI leads to the

development of CKD.

Note: what kills is not the prerenal AKI or post-renal AKI is still renal AKI.

Other AKI types are only formidable to the extent that they are complicated by renal AKI.

- RENAL AKI

Generally poor prognosis. nearly 100% mortality in anuric AKI!

This prognosis depends, of course, on the etiological agent.

Leptospirosis being the leading cause of AKI.

- POST-RENAL AKI

Fatal in 2 to 5 days without treatment.

After removal of the obstacle and correction of imbalances, it has a good prognosis.

TREATMENT

Goals of treatment:

- Etiological treatment: Remove the cause.
- Symptomatic treatment: Correction of hydro-electrolytic and acid-base imbalances + Restart diuresis.
- Manage complications.

ETIOLOGICAL TREATMENT

1. PRE-RENAL AKI:

Perfuse the kidney =

- Rehydration.
- Treatment of heart failure or rhythm disorders.
- Stop the administration of diuretics, NSAIDs.

2. AKI:

The identification of a toxic, toxicological, or infectious cause will be followed by etiological therapy:

- Elimination of the toxin (Stop administration of aminoglycosides).
- Restart diuresis.
- Resort to peritoneal dialysis if the toxin is dialyzable.

- Antibiotic therapy in case of infection: leptospirosis, metritis, etc.
- Avoid nephrotoxic antibiotics.
- Ovariohysterectomy if pyometra.

3. POST-RENAL AKI:

Removal of the obstacle after correction of hydro-electrolytic and acid-base imbalance:

- Urethral catheterization.
- Surgery: stones, tumors, ruptured urinary tracts.

SYMPTOMATIC THERAPY

❖ Fluid therapy

- The basis of treatment.
- Due to anorexia, vomiting, and a reduced ability to concentrate urine, dehydration is common in patients with ARF.
- Initial fluid therapy must consider 3 factors: the patient's dehydration, maintenance fluids, and insensible losses.

- In the absence of risk of congestive heart disease or hypovolemic shock; OR if it there is hyperkalemia, = Deficits from fluids are replenished. the intake of crystalloids (NaCl 0.9% for example) IV.
- Other balanced crystalloids can be used (LRS, Normosol, Ringer lactate) in the absence of hyperkalemia.

- **Water deficit:**

The degree of dehydration of the patient should be estimated; the total volume of fluids needed to correct the dehydration can be calculated using the equation:

Deficit in liters = % of dehydration × body weight (Kg)

The volume is administered IV over 8 to 12 hours.

% déshydratation x poids vif (en kg) x 1000 = quantité à administrer (en mL)

Pourcentage de déshydratation	Signes cliniques
< 5 %	• Aucun
5 %	• Pli de peau légèrement persistant (<2 secondes)
6-8 %	• Pli de peau persistant (>2 secondes) • Muqueuses buccales collantes • Temps de remplissage capillaire augmenté (>2 secondes) • Enophtalmie modérée
10-12 %	• Pli de peau persistant • Muqueuses buccales sèches • Temps de remplissage capillaire largement augmenté • Enophtalmie marquée • Choc hypovolémique (abattement, tachycardie, pouls filant, extrémités froides...)
12-15 %	• Troubles neurologiques • Mort imminente

- **Maintenance needs:**

A permanent urinary catheter should be placed aseptically to measure urine output.

Urine production/hour is equal to the maintenance fluid rate.

- **Insensible losses (fluid lost through the respiration and normal stools)** **via**

Can be estimated at 20 ml/kg/day + fluids lost due to vomiting or diarrhea.

Example:

- A 10 kg dog presenting for an AKI is dehydrated by 10% and produces 5 ml/hour of urine.
- Total dehydration is determined to be 1 liter (10 kg × 0.10), to be administered over 8 to 12 hours.
- Thus, the dehydration component of hourly fluid therapy is 83 ml/hour (1,000 ml/12 hours).
- The patient produces 5 ml/h and this represents the maintenance fluids.
- No vomiting or diarrhea has been reported. Insensible losses are therefore 8 ml/hour ([20 ml/kg × 10]/24).
- Fluid rate/hour for the next 12 hours should be 96 ml/h (83 ml/h + 5 ml/h + 8 ml/h).
- Urine production/hour is monitored regularly and the maintenance liquid component is

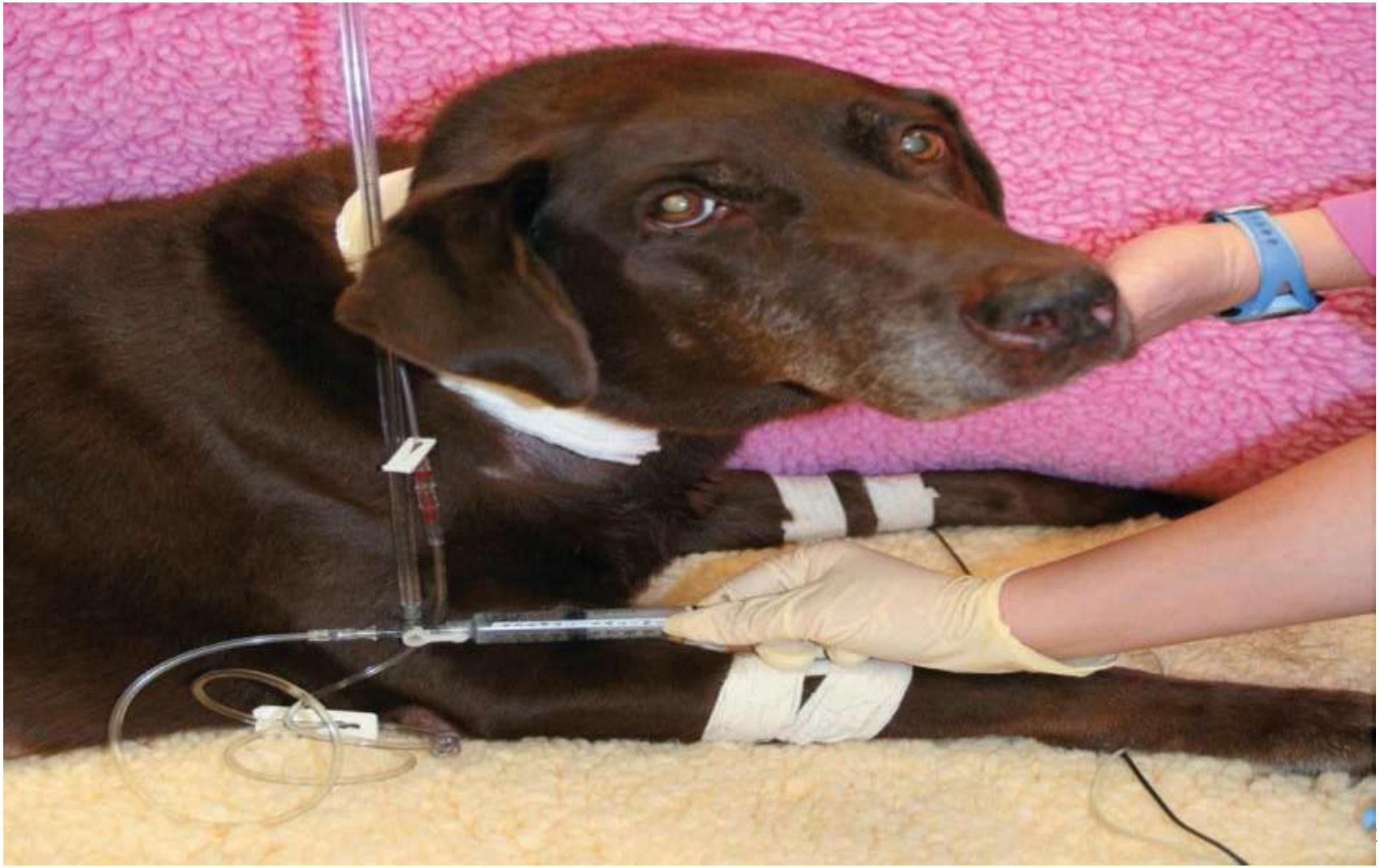
- Once dehydration is corrected, fluid therapy should only account for = maintenance fluids + insensible losses.
- To determine maintenance fluids, urine must be collected and quantified at regular intervals (e.g., every 4 hours) and the hourly urine production rate can be used as the 'maintenance' rate.
- Insensible losses can be estimated at 20 ml/kg/day + all fluids lost due to vomiting or diarrhea.

Example:

- The 10 kg dog is now well-hydrated. The patient produces 9 ml/hour of urine and this represents the maintenance fluids.
- No vomiting or diarrhea has been reported, so the insensible losses are 8 ml/hour (20 ml/kg × 10/24).
- Therefore, the hourly fluid rate for the next 12 hours should be 17 ml/hour (9 ml/hour + 8 ml/hour).
- Urine production is monitored regularly (e.g., every 4 hours) and the maintenance component is adjusted.

- Les patients atteints d'IRA présentent un risque élevé de surcharge hydrique et de décès (surtout pour les animaux oliguriques ou anuriques).
- Dans la mesure du possible, la pression veineuse centrale (PVC) doit être surveillée en plus du débit urinaire (normes = 5 CT ; 10 CN cm d’H2O)= Augmentation suggère un débit d'administration de liquide excessif.
- Poids du patient peut fournir des informations sur l'état d'hydratation du patient = indicateur insensible pour être utile comme seule méthode de surveillance.

Mesure de la pression veineuse centrale chez un chien.



NB:

- Le Monitorage cardiovasculaire peut être utile pour surveiller l'hyperhydratation
- Signes cliniques : Recherche des signes de d'hyperhydratation = Tachycardie, œdème pulmonaire.

NB:

- Lors de dehydrations significant associée à hypotension, the use of boluses (10-30 ml/kg) of high-flow crystalloids (up to 90 ml/kg) may be recommended.
- Colloids should be avoided.

❖ Forced diuresis techniques

- The goal should be a diuresis of at least 1 ml/kg/hour.
- Well-hydrated animals that produce < 0.25 ml/kg/h of urine are considered to be in oliguric AKI.
- Patients suffering from anuric AKI produce no urine.
- These conditions require aggressive treatment = forced diuresis.

- Sometimes, patients with AKI will produce large volumes of urine once dehydration is corrected =
- These polyuric patients are probably less severely affected and are generally easier to manage clinically, as they are less likely to develop fatal abnormalities and fluid overload; however, they still require a close monitoring.

- ***Mannitol***

- Sugar with osmotic power that increases intravascular volume = improves RBF (renal blood flow). .
- Reduces swollen tubular cells = increases tubular flow and combats tubular obstructions.
- In oliguric and anuric animals not overloaded with mannitol and well hydrated, it is considered the treatment of choice.

- Administered as an IV bolus of 0.25 to 1.0 g/kg over 30 minutes (infusion).
- If urine production improves, a rate of 1 to 2 mg/kg/minute may be established (CRI: Constant Rate Infusion = continuous infusion).

o Mannitol is contraindicated in:

- Patients with ethylene glycol toxicity as it may further exacerbate hyperosmolality and neurological signs.
- Patients with heart failure, severe fluid overload, and pulmonary edema.

If there is no response to treatment or in an overhydrated animal, treatment with furosemide should be attempted.

- ✓ ***Furosemide (Lasilix)***
  - Loop diuretic that increases urine output by inhibiting the reabsorption of NaCl.
  - Administered as a bolus (2 mg/kg IV).
  - If urine production increases, it is continued as a CRI = 0.25 to 1.0 mg/kg/hour (or 1 to 2 mg/kg IV QID).

If diuresis does not return, the following may be administered:

- Furosemide (Lasilix), 2 mg/kg IV.

+

- Dopamine (FINILAC) at 2-5 µg/kg/min IV in a perfusion fluid to increase renal blood flow (0.45% saline, 5% glucose).

- Dopamine increases DSR and glomerular filtration rate (GFR), promoting sodium excretion by the kidneys.
- Dopamine is used with caution; its effects depend on the dose administered and it is a positive inotropic catecholamine that raises blood pressure.

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- In the absence of effect, we renew the furosemide (4mg/kg IV) and double the dose of dopamine per minute.
- If diuresis occurs, administer furosemide 2mg/kg every 8 hours.
- In case of failure after 4 hours of treatment, an EER technique must be implemented.

NB:

- The toxicity of aminoglycosides should not be treated with furosemide as it may potentiate other renal injuries.
- Patients who produce significant amounts of urine in response to rehydration or treatment with mannitol/furosemide are less likely to require specific treatment for electrolyte and acid-base imbalances.
- Oliguric and anuric renal insufficiency patients who do not respond to medical management may quickly develop fatal hyperkalemia and metabolic acidosis.

MANAGE COMPLICATIONS

❖ Correction of hyperkalemia

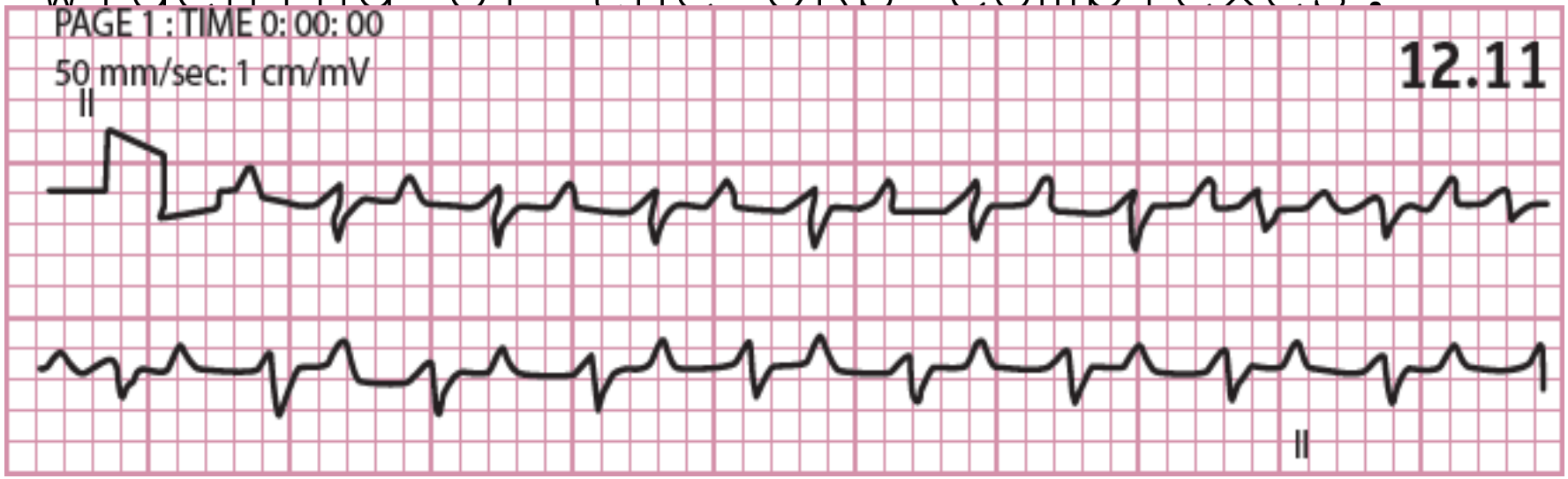
- Hyperkalemia is a potentially life-threatening electrolyte imbalance.

- Often encountered in AKI.

- An emergency that must be managed quickly, as it leads to severe cardiac disturbances and can be fatal.

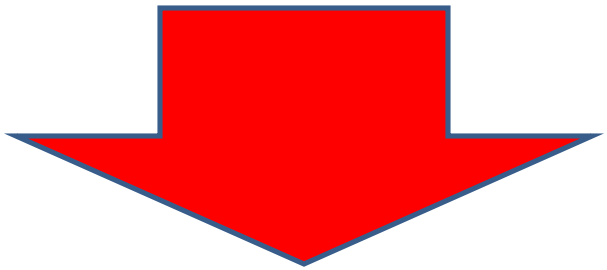
- The elevation of serum potassium leads to a reduction of the electrochemical gradient and transmembrane alters the excitability of nerve and muscle cells.
- muscle weakness, decreased Clinicall cardiac y, tachy contractility, arrhythmias, and neurological abnormalities. hyperkale

The classic ECG signs include bradycardia, disappearance of the P wave, peaked T wave, and widening of the QRS complexes.



Example of an ECG of patient with hyperkalemia (Lead II).

- These changes begin to appear when potassium approaches 6.5 mEq/l (norms = 3.7-5.8 CN; 4-4.5 CT).
- Cardiac arrest can occur at any moment.
- However, there are several short-term management strategies for this condition:



- Calcium gluconate (10% solution):

➢ 0.5–1.0 ml/kg administered IV over 10–15 minutes. Protects against cardiac toxicity for about 30 minutes = Protects the myocardium and counteracts the arrhythmogenic effects of hyperkalemia.

➢ Under ECG monitoring until the ECG abnormalities resolve.

- Regular insulin (0.1–0.25 units/kg) and glucose (1–2 g/unit of insulin):

➢ Potassium is transported into cells with glucose.

➢ Provides short-term correction = Allows for a decrease in serum potassium levels.

- Sodium bicarbonate (1–2 mEq/kg in 20 minutes):

➢ Hypokalemic action by transferring K+ ions into the cell.

➢ Moreover, its alkalizing property is interesting during metabolic acidosis.

➢ The effects can last 1 to 2 hours.

Note:

Emergency treatment can be supplemented with ion-exchanging resins (kayexalate) PO, 5 to 10 g/day to decrease intestinal absorption of potassium.

❖ Correction of metabolic acidosis.

- Metabolic acidosis is also common in AKI, as the renal tubules are responsible for the reabsorption of filtered bicarbonate.
- Moderate to mild metabolic acidosis (bicarbonates > 15 mEq/l) most often resolves with fluid therapy.
- The most severe acidoses (<12 mEq/l and pH <7.2) require bicarbonate supplementation.
- Norms (mEq/l) = 18-25 CN; 17-22 CT.

- A dose of bicarbonate can be calculated (mEq)= (body weight in kg × 0.3) × (16 - measured bicarbonate [mEq/l]).
- As a general rule, only 2/3 of the dose is administered = 1/3 IV over 30 minutes, then 1/3 can be given IV in the next 4 hours (with infusion fluids).
- The acid-base status should be reassessed before administering additional bicarbonate.

❖ Vomiting

- Very frequently, patients with AKI experience significant vomiting which can complicate treatment, worsen electrolyte abnormalities, and contribute to dehydration.
- The vomiting is likely due to both stimulation of the chemoreceptor area by uremic toxins and gastric irritation.
- These should be treated with a combination of anti-emetic and gastric protective medications.
- Until the vomiting is controlled, these medications should only be administered intravenously.

Vomiting protocols used in patients with acute kidney injuries. to control the of

Antiemetic protocols	Metoclopramide (Reglan): dopamine inhibition (1.0–2.0 mg/kg IV or CRI q24h)
	Maropitant citrate (Cerenia): NK1 inhibition (1.0 mg/kg SC q24h [dogs]; 0.5–1.0 mg/kg SC q24h [cats])
	Ondansetron (Zofran): 5HT3 inhibitor (0.1–0.2 mg/kg IV [slow push] q6–12h)
	Dolasetron (Anzemet): 5HT3 inhibitor (0.4–0.6 mg/kg IV q24h)
Gastric irritation	Omeprazole (Prilosec): proton pump inhibitor (0.7–1.0 mg/kg PO q12–24h)
	Sucralfate (Carafate): gastric coating (0.5–1.0 mg/kg PO [dog]; 0.25 mg/kg [cat])
	Famotidine (Pepcid): H2 receptor antagonist (0.5 mg/kg PO, SQ, or IV q24h)

❖ Treatment of diarrhea

Digestive dressings:

Smectite 500 mg/kg BID.

kaolin.

NUTRITIONAL SUPPORT

The purpose of nutritional support is:

- To meet energy, vitamin, mineral, and protein needs.
- To minimize azotemia and electrolyte and acid-base disturbances.

The ideal nutritional diet for dogs

and cats with ARF is not defined

but according to some studies, the diet

should be high in energy, low in

proteins, potassium, sodium and

phosphorus.

EXTRARENAL PURIFICATION (EER)

- If the initial administration of fluid therapy suitable for the estimated losses does not induce sufficient diuresis within the first 6 to 12 hours.

- Forced Diuresis is performed.

- If forced diuresis proves ineffective = Resort to EER techniques.

Extrarenal purification techniques (EER)

1- Peritoneal dialysis

Method of choice in acute oliguria.

- Supplanted by hemodialysis; still used; requires less equipment than hemodialysis.
- Well tolerated by animals from a cardiovascular point of view.
- Induces a septic risk due to bacterial contamination of the drain.

- Peritoneal dialysis (PD): Endocorporeal dialysis method, uses the peritoneum as a membrane allowing exchanges between blood (loaded with waste) and the dialysis fluid.
- The peritoneal membrane is semi-permeable.

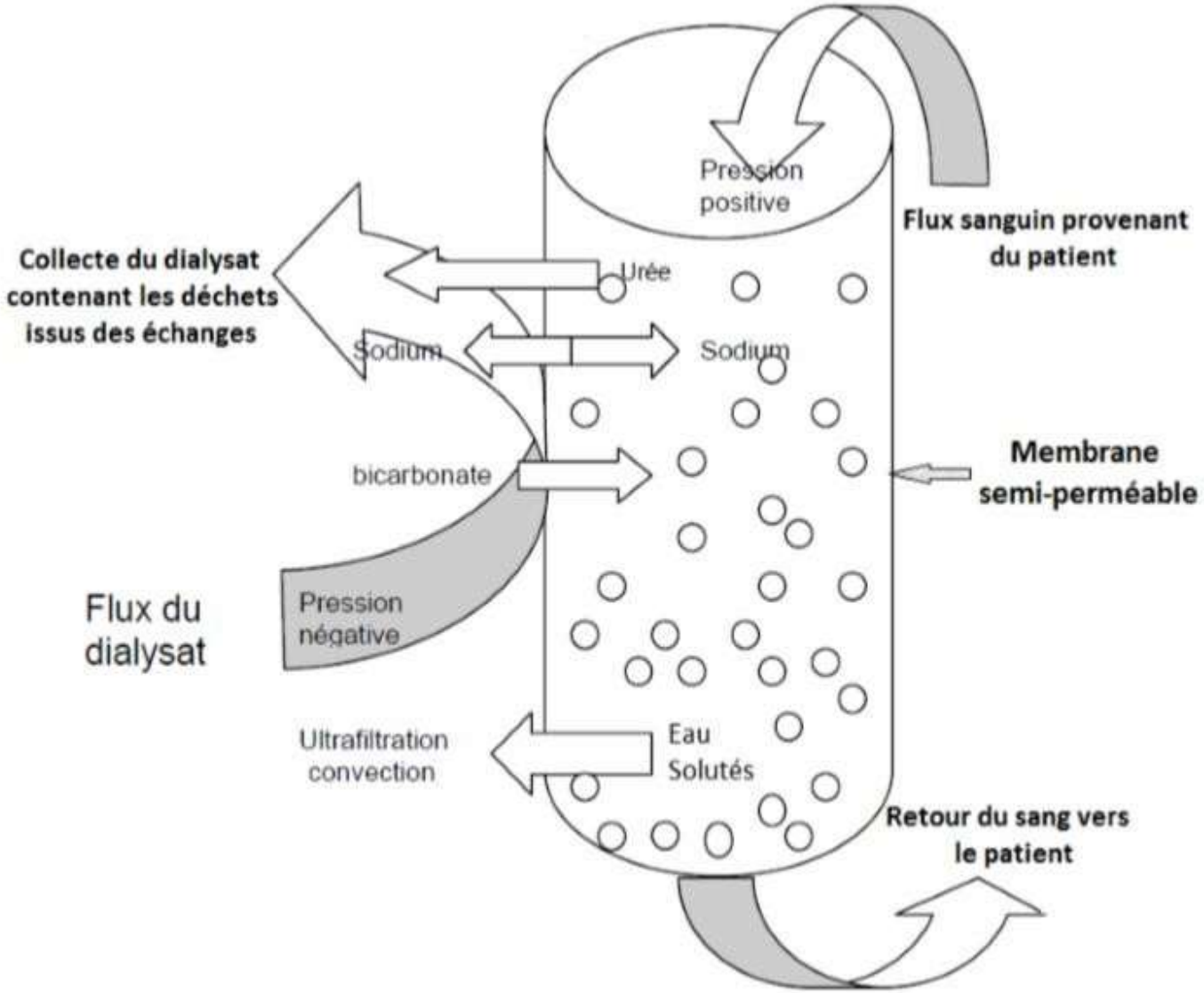


Figure 6 : Principes de diffusion et de convection (ultrafiltration) à travers une membrane semi-perméable (d'après Elliot, 2000)

The equipment consists of:

- Peritoneal dialysis catheters (Tenckhoff® drain, Blake silicon fluted drain®, Jackson Pratt® drain, Anicath®...).

- Perfuser.

Commercial peritoneal dialysis fluids have variable compositions:

	Formule A	Formule B
Sodium (mEq/l)	**141**	**141**
Potassium (mEq/l)	**0**	**0**
Calcium (mEq/l)	**3,5**	**3,5**
Magnésium (mEq/l)	**1,5**	**1,5**
Chlore (mEq/l)	**101**	**101**
Lactate (mEq/l)	**45**	**45**
Glucose (g/l)	**15**	**42,5**
Osmolalité (mOsm/l)	**366**	**505**

- Formula A for the patients normovolemic.
- Formula B: for patients with overload volemic (hyperhydration).

In Algeria, the veterinarian must resort to

human use solutions (hospital use):

Bi-compartment bag

Composition de :
PHYSIONEAL 40 avec glucose à 1,36 %
PHYSIONEAL 40 avec glucose à 2,27 %
PHYSIONEAL 40 avec glucose à 3,86 %

Composition de la solution finale (mmol/L) après le mélange :			
	1,36 %	**2,27 %**	**3,86 %**
Glucose anhydre ($C_6H_{12}O_6$)	75,5	126	214
Sodium (Na^+)	132	132	132
Calcium (Ca^{++})	1,25	1,25	1,25
Magnésium (Mg^{++})	0,25	0,25	0,25
Chlorure (Cl^-)	95	95	95
Bicarbonate (HCO_3^-)	25	25	25
Lactate ($C_3H_5O_3^-$)	15	15	15

Concentration de glucose de la solution	**1,36 %**	**2,27 %**	**3,86 %**
Osmolalité (mOsm/l)	344	395	483

Technique:

- Introduction of the catheter by simple "puncture-tunneling" of the abdominal wall or by small laparotomy (depending on the type of catheter).

- In a paramedian position in a declive area of the abdomen.
- The position of the catheter is chosen to minimize the risks of obstruction as much as possible.
- In an aseptic manner to minimize the risk of septic peritonitis.

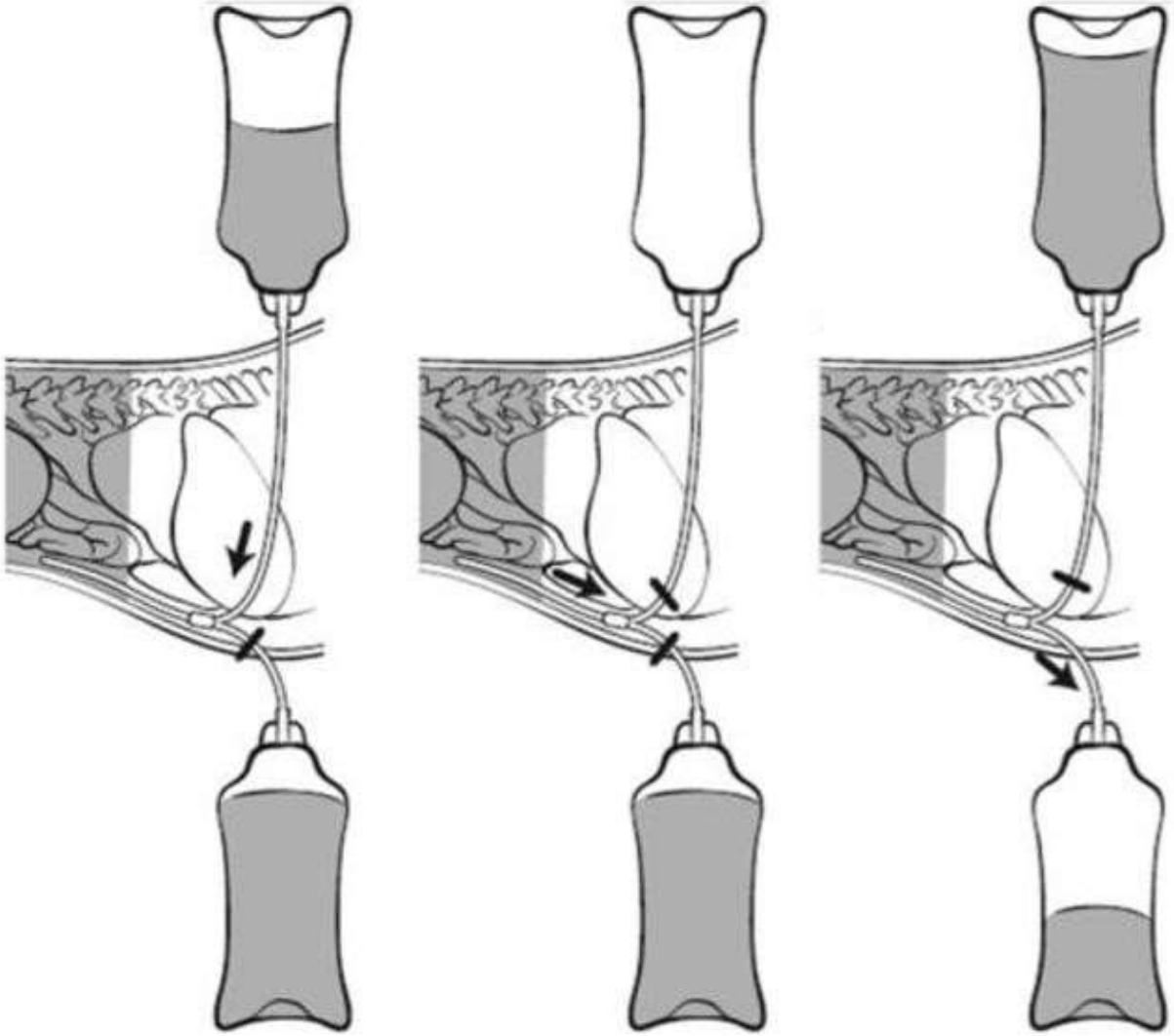
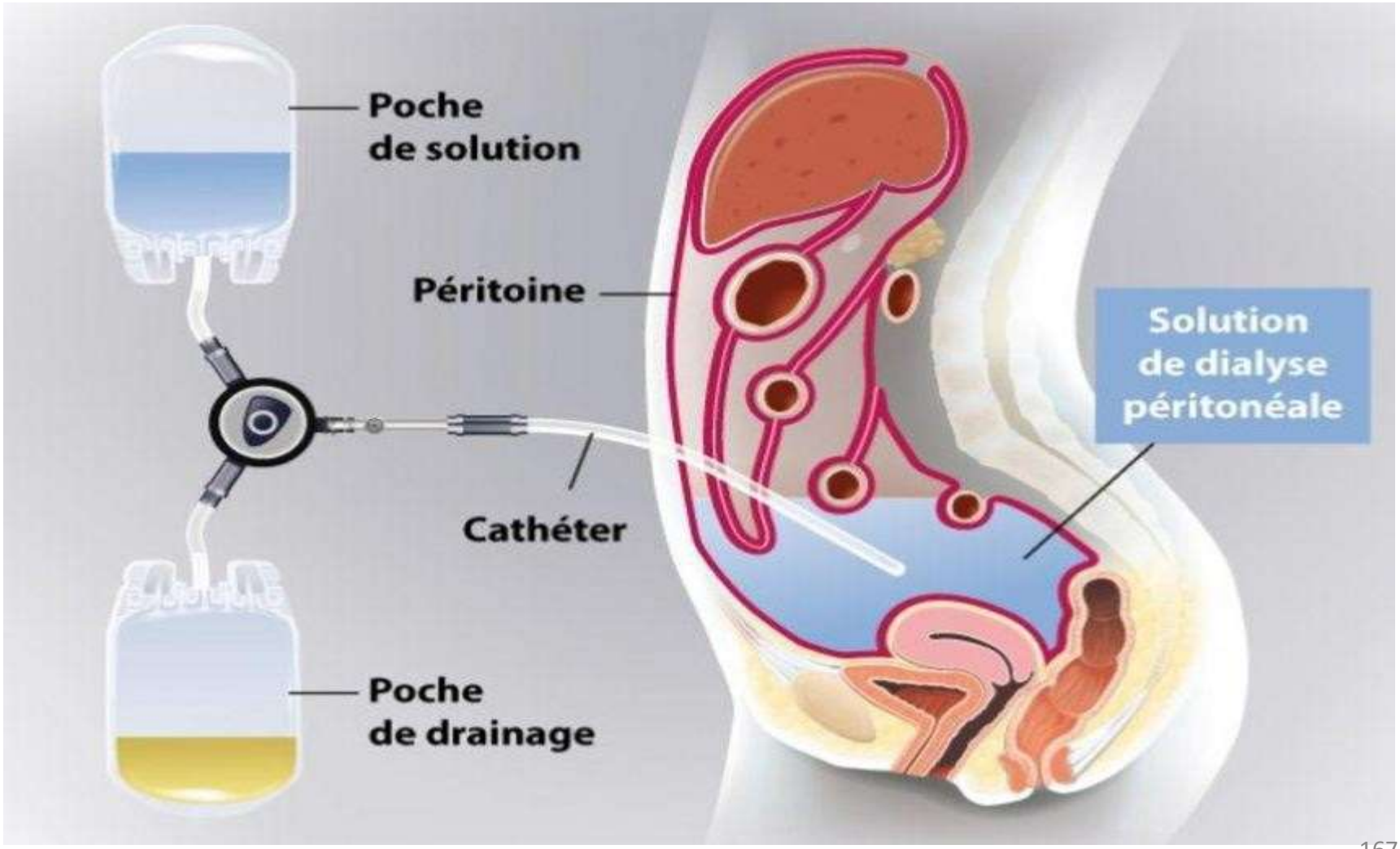


Figure 5 : Protocole de dialyse péritonéale (d'après Cooper et Labato, 2011)

Peritoneal dialysis in men



- Warmed dialysate (2-3°C above the patient's body temperature).
- Inject the dialysate into the peritoneal cavity at 10-20 ml/kg (up to 59 ml/kg) over a period of 5 to 10 minutes.

The fluid is left in place in the abdomen for 30 to 40 minutes and then recovered by siphoning (by gravity over about twenty minutes).

The amount of liquid recovered must be:

- The same as that of liquid injected in the case of normovolemic animals.
- Higher in the case of animals with fluid overload.

Note:

In the first exchange, the amount of liquid

the recovery is low.

From the second exchange, 90%-95% of the amount

injected must be collected.

- The sessions are repeated every 1 to 2 hours: at least 4-5 dialysis cycles/24 hours.

- Sessions must be conducted with the utmost possible asepsis.
- With each catheter manipulation, inject an antibiotic (Ampicillin 30-50mg/kg) through it.

The catheter is heparinized after each dialysis session

(500 UI/l, 0.5ml per liter) to prevent

obstruction of the catheter by fibrin.

The effectiveness of peritoneal dialysis is based on:

- The clinical improvement of the animal.
- On the hourly dosage of urea during the sessions:

➢ Effective dialysis reduces uremia by 0.1 to 0.3 g/l/h.

On average, the duration:

- Lasts between 5 and 10 days
- It can, in some cases, extend to 3-4 weeks.

The complications are of a technical nature:

- Catheter obstruction.
- Infectious (risk of peritonitis).
- Metabolic (hypoalbuminemia, fluid overload or peritoneal effusions).

The survival rate with this technique varies from

24 to 67 %.

2- Hemodialysis

Extracorporeal sanguine par circulation dialysis has become over the last 20 years the therapy of choice in the management of ARI.

Patient under

Its low availability and high cost make it hardly accessible;

Performed only in veterinary hospital centers or in certain specialized clinics and currently, only a few centers in France and Europe offer it.

Hemodialysis is considered:

- When renal parameters worsen or when they do not improve significantly after 24 or 48 hours of fluid therapy:

- Severe azotemias (creatinine > 800 μmol/l = 90.49 mg/l).
- Onset of oliguria.
- Signs of volume overload.
- Persistence of hyperkalemia and/or metabolic acidosis despite infusion and forced diuresis must.

SOME ETIOLOGIES

TREATMENTS

❖ Leptospirosis

- Patients should be treated as indicated above, with particular attention to fluid therapy.
- As much as possible, doxycycline should be used as the initial antimicrobial treatment as it treats both leptospiremia and eliminates the carrier state.
- However, doxycycline is metabolized by the liver and excreted in the bile.

- Doxycycline concentrations can supra-physiological serum levels occur in patients presenting with liver failure, which is common in patients with leptospirosis.
- In patients showing signs of liver involvement, antibiotics from the beta-lactam category (penicillin, ampicillin) should be used for 2 weeks to eliminate leptospiremia. This is then followed by 2 weeks of doxycycline to clear the carrier

❖ Ingestion of specific toxins

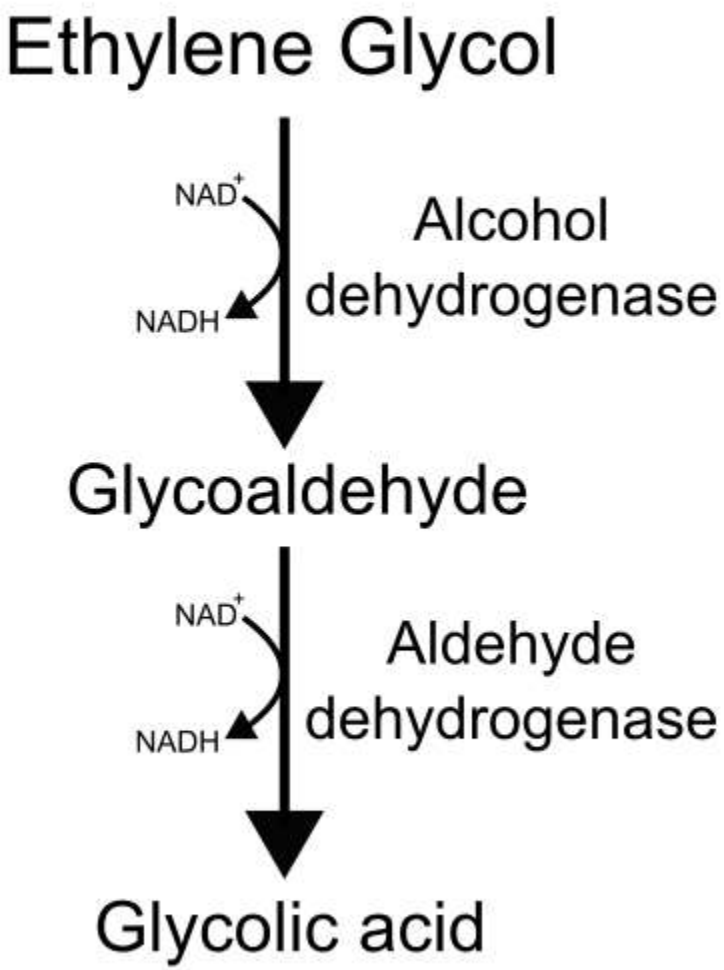
❑ Ethylene glycol

- Exposure is always a medical emergency.
- There are tests for the detection of this toxin.
- In the absence of a diagnostic test, treatment withethylene glycol should begin whenever a combination of compatible laboratory results (severe metabolic acidosis, increased anion gap, hypocalcemia, calcium oxalate crystalluria) is observed in an animal showing clinical signs.

appropriat
e.

- If ingestion is discovered within the first hour, vomiting should be induced and activated charcoal administered.
- The initial serum chemistry must be obtained and repeated at 24 and 48 hours.
- Methylpyrazole, an antidote, should be administered.
- The first step in the metabolism of ethylene glycol into toxic intermediates occurs in the liver by alcohol dehydrogenase.
- Methylpyrazole binds to alcohol dehydrogenase and inactivates it, allowing ethylene glycol to leave the body unchanged via the

Ethylene Glycol Metabolism



Fomepizole

- Although ethanol may be administered IV as an antidote, methylpyrazole is much safer and more effective.
- IV fluids should be started at a rate of 4 ml/kg/hour and urinary output should be monitored for at least 48 hours.
- If urine production decreases, follow the fluid therapy recommendations for AKI described above.

- In dogs, the greatest benefit of medical management is observed in the first 5 to 8 hours, and in cats within 3 hours of ingestion.
- In one study, cats treated with 4-methylpyrazole 3 hours or less after exposure had a 100% survival rate, while those treated with ethanol had a 25% survival rate.
- However, 4 hours after ingestion of ethylene glycol, there was 100% mortality regardless of treatment.

- It has been reported that cats treated with hemodialysis after the onset of renal failure due to ethylene glycol had a significantly better survival rate.

- **Ethylene glycol toxicity treatment protocol:**

➢ **Dog = 4-MP (methylpyrazole 50 mg/ml): 20 mg/kg IV first dose; 15 mg/kg at 12 hours; 15 mg/kg at 24 hours; 5 mg/kg at 36 hours.**

➢ **Cat = 4-MP (methylpyrazole 50 mg/ml): 126 mg/kg initial slow IV dose; 31.25 mg/kg IV at 12 hours; 31.25 mg/kg IV at 24 hours; 31.25 mg/kg IV at 36 hours**

➢ **Alternative treatment =**

✓ A 7% ethanol solution.

✓ For cats and dogs, give a loading dose of 8.6 ml/kg of 7% ethanol (slow IV), then continue with a CRI of 1.43 ml/kg/hour.

✓ Remember to only use clear alcohols.

❑ NSAIDs

- Due to its rapid absorption and its depressive effect on the CNS, vomiting should only be induced if ingestion is detected immediately.
- The initial serum chemistry should be obtained and repeated at 24 and 48 hours.
- IV fluids should be started at a rate of 4 ml/kg/hour and urinary output should be monitored for at least 48 hours.
- If urine production decreases, follow the fluid therapy recommendations for AKI described above.

- Misoprostol, a synthetic analogue of prostaglandin E1, can be administered to dogs at a dose of 2.0 to 5.0 μg/kg q8h.
- Due to its long half-life, naproxen toxicity should be managed for at least 72 hours.

❑ Rodenticides based on cholecalciferol

- If ingestion is discovered within the 24 the first hours, vomiting must be induced of vomiting and administering activated charcoal.
- Due to enterohepatic recirculation, administration of activated charcoal should be repeated.
- The initial serum chemistry must be obtained and then repeated every 12 hours for 4 days.
- Intravenous fluids (0.9% sodium chloride) should be started at a rate of 4 ml/kg/hour and the urinary output should be monitored for at least 48 hours.

- Serum NaCl is preferred as it increases calcium excretion.
- If urine production decreases, follow the fluid therapy recommendations for AKI described above.
- A combination of furosemide (2 mg/kg q6h) and prednisone (2–3 mg/kg q12h) should be administered to reduce calcium reabsorption and increase its excretion.
- If oral intake is possible, oral phosphate binders (such as aluminum hydroxide) may be used as needed.

- If calcium and phosphorus levels remain high, a single dose of 1.3 to pamidronate of 2.0 mg/kg administered IV over 2 hours may be effective.
- Often, a single dose is sufficient for the entire treatment.
- Calcium and phosphorus levels should be monitored for 6 weeks.

❑ Raisins, dried raisins, ingestion of lilies

- If ingestion is discovered within the first 4 hours, vomiting should be induced and activated charcoal administered.
- The initial chemistry of the serum must be obtained and then repeated at 24 hours.
- IV fluids should be started at a rate of 4 ml/kg/hour and urine output must be monitored for at least 48 hours.
- If urine production decreases, follow the fluid therapy recommendations for ARF described above.

- The prognosis for cats presenting for lily ingestion is guarded. In one study, 50% of cats that presented for lily plant ingestion died despite aggressive treatment.
- Dogs suffering from ARF secondary to grape ingestion also have a guarded prognosis. In one study, more than half of affected patients survived; 65% of those who survived had a complete resolution of signs.

- All exposures should be considered potentially fatal.
- It is important to realize that products containing raisins such as bread, cakes, etc. are also potentially toxic.