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Chronic kidney disease

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Definition/overview

Chronic Kidney Disease (CKD) is a clinical syndrome characterized by a progressive decrease (or even loss) in the kidney's ability to:

- Concentrate urine and maintain electrolyte and acid-base balance.
- Excrete nitrogenous wastes and other substances for urinary elimination.
- Fulfill endocrine functions (erythropoietin); produce renin (enzyme = blood pressure control) and activate vitamin D.

- This deterioration of kidney function is secondary to the development of chronic lesions in the renal parenchyma (extensive lesions), manifested by a progressive and irreversible loss of nephrons.
- Azotemia develops only when 75% or more of the nephron population becomes non-functional.
- Isosthenuria occurs when more than 66% of the nephron population becomes non-functional.

Importance

- Affection is the most common type of kidney disease in pets.
- It is estimated that CKD affects 0.5% to 1.0% of older dogs and 1.0% to 3.0% of older cats.
- Progresses, regardless of treatment, to the final stage of uremic syndrome and the death of the animal.

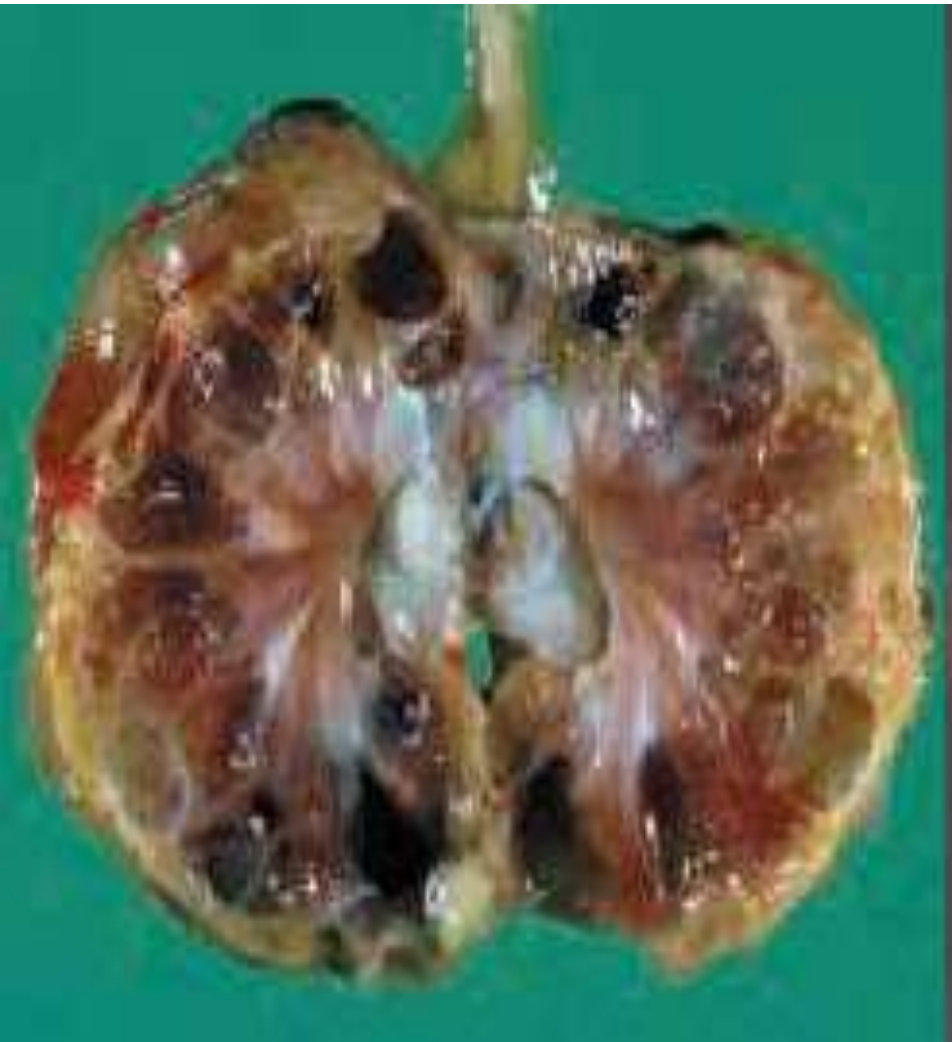
Causes

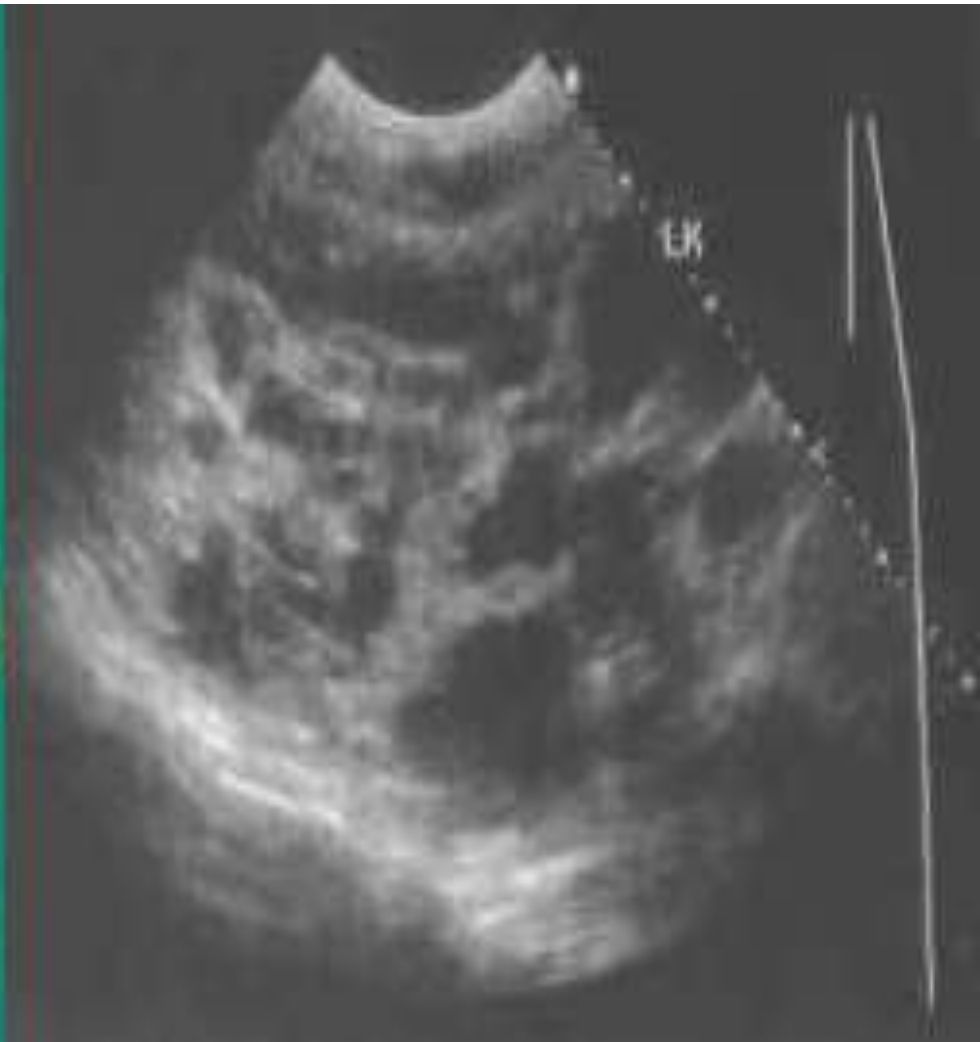
CKD is often divided into two categories based on the underlying etiology: congenital and acquired.

❖ ***Congenital causes:***

- The animal is either born with lesions present in the kidneys (e.g. aplasia) or born with a condition that will lead to kidney disease in the future (e.g. renal polycystosis).
- Most cases of congenital kidney failure are considered hereditary.
- The mode of genetic transmission and pathogenesis are often unknown.
- Symptoms gradually manifest early in the animal's life, often during the first year.

Polycystic kidney disease (cat)





Congenital causes of CKD in dogs and cats

Cause	Race
Amyloïdose	Shar Pei, Beagle, Abyssin, Oriental Shorthair
Dysplasie rénale	Shi Tzu, Lhassa Apso, Golden Retriever, Soft-coated Wheaten Terrier (Terrier irlandais à poil doux), autres races
Glomérulopathies	Soft-coated Wheaten Terrier, Cocker Spaniel
Syndrome de Fanconi	Basenji
Maladie polykystique des reins	Cairn Terrier, persan

❖*Acquired causes:*

- ❑Acquired CKD: Result of damage to the renal parenchyma that causes nephron loss and a progressive decline in kidney function.
- ❑In most cases, the nature of the etiology is never discovered.
- ❑In some cases, it is possible to determine and treat the underlying cause of CKD (e.g. Pyelonephritis).

- Regardless of the etiology, most cases of CKD have similar clinical presentation, progression, and treatment.

Pathophysiology

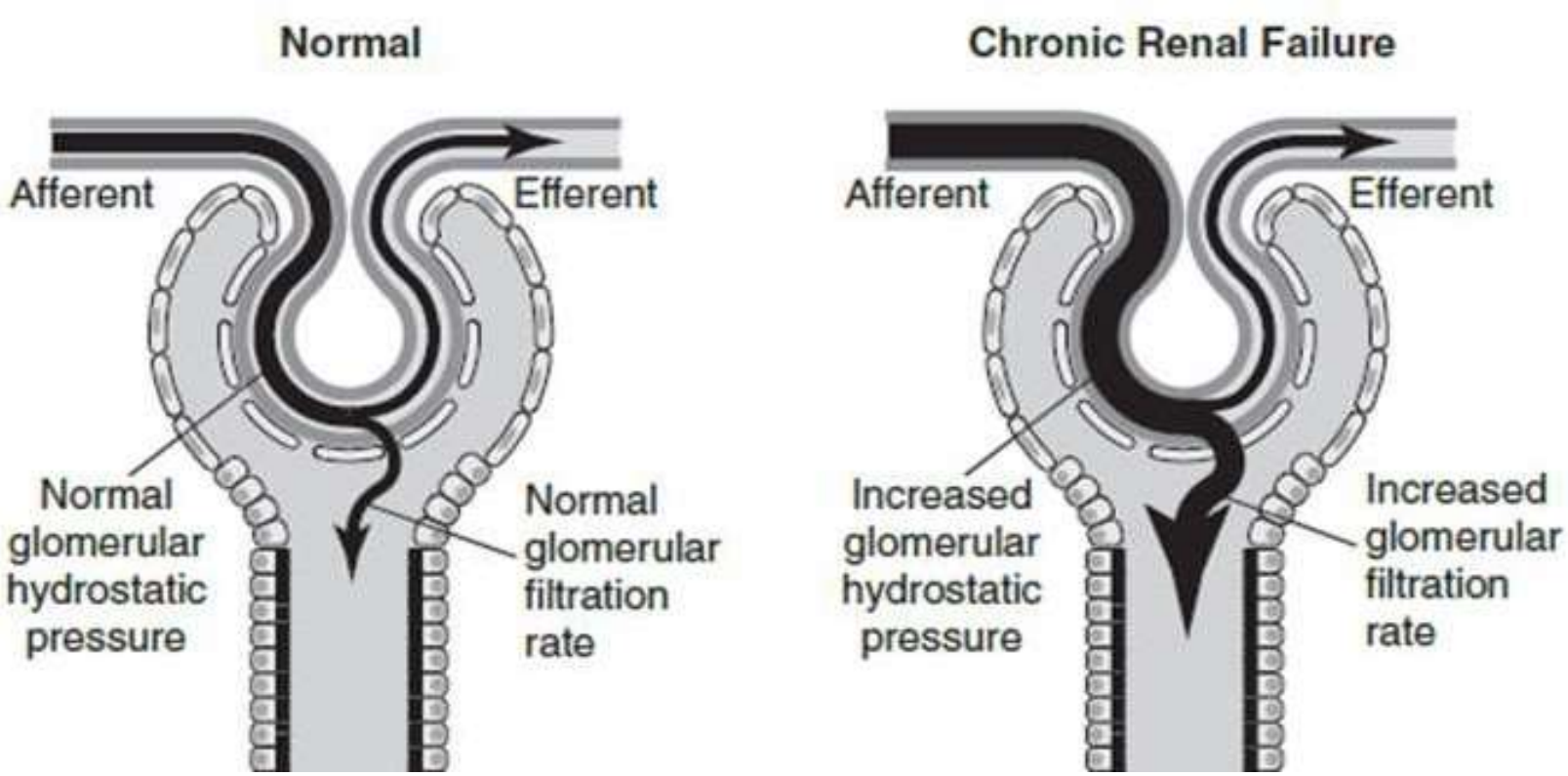
- Although the exact pathophysiology of CKD is not known, it is believed that the problem is related to an initial injury that reduces the number of functional nephrons.
- It may be a sequel to IRA,
  a congenital anomaly or the result of a
  disease
  chronic process (e.g.

- In CKD, there is an astonishing adaptation of the remaining renal parenchyma (non-injured) to the needs of the organism.
- The function of the remaining nephrons increases by 50 to 200% in order to compensate for the activity of the lost nephrons, characterized by the establishment of a hyperfiltration phenomenon:

- The dilation of the afferent glomerular arteriole ensures increased pressure to the glomerular capillaries (increase in intraglomerular capillary pressure) and an increase in renal plasma flow (RPF).
- An increase in glomerular filtration rate (GFR) in the nephron due to vasodilation of the afferent glomerular arteriole and the vasoconstrictive action of the efferent glomerular arteriole.

- A certain increase in GFR is also attributed to an increase in glomerular volume, which also increases the filtration surface.

Adaptation of residual nephrons (development of the super-nephron) during CKD. The increase in glomerular filtration rate (GFR) through vasodilation of the afferent arteriole + increase in glomerular volume that increases the filtration surface.



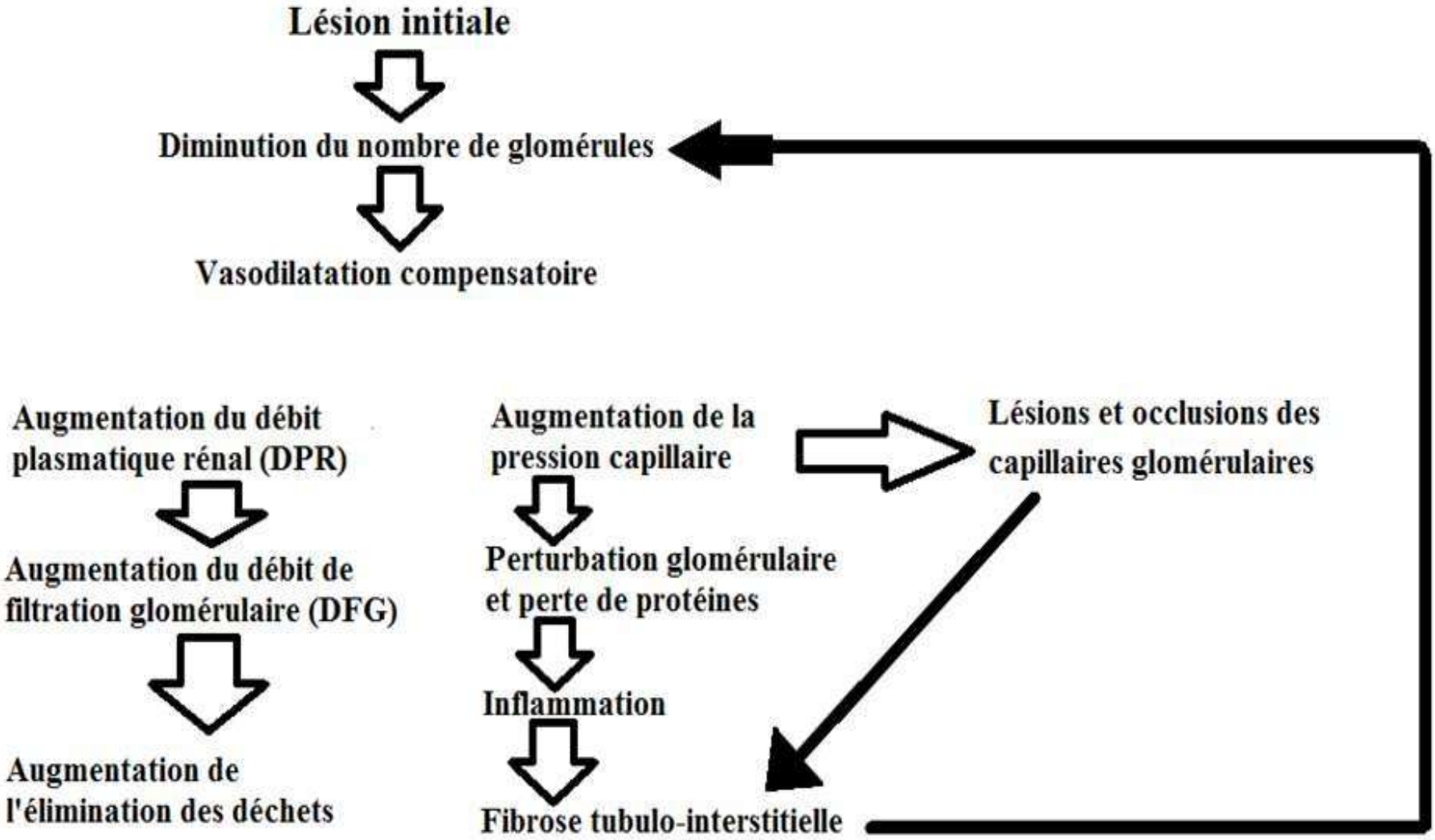
- Hyperfiltration increases the clearance of nitrogenous waste by each surviving nephron.
- High intraglomerular capillary pressure ultimately leads to mechanical disruption of the capillaries and loss of protein across the glomerulus.

- Excess filtered protein is reabsorbed by the epithelial cells of the proximal convoluted tubule, broken down by cellular lysosomal mechanisms, and reintegrated into the blood as amino acids.
- The process of protein breakdown releases reactive oxygen species, which stimulate the release of inflammatory cytokines.
- The resulting inflammation damages the epithelial cells of renal tissues.

- Increased intraglomerular capillary pressure also leads to damage and potential occlusions of glomerular capillaries.
- Continuous damage to tubular epithelial cells, combined with glomerular capillary injury, results in tubular-interstitial fibrosis, characteristic of CKD.
- Thus, what begins as a compensatory mechanism ultimately perpetuates further renal damage.

- Each time new nephrons are destroyed, a compensatory mechanism kicks in.
- Compensatory phenomena limit the clinical progression of the disease until structural and functional injuries exceed a threshold beyond which clinical signs of CKD appear.

Pathophysiology of chronic kidney failure



- ***Uremic syndrome***

- Nitrogenous waste products from the digestion and catabolism of proteins (urea, creatinine, ammonia, guanidine and its derivati accumulate when renal function is reduced.ves)
- Some of them contribute to the clinical consequences of uremic toxicity associated with CKD.
- However, the pathogenesis of uremic syndrome is complex and not fully elucidated.
- Many toxins are involved and no substance taken in isolation is likely to explain the diversity of uremic symptoms.

Nitrogenous metabolites or responsible for the clinical and biological manifestations of CKD

Métabolites azotés	
• **Urée** • **Créatinine** • **Acide guanido-acétique** • **Méthylguanidine**	• Signes digestifs : anorexie, vomissements, diarrhée, ulcérations des muqueuses, stomatite, perte de poids. • Polyurie osmotique d'où polydipsie. • Hémolyse. • Anomalie plaquettaire : trouble d'hémostase primaire (hémorragie). • Trouble neurologique. • Immunodéficience.
Métabolites non azotés	
• **H+SO4- (anions organiques)**	• Acidose; ostéodystophie rénale.
• **Phosphates**	• Hyperpathyroidisme secondaire; acidose ; calcification rénale et altération de la fonction rénale.

Evolution

- Progresses to terminal uremia through continuously transitioning stages.
- The progressive destruction of nephrons is partially compensated by the hypertrophy and increased function of the remaining nephrons.

1- Early stage (stage of total compensation)

- Latency phase where the condition evolves wit hou t symptoms.
- The remaining nephrons are sufficient to ensure normal kidney function.
- More than 50% of nephrons are already gone: this is what show a slight decrease in concentration capacity and glomerular filtration.

- Urea and creatinine levels are normal (stage of total compensation).
- This stage may be accompanied by of a slight polydipsia.
- This stage leads to the compensated retention stage.
- The transition is gradual or sudden (under the effect from stress for example).

2- Compensated retention stage

- Characterized by a low or moderate increase in blood urea and creatinine levels:

  - Urea (10-14 mmol/l or 1-1.4g/l).
  - Creatinine (<220 mmol/l or <22mg/l).

- Mild clinical signs of uremia.

3- Decompensated retention stage

Leads to advanced renal failure:

- Symptoms are initially manageable with medical measures. Moderate uremic symptoms, urea=1.5-2g/l; creatinine=20-40mg/l).
- Then terminal uremia, which can often only be influenced by dialysis.

Clinical study

❖ Commemoratives

Vary depending on whether the animal is presented at the stage of:

- ❑ Complete compensation, or
- ❑ Compensated retention, or
- ❑ Decompensated retention.

- Polyuria-polydipsia are often the first signs.
- These signs often escape the owners until that nocturia appears.

- In many cases the first symptoms occur following stress such as:

Overwork, general anesthesia, extra-renal conditions, etc.

The owner often notices:

- Frequent vomiting (occasional or permanent).
- Sometimes diarrhea; in severe cases, melena may develop.
- Decreased or irregular appetite.

- Reduced (tolerance to exercise is fatigue).
- Dull coat, gradual weight loss and weight reduction (despite a normal appetite).
- Sometimes neurological signs: Depression, lethargy, tremors, seizures, etc.

❖ Clinical manifestation

oSymptoms are by the determined

stage and degree of the IRC.

A- Initial phase

The initial period of the IRC is practically silent and is hardly manifested except by low, but persistent, proteinuria.

B- Stable phase

The state phase, which usually lasts several months, allows for the observation of the association of clinical symptoms and biological signs.

Certain clinical symptoms are common to all CKD:

- General condition impairment.
- Polyuria-polydipsia syndrome.
- Digestive and hematological symptoms.
- The cardiovascular

o Modification of the general condition

- Asthenic behavior: The animal is less lively, more fatigable, sleeps frequently, and shows a general appearance of an older individual.
- Modification of the coat state: Dry and dull.
- These animals show a certain predisposition to chronic skin conditions and alopecias

- Polyuric-polydipsic syndrome

Often constitutes the reason for consultation:

Very often the owner notices that their animal:

- Drinks excessively (Example: 1.5 l per day for a 20 kg dog).
- Produces abnormally abundant and clear urine.

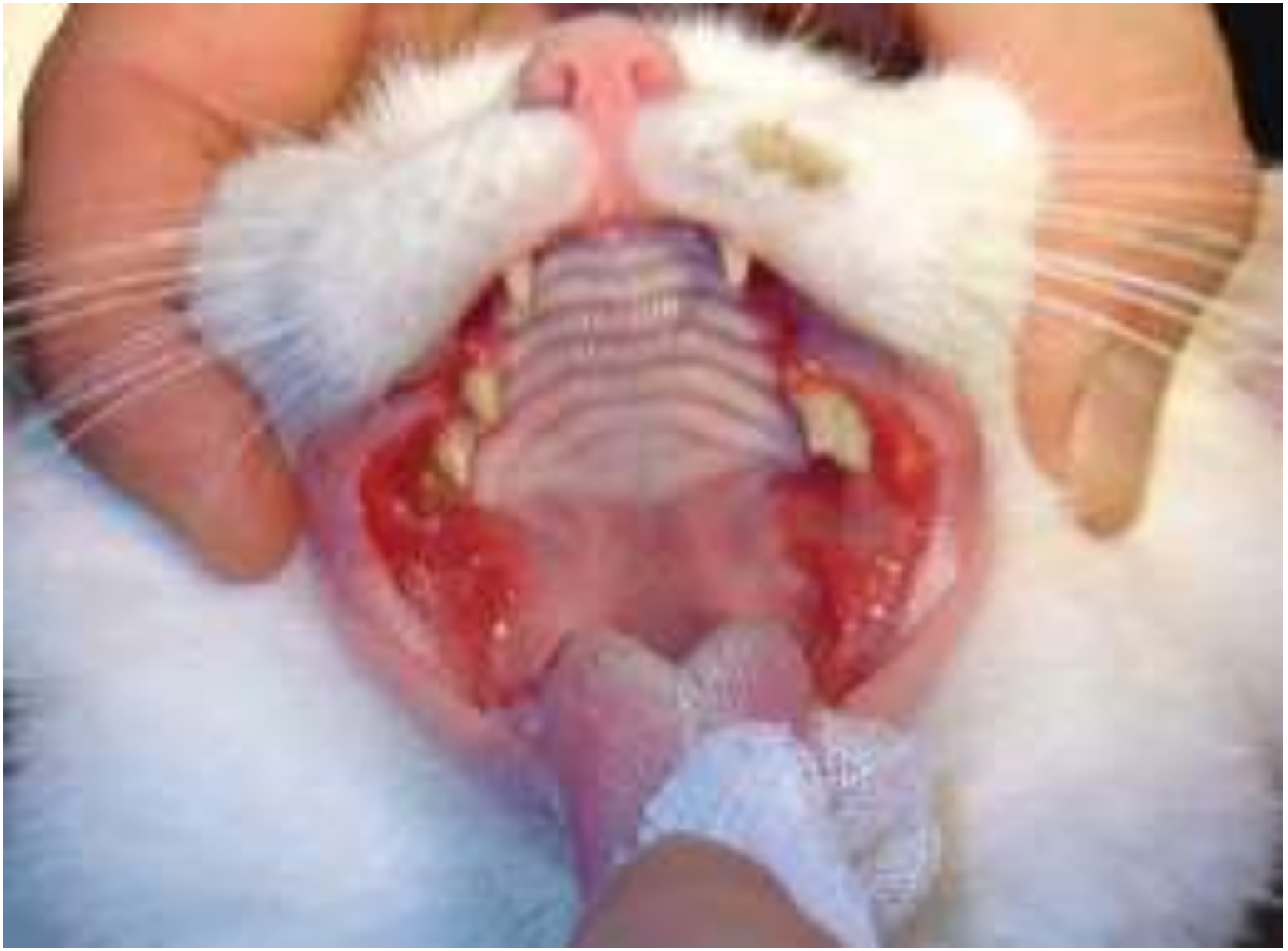
o Digestive symptoms

Essentially:

- Picky appetite.
- Initially spaced vomiting, then increasingly frequent.
- Finally episodes of diarrhea.

- Upon opening the oral cavity, the clinician always perceives a bad odor that can sometimes become frankly urine-like.

- The examination of the oral cavity often allows for noting the presence of mucosal exulcerations or even varying ulcers in the area of the canines and upper premolars.



- A brownish tartar covers more or less totally the teeth implanted in an inflamed gum.
- The coloration of the tongue that turns red brownish especially at the tip and on the edges (appearance of a cooked tongue) is very indicative of renal insufficiency.

- Hematological symptoms

Are less obvious: it is a more or less marked anemia.

- Cardiovascular syndrome

Toxins, metabolic acidosis, hypokalemia (sometimes hyperkalemia) have a depressant effect on the myocardium and cause bradycardia and arrhythmias.

- Osteo-renal syndrome (secondary hyperparathyroidism)

Leads to a state of demineralization of the skeleton.

Often, this syndrome remains subclinical or is only expressed by some poorly characterized lameness.

In cases of demineralization of the skeleton in particular, one can note (in the bones of the face, the dog):

- Abnormal mobility and instability of the teeth (rubber jaws).
- Spontaneous fractures.

o Biological signs

The urine of the animal affected by CKD in the stable phase is:

- Abundant (polyuria), pale with acidic pH.
- Low density = isosthenuria (≤1010) (clear urine less dense).

In these urines:

- Proteinuria is discreet (mild proteinuria).
- Mild glycosuria.
- The examination of the centrifugation pellet

  = Rarely a small number of cylinders.

Interpretation of proteinuria according to urinary density

Échantillon	1	2
Densité urinaire	1,040	1,010
Protéinurie	++	++
Conclusion	incertaine	significative

Plus la densité urinaire est faible, plus la protéinurie est significative.

In the blood, nitrogen catabolism products are present at a high rate:

- Urea: 0.5 to 1.5 g/l.
- Creatinine: 20 mg/l.
- Normocytic normochromic anemia, with a normal or slightly decreased reticulocyte count.

o Evolution of the steady state phase

- ✓The steady state phase of CKD can evolve over several months.
- ✓The kidneys may be abnormal upon palpation: small, firm, nodular, etc.

- ✓Under the influence of an evolving episode of lesions or a failure of the compensation mechanism, CKD enters its terminal phase.

C- Terminal phase

The terminal phase of CKD is often:

- Uremic.
- Acidotic.
- Oliguria.

o General symptoms

- Marked asthenia.
- Rapid and significant weight loss.
- Hypothermia.
- Extracellular dehydration (presence of skinfold sign).

Cat with renal insufficiency under skin fluid receiving chronicle. -

- Digestive symptoms

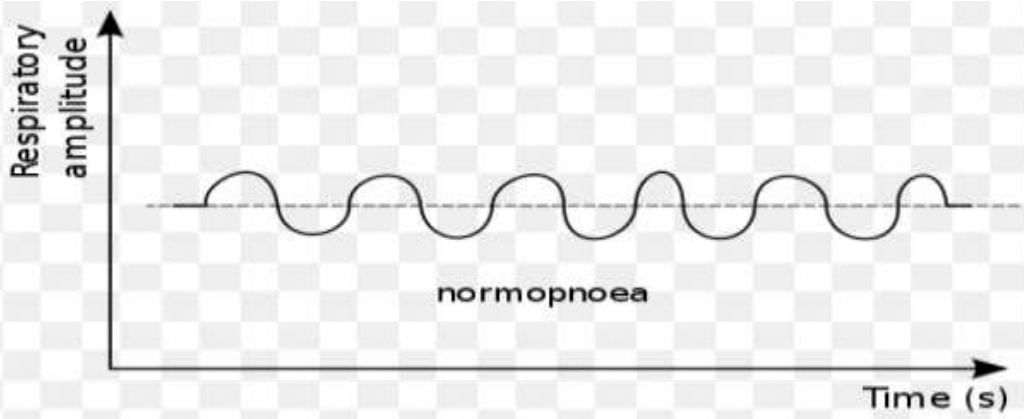
At this stage, vomiting followed by diarrhea with melena is the norm.

The oral cavity has a distinctly urine-like odor; ulcers and the brownish coloration of the tongue are very characteristic.

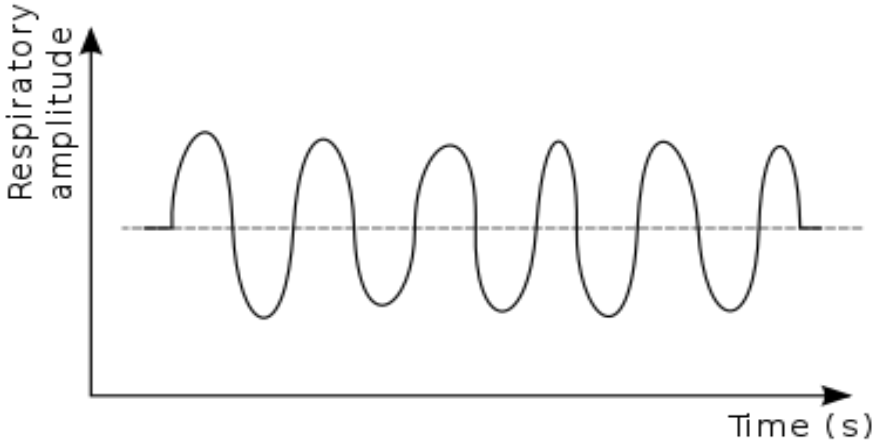
o Respiratory symptoms

- ✓ Respiratory symptoms vary.
- ✓ In some animals, breathing is slow and deep due to acidosis (sign of dyspnea = Kussmaul breathing, Cheyne-Stokes).
- ✓ In others, presenting with pulmonary edema, one may note an acceleration of breathing (sign of dyspnea).

Normal respiration

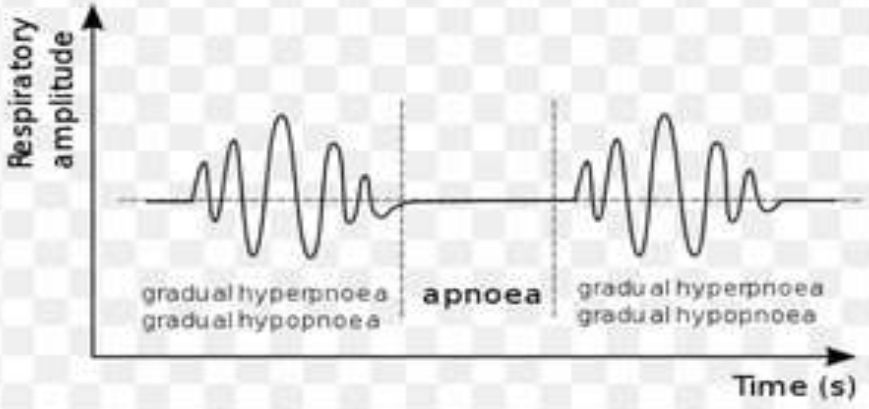


Kussmaul breathing



— Metabolic acidosis (Diabetes mellitus)
— Hyperpnoea
K = Ketones (Diabetic ketoacidosis)
U = Uremia
S = Sepsis
S = Salicylates
M = Methanol
A = Aldehydes
(U)
L = Lactic acid/Lactic acidosis

Cheyne-Stokes respiration



— Periodic breathing:
Gradual hyperpnoea/hypopnoea and Apnoea
— Sleep/Hypoxemia/Drugs
— Hypoperfusion of the brain (respiratory center)

o Neurological symptoms

Neurological symptoms often occur in the terminal phase of CKD.

Sometimes, neurological disorders are the first symptoms of uremia noticed by the owner.

Neurological disorders indicating encephalopathy

of varying severity:

Lethargy, depression, comatose state, tremors, or sub-contractures

jerky muscle contractions, pruritus, hyperexcitability,

tetany, epileptic seizures, etc.

o Cardiac symptoms

- Mitral insufficiency.
- Symptoms of pulmonary edema.
- In 60% of uremia cases, there is: Left ventricular hypertrophy associated with a state of hypertension.

- When present, the cardiovascular syndrome manifests as:

- Increased pulse strength.
- Increased precordial impact strength.
- Enlargement of the area of dullness in the precordial region.
- Increased intensity of the first heart sound.
- On radiographic examination: enlargement of the ventricular radiological shadow.

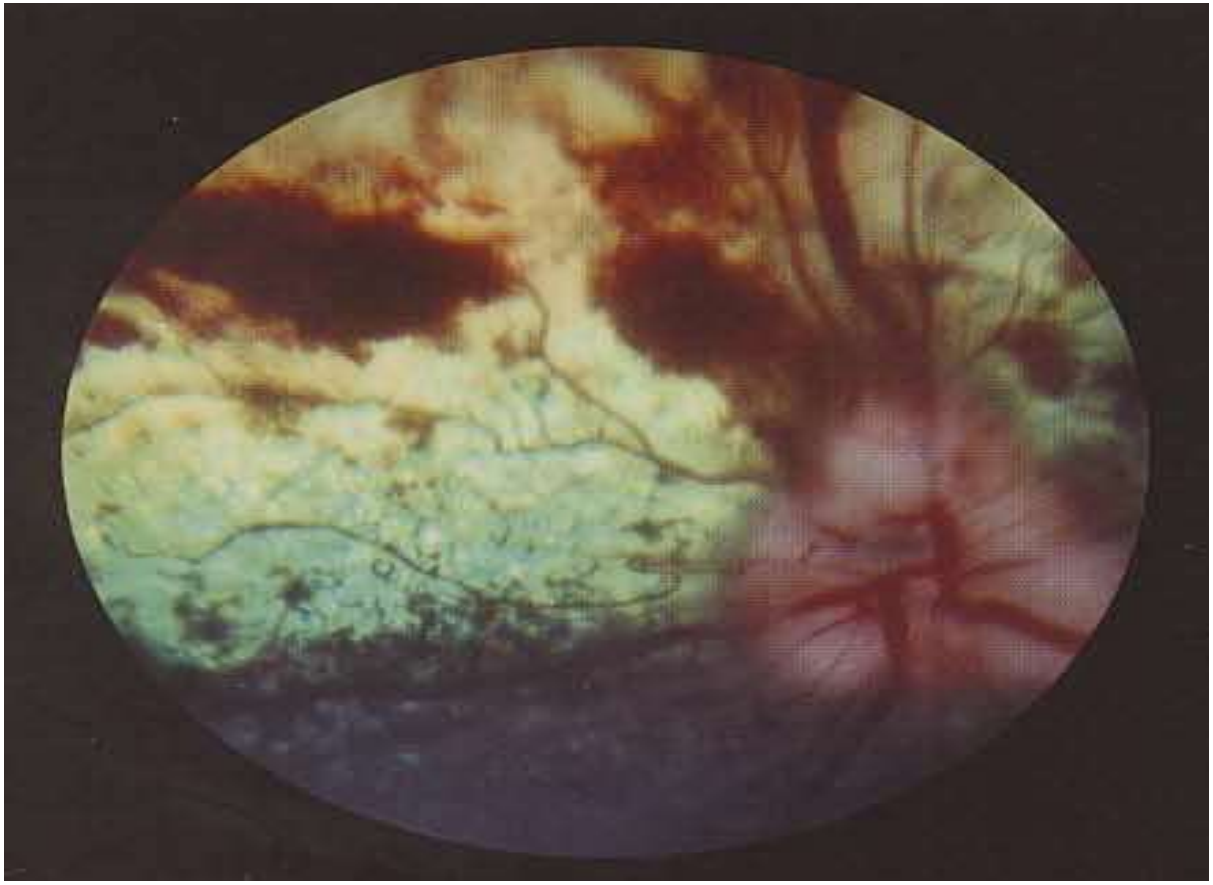
o Other sub-clinical disorders

- Immunodepression.
- Calcifications of soft tissues.
- Healing disorders and blood coagulation issues.
- Insulin resistance (hyperglycemia).

- Pancreatic disorders (hyperamylasemia).
- Increased sensitivity to glucocorticoids.
- Vitamin and iron deficiency.
- Renin-angiotensin-aldosterone system disorders.
- Uremic pericarditis and pneumonia.

NB:

In cats, blindness secondary to hypertension is not uncommon and is often the primary reason why owners consult a veterinarian.



Retinal hemorrhage in a 6-year-old cat; due to hypertension (> 140 mmHg; following chronic kidney disease).

o Biological signs

At this stage, biological signs are dominated, on part by oliguria, and one hand, by:

- A very high elevation of uremia that (always >2g/l can reach 5 or 6 g/l).
- Creatinine >50 mg/l.

Ventro-flexion of the neck of the cat with severe hypokalemia

oEvolution of the terminal phase

The animal enters uremic coma which ends in death within a few days.

Lesions

The lesions of CKD are primarily renal lesions but also extra-renal.

oExtra-renal lesions

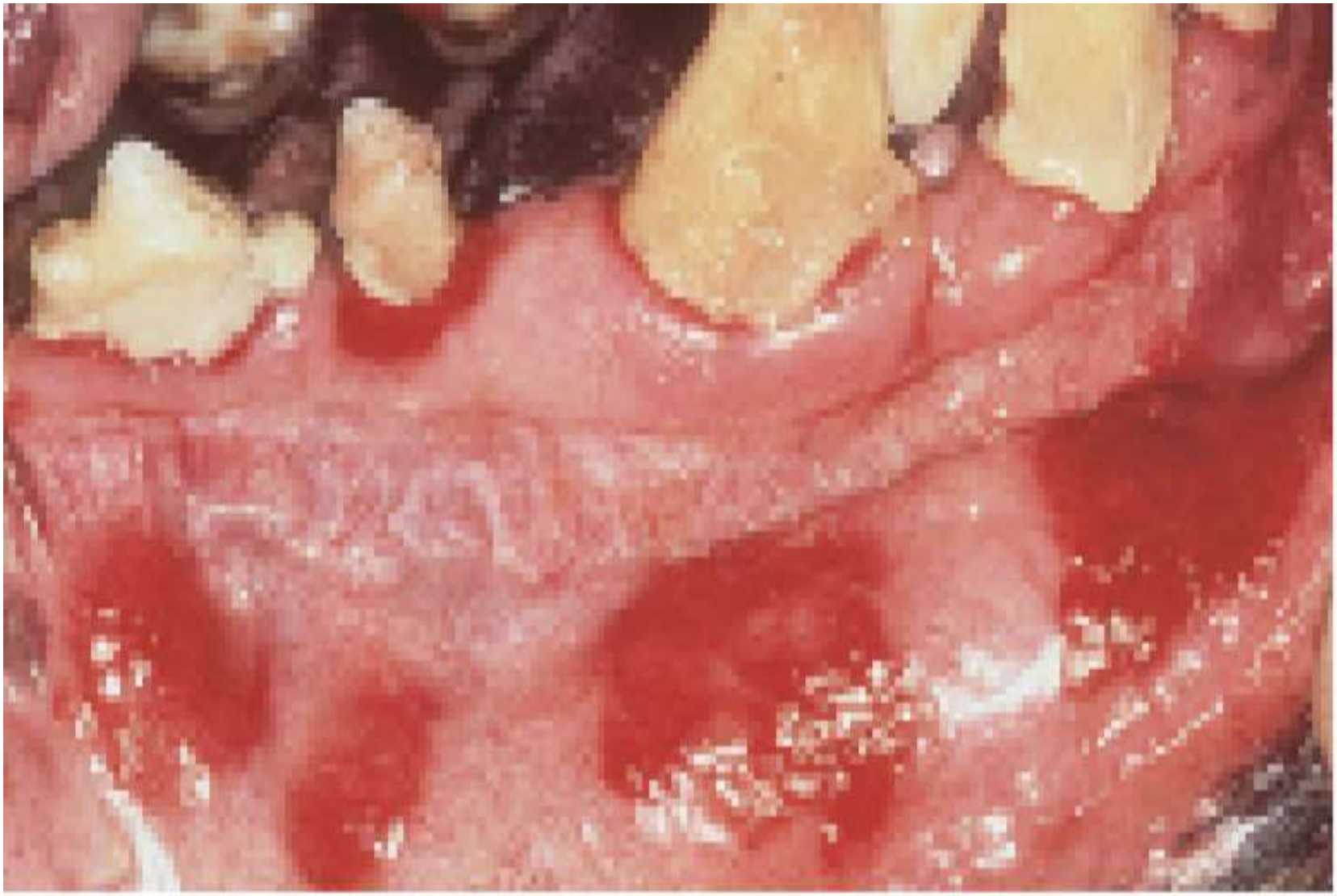
- Dehydration.
- Necrotic lesions of the pleura.
- Pulmonary edema associated with left ventricular hypertrophy.

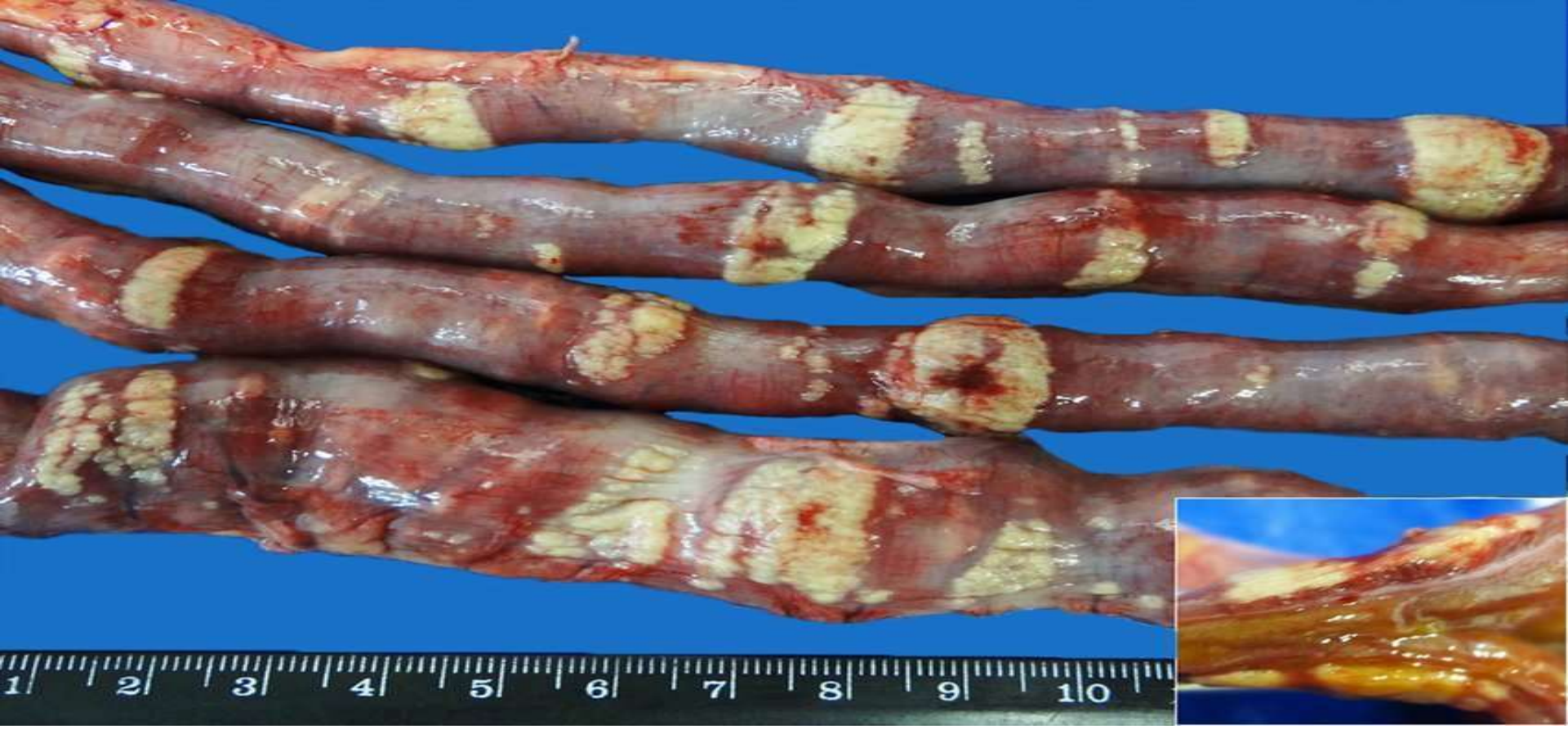
Oral cavity ulcers: Brown discoloration of the tongue and the presence of dental tartar.

On the anatomopathological level:

- Hemorrhagic ulcerative gastritis.
- Necrotizing and hemorrhagic enterocolitis.

Uremic stomatitis/gingivitis.





CKD in a dog. Uremic enteropathy. Several irregular white patches of varying sizes in the serosa of the small intestine that extend into the muscular layer = Marked multifocal dystrophic mineralization.

Uremic gastropathy. Marked edema and thickening of the folds of the gastric mucosa (Dog stomach).

Small multifocal white foci in the myocardium (dystrophic mineralization
).

Differential diagnosis

- Isosthenuria, azotemia, proteinuria, and renal atrophy primarily confirm CKD when observed simultaneously.
- AKI: Anemia, polyuria-polydipsia, and renal atrophy are generally absent.

- Glomerulonephritis:

Accompanied by significant proteinuria, normal-sized kidneys, sometimes a sign of nephrotic syndrome (hypoalbuminemia, hypercholesterolemia, tendency to edema).

- Pyelonephritis:

Inflammatory urinary sediment, pyuria, kidneys of irregular shapes, sometimes blood leukocytosis, slight decrease in urinary density, modification of the renal pelvis and ureter on intravenous urography.

Diagnosis

Established based on data from the medical history and records, clinical examination, and laboratory blood analyses.

Once the presence of azotemia is confirmed, possible differential diagnoses (prerenal azotemia, postrenal azotemia, renal AKI) must be ruled out.

Complete Blood Count (CBC), blood biochemical profile, urine analyses and culture, imaging must be performed.

The diagnosis of CKD is all the easier as one approaches the terminal phase.

❑ Urine analyses and culture

- ❖ The most common urine analysis result in CKD is isosthenuria (1.007–1.015); however, some cats may still concentrate their urine in the early phases of CKD.
- ❖ Mild azotemia in the presence of very concentrated urine is a hallmark of prerenal azotemia.
- ❖ The discovery of large amounts of glucose (with normal blood glucose levels) is suggestive of proximal tubular dysfunction and can be observed in dogs with Fanconi syndrome.

Syndrome de Fanconi	Échec du transport du tubule proximal Non réabsorption : Sodium, bicarbonates, potassium, glucose, acides aminés. 10 à 16 % des Basenji sont atteints, documentés également chez d'autres races
Diagnostic	Les même signes d'IRC + glucosurie avec une glycémie normale sont évocateurs, l'aminoacidurie est diagnostiquée
Traitement	Supplémentation orale : bicarbonate (Objectif : sérum >12 mmol/l [12 mEq/l]) ; potassium (Objectif : sérum 4–6 mmol/l [4–6 mEq/l]) ; calcique (Objectif : sérum 2,25–2,5 mmol/l [9–10 mg/dl]) Régime d'insuffisance rénale
Pronostic	Bon avec un traitement approprié

- The detection of large amounts of protein, in the absence of hematuria, bacteria, or white blood cells in the urinary sediment, may be the result of glomerular lesions.
- Proteinuria requires the performance of:

  UPC ratio (Proteinuria/Creatininuria Ratio) = Prognostic Value.

  UPC < 0.2 is normal for most dogs and cats

- Research suggests that:
  - Cats with IRIS + a UPC ratio <0.43 lived for about 2 years from the time of diagnosis.
  - Those with a UPC ratio > 0.43 lived for only about 9 months.
- Even if no bacteria are detected microscopically in the urine, an anaerobic urine culture should always be performed to help rule out chronic pyelonephritis as a contributing factor to the progression of IRIS.

❑Blood biochemical profile

- Elevation of urea and creatinine levels in the blood.
- Creatinine may not be as high as one might expect.
- Elevations of serum phosphate.
- Calcium is often slightly to moderately elevated due to secondary hyperparathyroidism.
- Serum bicarbonates decrease with the degree of renal dysfunction.

- Potassium levels are generally maintained within the normal range, but hypokalemia may be observed in cats.
- Recently, a new blood test, symmetric dimethylarginine (SDMA), has become available.
- Preliminary studies have shown that SDMA is an accurate indicator of chronic kidney disease (CKD) and can become elevated 9 months before creatinine in dogs and 17 months earlier in cats.

❑Diagnosis of Polyuria-Polydipsia Syndrome

Any animal exhibiting a polyuria-polydipsia syndrome must undergo blood and urine analysis:

- Urea (blood, urine); Creatinine (blood, urine).
- Glucose (blood, urine).
- Proteinuria.

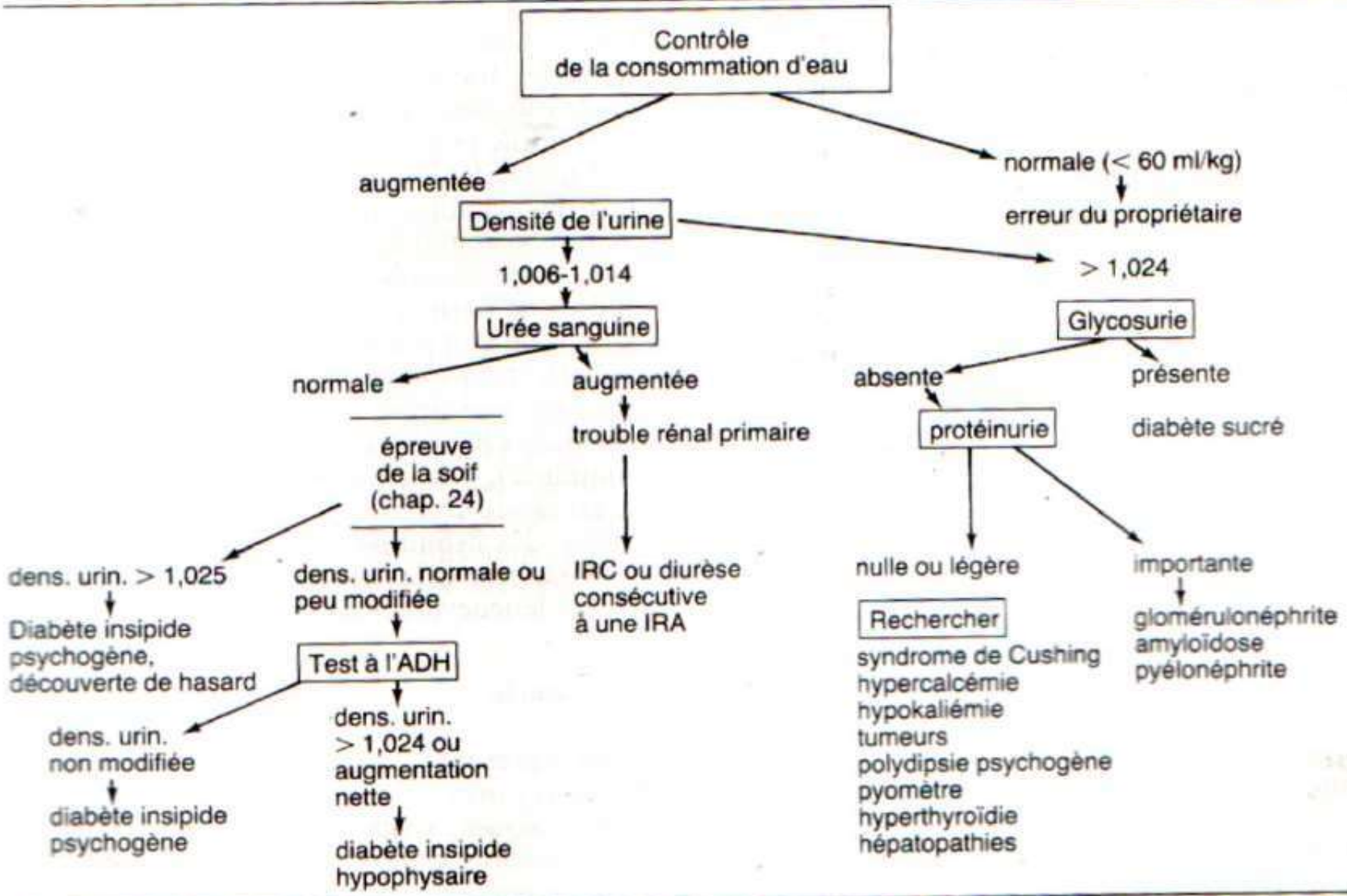
During the steady state phase of CKD =

- ✓Poor general condition and tendency to lose weight.
- ✓Proteinuria.
- ✓Low urinary density.
- ✓Moderate cylindruria.

Diagnosis of polyuric-polydipsic syndromes

	Volume d'eau consommée	Sang		Urines	
		Urée	Glycémie	Densité	Eléments anormaux
Néphrite chronique	+	0,5-1,5 g/l	±	1010	Albumine
Diabète sucré	++	Normale	>1,5g/l (à jeun)	1030	Glucose
Diabète insipide	+++	Normale	Normale	1010	0
Syndrome de Cushing	++	Normale		1020	0
Gastro-entérite	+	Normale	Normale	Normale	0
Pyromètre	+			Normale	Albumine

Algorithme des polyuries-polydipsies

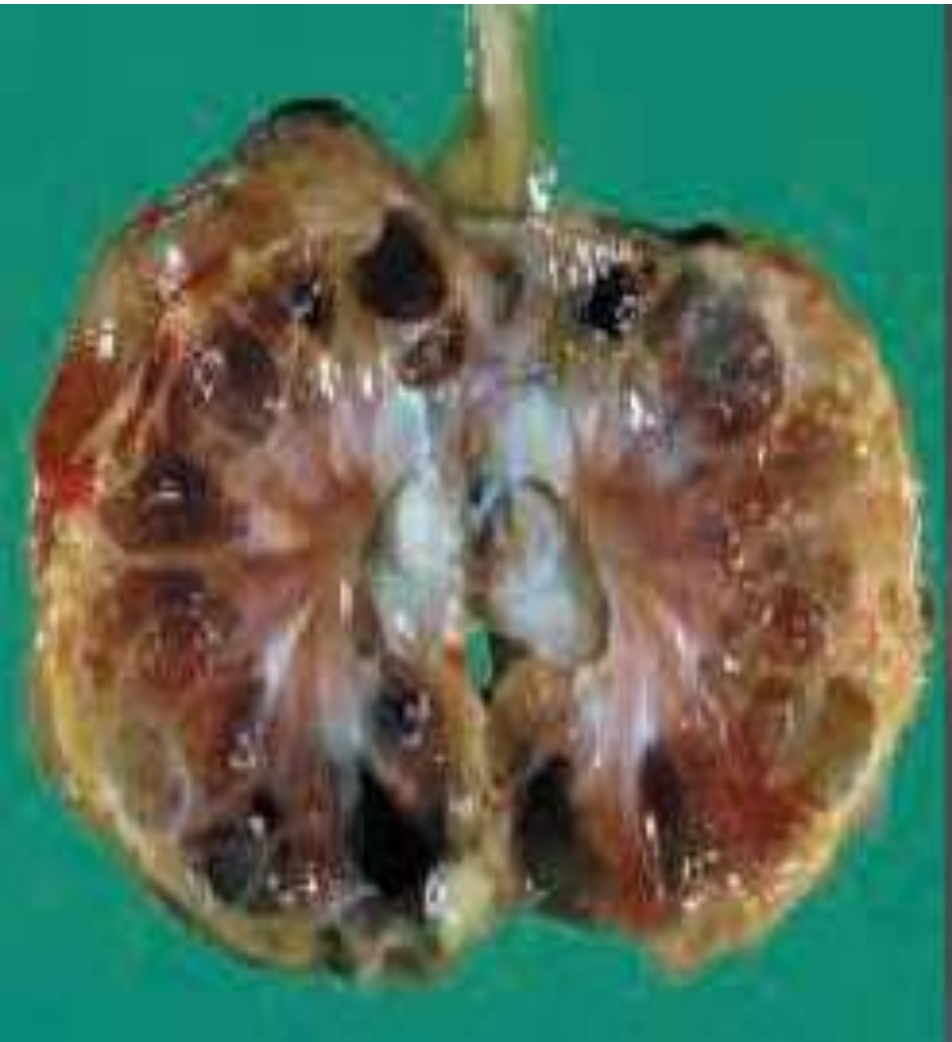


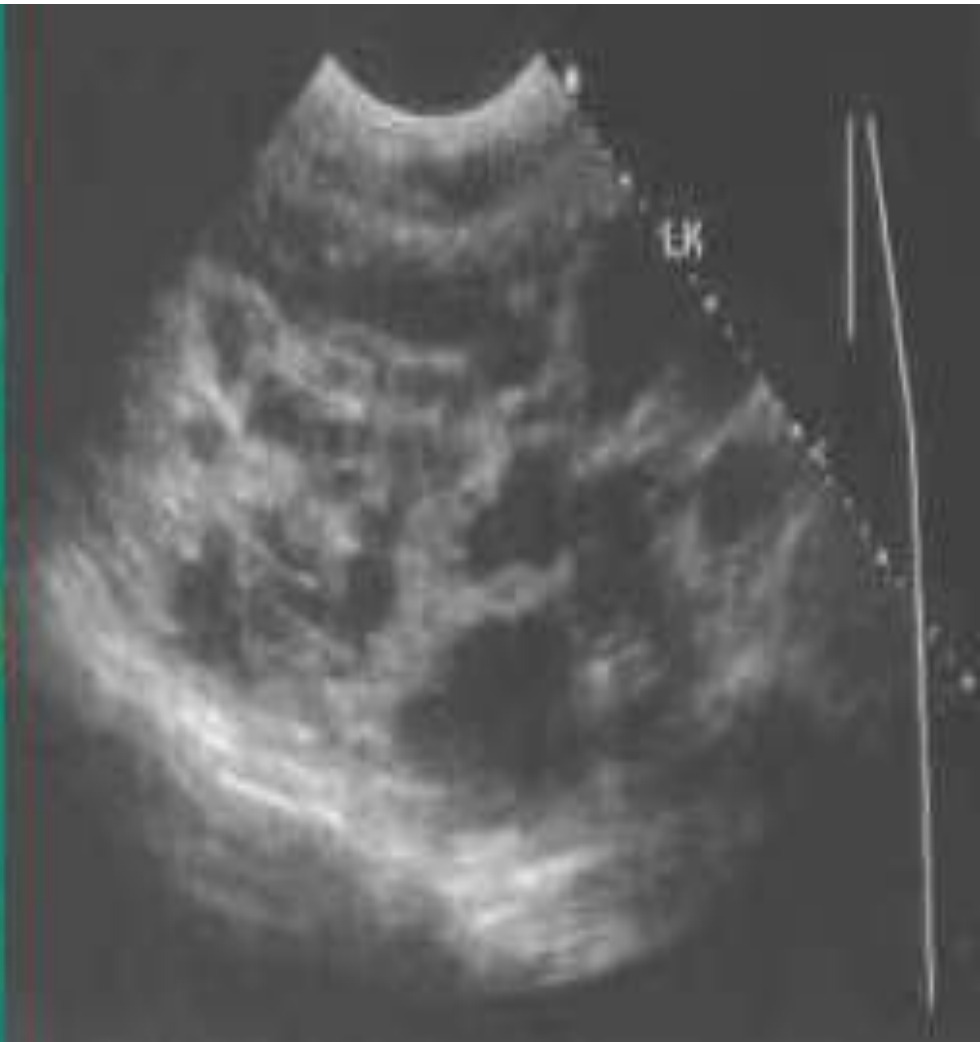
Rechercher par l'anamnèse si les aliments sont salés et si l'animal reçoit des médicaments (glucocorticoïdes, diurétiques, gentamycine, phénytoïne, œstrogènes, vitamine D). Rechercher par l'examen clinique : fièvre, diarrhée, signes d'urémie, hypertrophie hépatique, troubles endocriniens (pyomètre, diabète sucré et syndrome de Cushing).

❑ Radiography and ultrasound

- Ultrasound is the imaging modality preferred = Offer provides an unmatched view of renal architecture and vascular pathways + can also be used to obtain renal biopsies when indicated.
- Generally, CKD is characterized by bilateral loss of renal mass (renal atrophy).
- However, certain pathological processes, such as renal polycystosis, have a characteristic ultrasound appearance.

Renal cystic disease (cat)

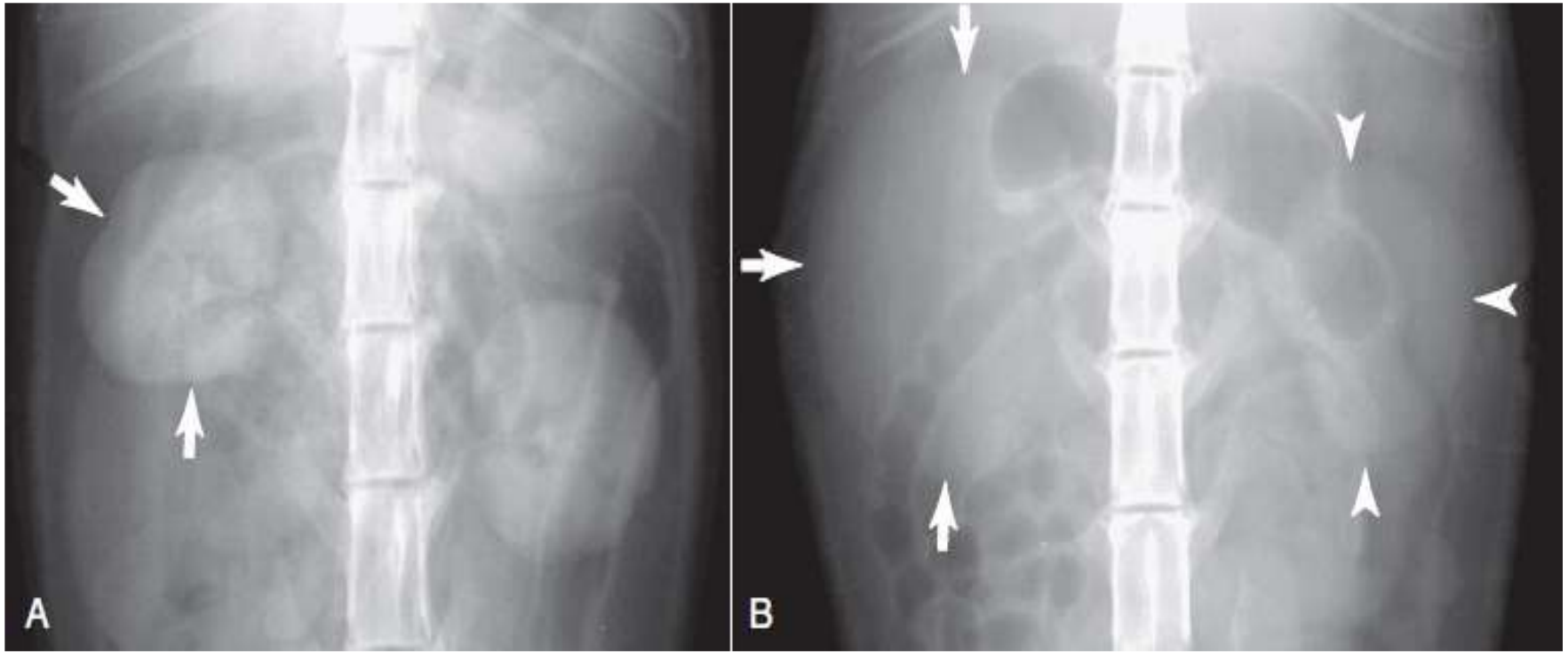




On X-ray = ventrodorsal views:

- In the dog, Length = 2.5 to 3.5 times the length of L2.
- In the cat

It is slightly less, between 2.4 and 3 times the length of L2.



A, Small and irregular kidneys. Both kidneys are small in relation to the length of L2. The arrows point to irregular flattened areas.

B, note the disparity between the size of the left and right kidneys. The left kidney (arrow heads) is small relative to the length of L2, while the right kidney is slightly enlarged (small arrows).

- Hypertrophied kidneys (in cases of CKD) suggest an underlying pathological process with secondary renal impairment (e.g., lymphoma, feline infectious peritonitis [FIP], hydronephrosis), primary renal neoplasia, or acute kidney injury.
- Slight dilation of the renal pelvis (pylectasis) is often observed with chronic renal infections.
- Congenital renal dysplasia and aplasia are characterized by abnormal renal architecture with loss of demarcation between the cortex and medulla.

❑ Measurement of blood pressure (BP)

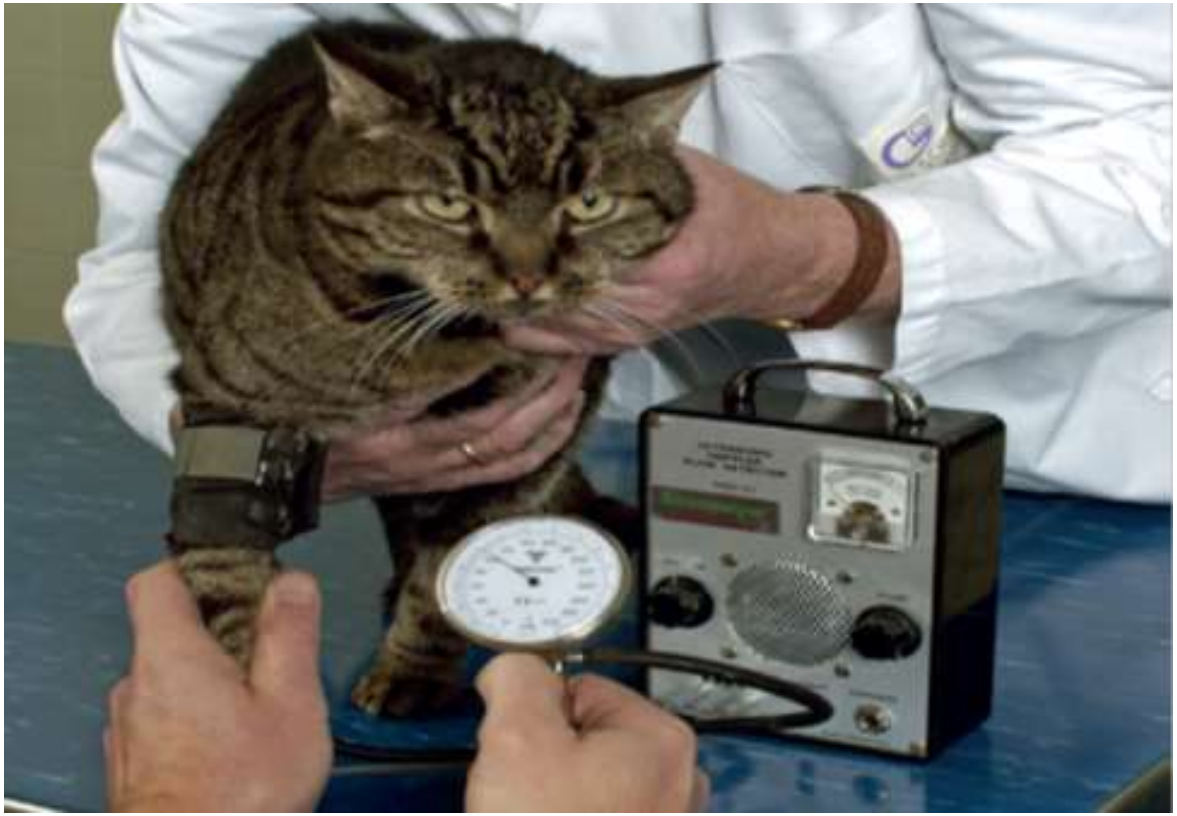
- Normal BP in cats ranges from 120 to 140 mm Hg systolic and 70 to 90 mm Hg diastolic.
- Dogs show some breed variation with an average BP of 133 mm Hg systolic and 75 mm Hg diastolic.

Normal Arterial Blood Pressure Values in Adult Dogs & Cats[5]

BLOOD PRESSURE VALUES	DOGS	CATS
Systolic arterial pressure	90–140 mm Hg	80–140 mm Hg
Diastolic arterial pressure	50–80 mm Hg	55–75 mm Hg
Mean arterial pressure	60–100 mm Hg	60–100 mm Hg

Hypertension has been defined as systolic pressures of 140 to 185 mm Hg or higher.

Severity	*BP Level*
Mild	>150/95 mm Hg
Moderate	>160/100 mm Hg
Severe	>180/120 mm Hg



Measurement of systolic blood pressure in a cat using the Doppler system. The position of the cuff allows for the measurement of blood pressure in the brachial artery. Slightly bending the cat's elbow and placing a finger on the cuff helps prevent it from sliding down. The transducer is placed on the artery, distally from the cuff.

- Hypertension is a common complication of CKD that ultimately affects the majority of cats and dogs.
- Not only can hypertension have negative consequences for the eyes, heart, and nervous system, but it can also exacerbate other kidney injuries; therefore, identifying and treating these patients is essential.
- Given that hypertension can develop at any time during the disease process, checking blood pressure is routine in all patients with CKD.

❑ Diagnosis confirmation

Isosthenuria, azotemia, anemia, the polyuria-polydipsia syndrome, and renal atrophy virtually confirm CKD when observed simultaneously.

❑ Classification of CKD

Patients with CKD are classified according to the guidelines developed by the International Renal Interest Society (IRIS) based on:

- Kidney function.
- Proteinuria.
- Blood pressure.

Table. Stages of CKD based on serum creatinine values (mg/dl [µmol/l]) (IRIS).

	Chien	Chat
Stade 1	<1,4 [<125]	<1,6 [<140]
Stade 2	1,4–2,0 [125–179]	1,6–2,8 [140–249]
Stade 3	2,1–5,0 [180–439]	2,9–5,0 [250–439]
Stade 4	>5,0 [>440]	>5,0 [>440]

Table. Classification of proteinuria based on the urine protein/creatinine ratio (UPC) (IRIS).

	Chien	Chat
Protéinurique	>0,5	>0,4
Protéinurie limite	0,2–0,5	0,2–0,4
Non protéinurique	<0,2	<0,2

Table. Classification of hypertension (IRIS).

	Tension artérielle systolique
Stade 1	150 mmHg
Stade 2	150–159 mmHg
Stade 3	160–179 mmHg
Stade 4	>180 mmHg

Example:

- A 15-year-old cat with a creatinine level of 3.0 mg/dl (265 μmol/l), an UPC (urine protein:creatinine ratio) of 2.0, and a blood pressure of 170 mmHg would be classified as proteinuric stage 3, hypertensive stage 3.
- The use of this classification system not only allows for a common nomenclature to describe and discuss patients but also enables the development and application of appropriate guidelines for the prognosis and treatment of CKD.

Prognosis

The prognosis of CKD is serious as cure is never achieved due to its irreversible nature.

- The blood urea level observed over several samples taken a few weeks apart allows for an approximate assessment of the patient's survival duration.
- UPC ratio = Very high prognostic value (UPC <0.2 under normal conditions).

When uremia:

- Remains <1g/l: the patient may survive for several years if subjected to an appropriate diet.
- 1-2g/l: the survival duration will not exceed a few months.
- ">2g/l : death within a few weeks.

Treatment

Renal lesions are extensive and irreversible, which is why no therapy has a curative aim, and treatment can only propose measures that may prolong the animal's life.

Only hygiene and dietary measures are justified, aimed at limiting the accumulation or production of nitrogenous metabolites.

A- Etiological therapy

Rare; it is only possible in rare cases:

hypercalcemia, kidney stones, pyelonephritis.

B- Symptomatic therapy

- ❑ Fluid therapy
- ❑ Control of acidosis
- ❑ Potassium
- ❑ Proteinuria
- ❑ Treatment of anemia
- ❑ Anorexia

❑ Fluid therapy

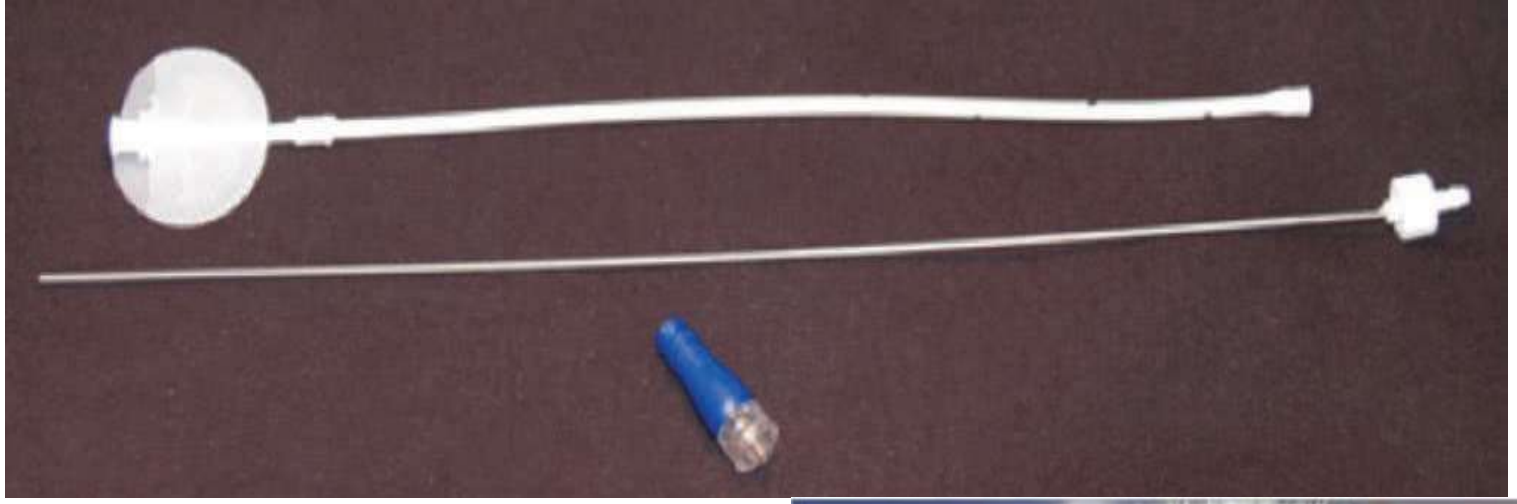
- Many patients with CKD present a certain degree of dehydration = Dehydration leads to hypoperfusion and pre-renal azotemia.
- Good rehydration often results in significant reductions in azotemia.
- The degree of dehydration must be assessed and, if significant, a replacement fluid plan should be calculated and administered IV over 12 to 24 hours.

- **Rehydration serum of choice: NaCl 0.9%; Ringer lactate; Mixed solution: 2.5% glucose and 0.45% saline alternately, etc.**
- Chez les patients légèrement déshydratés, des liquides SC peuvent être administrés.
- L'administration quotidienne de liquides SC à domicile peut aider à prévenir la déshydratation, à réduire l'azotémie et à améliorer considérablement la qualité de vie du patient .

Chat atteint d'insuffisance rénale chronique recevant des fluides sous-cutanés.

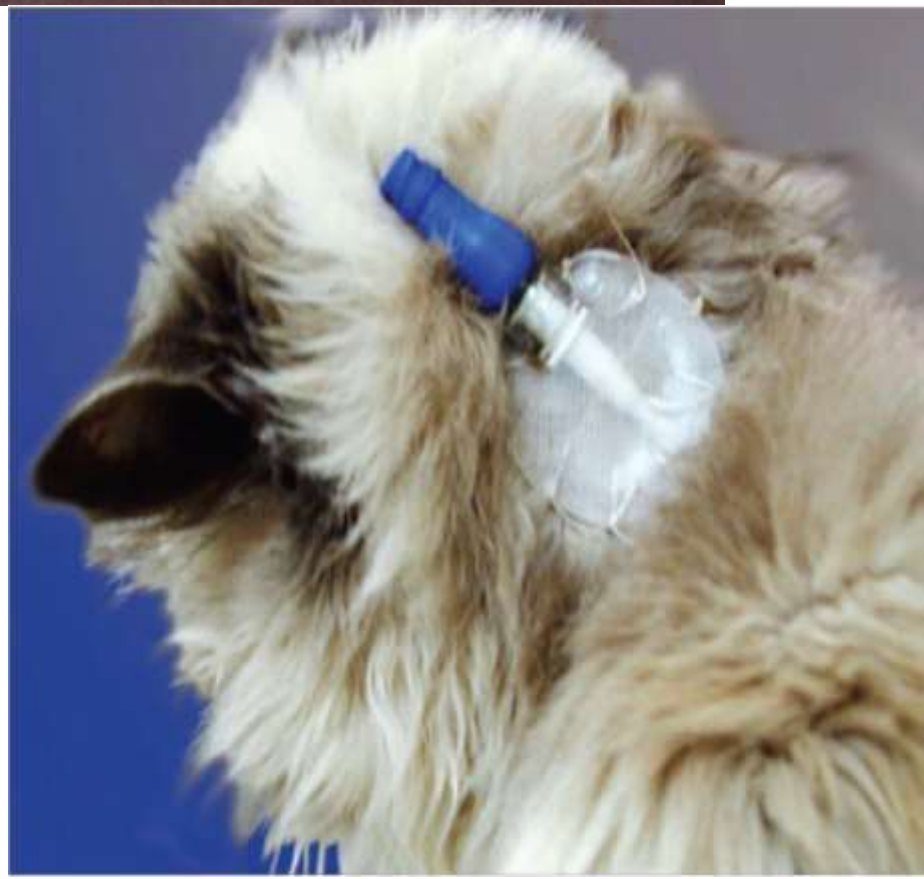
Dans les cas où le patient ne coopère pas ou que le propriétaire ne veut pas administrer de liquides SC:

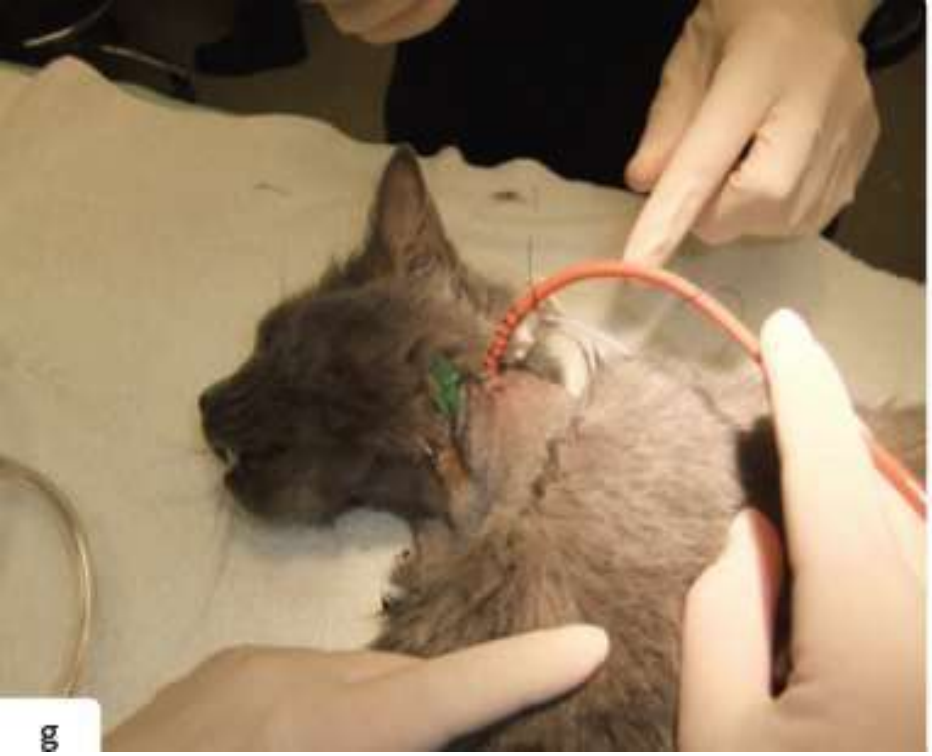
- Un port de liquide SC (GIF-Tube®) peut être inséré. Ce port offre un accès facile pour l'administration de liquide et évite le besoin d'aiguilles.
- Alternativement, un tube d'oesophagostomie peut être placé. Ceux-ci s'insèrent facilement, peuvent rester en place pendant de longues périodes et peuvent être utilisés pour répondre aux besoins hydriques et nutritionnels du patient.

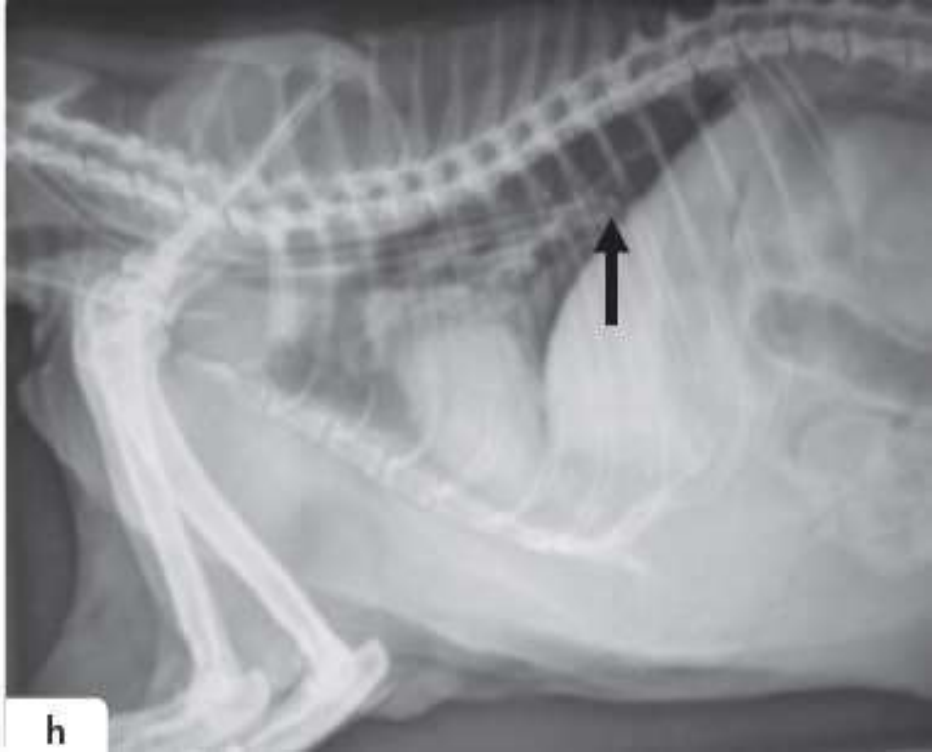


- Gif-Tube.
- Patient avec un Gif-Tube inséré .

Certains chats ne toléreront pas ces tubes.







(g) Placement of the esophagostomy tube. The patient is anesthetized and monitored. Although most tubes are placed in the left lateral cervical region, the right can also be used. A red rubber or silicone tube is selected and marked so that the end of the tube is located in the esophagus between the 6th and 9th intercostal spaces. (h) The X-ray confirms the correct placement. Note that the end of the tube: Caudal to the heart and cranial to the lower esophageal sphincter (arrow).

❑ Control of acidosis

- One of the main functions of the kidney is to maintain acid-base balance.
- The renal tubules reabsorb filtered bicarbonates, regenerate new bicarbonates, and excrete acids.
- As CKD progresses, the kidneys' ability to fulfill this function fails.
- Even when mild, chronic acidosis enhances protein catabolism, promotes bone demineralization, and contributes to the range of clinical signs exhibited by the renal insufficient patient.

- Changing the diet to a buffered regimen (particularly for those on acidified diets) helps prevent and correct metabolic acidosis.
- When the patient follows an appropriate diet, additional oral alkalinizing treatment is indicated only when the total CO2 is <18 mEq/l or when serum bicarbonates are
  <17 mEq/l (CN= 18-25 mEq/L; CT17-22mEq/L).
- Initially, sodium bicarbonate at a dose of 5–10 mg/kg q8–12h or potassium citrate at 40–60 mg/kg q8–12h may be administered.
- The exact dose initially requires frequent monitoring (repeated measurement of bicarbonates) and must be tailored to each patient.

❑ Potassium

Hypokalemia is a common observation in cats with CKD; associated with muscle weakness + muscle mass loss + ileus +

potentially fatal cardiac arrhythmias.

However, the most frequently observed manifestation is anorexia.

Ventroflexion of the cat's neck

- The mechanism by which cats develop hypokalemia is unknown; however, it is generally believed to be a combination of malnutrition and excessive renal losses.
- In one study, one-third of healthy cats fed a low-potassium diet developed interstitial nephritis and fibrosis.
- For this reason, most feline renal failure diets are supplemented with potassium and, in most cases, will prevent hypokalemia.
- In patients who do not respond to dietary management, oral supplementation of potassium citrate (20–30 mg/kg PO q24h) or potassium gluconate (2–6 mEq/cat q24h) may be administered.

❑Hyperphosphatemia (and Osteorenal Syndrome = secondary hyperparathyroidism)

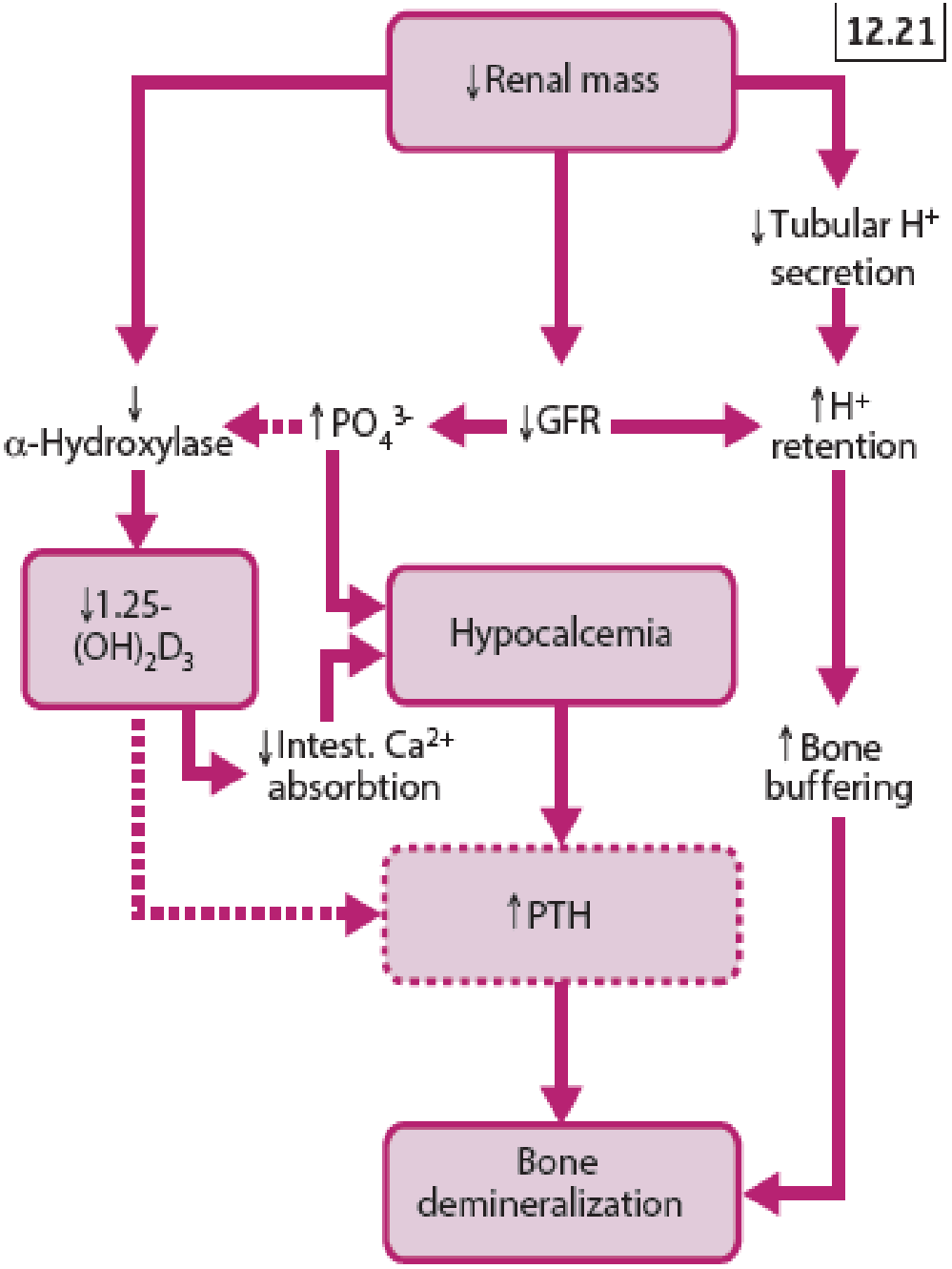
- Due to its role in muscle and nerve conduction, calcium is highly regulated in the body.
- Parathyroid hormone (PTH) is released by the parathyroid gland in response to slight decreases in circulating calcium.
- PTH causes the release of stored calcium and stimulates an enzyme in the renal tissue, alpha-1 hydroxylase, to convert calcidiol to calcitriol.
- Calcitriol: The active form of vitamin D that stimulates calcium absorption in the intestinal tract and provides negative feedback on the release of PTH.

- Phosphorus is normally absorbed from the diet
  = used in metabolic processes and then undergoes renal excretion.
- As renal mass decreases and GFR declines, excessive levels of phosphorus accumulate in the blood.
- Phosphorus acts to inhibit alpha-1 hydroxylase, thus preventing the formation of calcitriol and suppressing the negative feedback on the release of PTH.
- Thus, hyperphosphatemia leads to decreased calcitriol, continuous release of PTH by the parathyroid, and release of calcium and phosphorus from the bones.

- Mineralization of soft tissues becomes a concern when 'Ca-P product' approaches 70(mg/dl) = (4xSerum calcium)x (3.1xSerum phosphorus).
- This is often observed in patients with advanced CKD.
- In addition to its role in calcium regulation, calcitriol may also play a role in slowing the progression of kidney disease. = Control of hyperphosphatemia is essential.

Pathogenesis of secondary renal hyperparathyroidism in CKD.

The renal production of calcitriol normally inhibits production and release of the parathyroid hormone by the parathyroid gland. The arrows discontinue indicate an action inhibitor.



- A apart from hemodialysis, there is no treatment that rapidly reduces serum phosphorus levels, although fluid therapy may help dehydrated patients.
- Given that the main source of serum phosphorus is dietary, the first step is to modify the patient's diet to a low-phosphorus diet.

- In many cases, this will control adequately serum levels. phosphorus

If after 2 to 3 weeks, hyperphosphatemia has not resolved, a phosphate binder should be added to the diet:

- Aluminum hydroxide and aluminum carbonate (30–80 mg/kg q24h divided and given with meals) are commonly used and are effective at binding phosphorus in the intestine.
- Lanthanum carbonate (Fosrenol®= 30 mg/kg divided and given with meals; Renalzin® = veterinary medication) is an excellent alternative and should be crushed and well mixed with food.

- Calcium acetate (60–90 mg/kg q24h divided with meals) may also be effective at binding phosphate but increases calcium absorption in the intestine and may contribute to hypercalcemia; therefore, monitoring of serum calcium is essential in this case.
- Regardless of the chosen binder, the medication should be started at the lowest dose and then adjusted as needed based on serum phosphorus levels.
- Two weeks should be allowed to judge the results.

- Since high PTH levels result from inhibition of calcitriol (Vitamin D3) synthesis, exogenous calcitriol supplementation has been proposed as a treatment for secondary hyperparathyroidism.
- Furthermore, studies suggest that calcitriol therapy slows the progression of CKD and improves survival in dogs with CKD; however, similar results have not been documented in cats.
- Therefore, dogs with CKD should receive calcitriol treatment (and cats).

- Calcitriol (2.0–2.5 ng/kg/day) has been effective in normalizing serum PTH levels; however, the required doses vary significantly and must be tailored to each patient.
- Dose: CN= 2.0–2.5 ng/kg/day; CT=0.01–0.04 μg/kg/day PO.
- Ionized calcium and PTH should be monitored.
  = The goal is to minimize PTH without inducing hypercalcemia.
- The use of calcium-containing phosphate binders should be avoided.

❑ Proteinuria

- Proteinuria may accelerate the progression of CKD and measures to mitigate protein loss should be taken when the UPC ratio exceeds 0.4 in cats and 0.5 in dogs.
- Treatment typically involves following a renal insufficiency diet and administering an ACE inhibitor.
- The goal of therapy is to reduce the UPC ratio by at least 50% (preferably within the normal range).
- Although enalapril can be used, it is eliminated exclusively through the kidneys, while benazepril (0.25–0.5 mg/kg PO q12–24h), which has both renal and hepatic clearance, is preferred.

- If significant reductions in proteinuria cannot be achieved with an ACE inhibitor alone, angiotensin receptor blockers may be added.
- Pharmacological data are scarce. However, irbesartan (1–5 mg/kg PO q24) has been proposed.

❑ Treatment of anemia

- The cause is anemia in CKD includes multifactorial and a decreased lifespan of red blood cells due toxins uremic, altering to nutritional deficiencies the production of red blood cells and intestinal bleeding.
- The most important cause of anemia is decrease in the production of erythropoietin by the renal interstitial cells.

- Erythropoietin is a glycoprotein that increases the number of stem cells engaged in the bone marrow that will develop into erythrocytes.
- In the absence of erythropoietin, erythroid stem cells undergo apoptosis (programmed cell death).
- The release of erythropoietin depends on oxygen sensors located on the renal interstitial cell membranes.
- These sensors upregulate erythropoietin production during hypoxia and downregulate it when blood oxygen levels are normal.

- Patients who exhibit symptoms of anemia or dangerously low the hematocrit is (<20 %) need a should receive transfusion immediately compatible.
- Patients with a low hematocrit who are not symptomatic or critical should begin treatment with recombinant erythropoietin.
- Two alternatives exist: epoetin alfa (Epogen®) and darbepoetin alfa (Aranesp®).

- Epoetin alfa=

- Widely used in the veterinary field.
- Human recombinant protein.
- Can stimulate an immune response that may inactivate endogenous erythropoietin as well as the exogenous hormone.
- Should be reserved for patients with significant anemia.
- Induction dose = 44 to 120 units/kg SC three times a week.

- Response time is variable, but increases in hematocrit are generally observed in 1 to 2 weeks (the goal is to reach the target hematocrit within one month).
- Once the hematocrit has returned to 24-28%, the dose is reduced to the minimum necessary to maintain efficacy. Often, 44 to 88 units/kg SC 1 to 2 times per week is sufficient.
- Hematocrit should be rechecked every 2 weeks, then monthly.
- The absence of an increase in hematocrit despite increasing doses of epoetin alfa is strongly indicative of an immune response. The medication should be stopped immediately, and its use can be reconsidered in 3 to 4 weeks.

- Darbepoetin alfa =
- More expensive, but experience suggests it is much less likely to stimulate an immune response.
- Induction dose = 1.5 units/kg SC once a week until the patient's hematocrit reaches the lower end of the normal range. Then a dose every two weeks.
- Initially, hematocrit should be checked weekly and then monthly to avoid overdose.
- Due to the high demand for iron necessary for erythropoiesis, it is recommended that patients receiving epoetin alfa or darbepoetin alfa receive iron supplementation (10 mg/kg IM every 3 to 4 weeks.

❑Dietary regimen

- The cornerstone of CKD treatment is correcting dehydration and providing nutritional support.
- Dietary formulations for patients with CKD have traditionally focused on protein restriction in the hope of slowing the progression of kidney failure.
- Protein restriction helps reduce uremia and significantly improves the patient's quality of life.

- Controlling acidosis, hyperphosphatemia, and hypokalemia is useful.
- Studies show that appropriate regulation of serum phosphorus alone can improve the survival of patients with CKD.
- However, it is now thought that the omega-3/omega-6 fatty acid ratio may also play an important role in slowing the progression of kidney disease.
- All major commercial renal diets are generously supplemented with omega-3 fatty acids.

Example:

❖ Hill's® Science Diet k/d (alkalinization, restriction of sodium, phosphorus, lipid, and calcium).

❑ Anorexia

- Patients with CKD often suffer from anorexia.
- Although the exact cause of the lack of appetite is unknown, it is likely related to uremic toxins associated with gastrointestinal tract irritation.
- Owners should try several brands of food and different formulations to find one that their pet will eat.

- Some owners report good success with rotating several different diets across small frequent meals per day.

- Warming wet food can make a renal diet more palatable, especially for cats.
- Mirtazapine, a tetracyclic antidepressant, may help improve appetite in anorexic cats (1–3 mg/cat PO q72h).
- Since hypergastrinemia can occur with CRF, many patients respond to H2 histamine receptor antagonists such as famotidine (0.5 mg/kg IV or PO q24h).

- When present, nausea and vomiting can usually be alleviated by dopamine or serotonin inhibitors (5HT3 antagonists such as ondansetron 0.1–0.2 mg/kg IV q6–12h).

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

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)

❑ Advanced renal therapies

- Kidney transplantation for cats with CKD is performed at referral centers in certain countries.
- The patient must be free of infectious diseases such as feline leukemia virus, feline immunodeficiency virus, and toxoplasmosis.

- Recent chest X-rays and an abdominal ultrasound are necessary to show the absence of malignant tumor.
- Additionally, an echocardiogram may be necessary to demonstrate that the patient does not have significant heart disease.

- A good candidate would be a middle-aged cat suffering from increasing azotemia despite appropriate treatment and is still in good physical condition.
- Although kidney transplantation has been performed in dogs, the success rates are not encouraging due to issues with tissue rejection.
- Hemodialysis for patients with CKD is available at some centers in many countries. Although technically feasible, the cost and the need for treatments several times a week have made this option impractical for most pet owners.