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Canine leptospirosis

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Infectious and contagious disease, due to the multiplication - in the blood and then certain tissues

- of different serovars of the bacterial species

Leptospira interrogans.

Characterized by a dominant involvement of the

liver and kidneys; and by vascular lesions.

Leptospirosis is a zoonosis.

Importance

Leptospirosis is a zoonosis with a global **distribution.**

Affecting the **most species of mammals.**

The clinical forms are characterized by:

High mortality (or sequelae).

Clinical leptospirosis is common

in dogs but seems rare in cats.

Public health

Controlling leptospirosis is important not

only from the animal perspective but also from the

public health perspective = Zoonosis.

Dogs and cats can excrete leptospires in their urine

without showing clinical signs of the disease = Can

lead to human exposure.

Risk zones

- Recreational areas = rivers, ponds, puddles, etc.

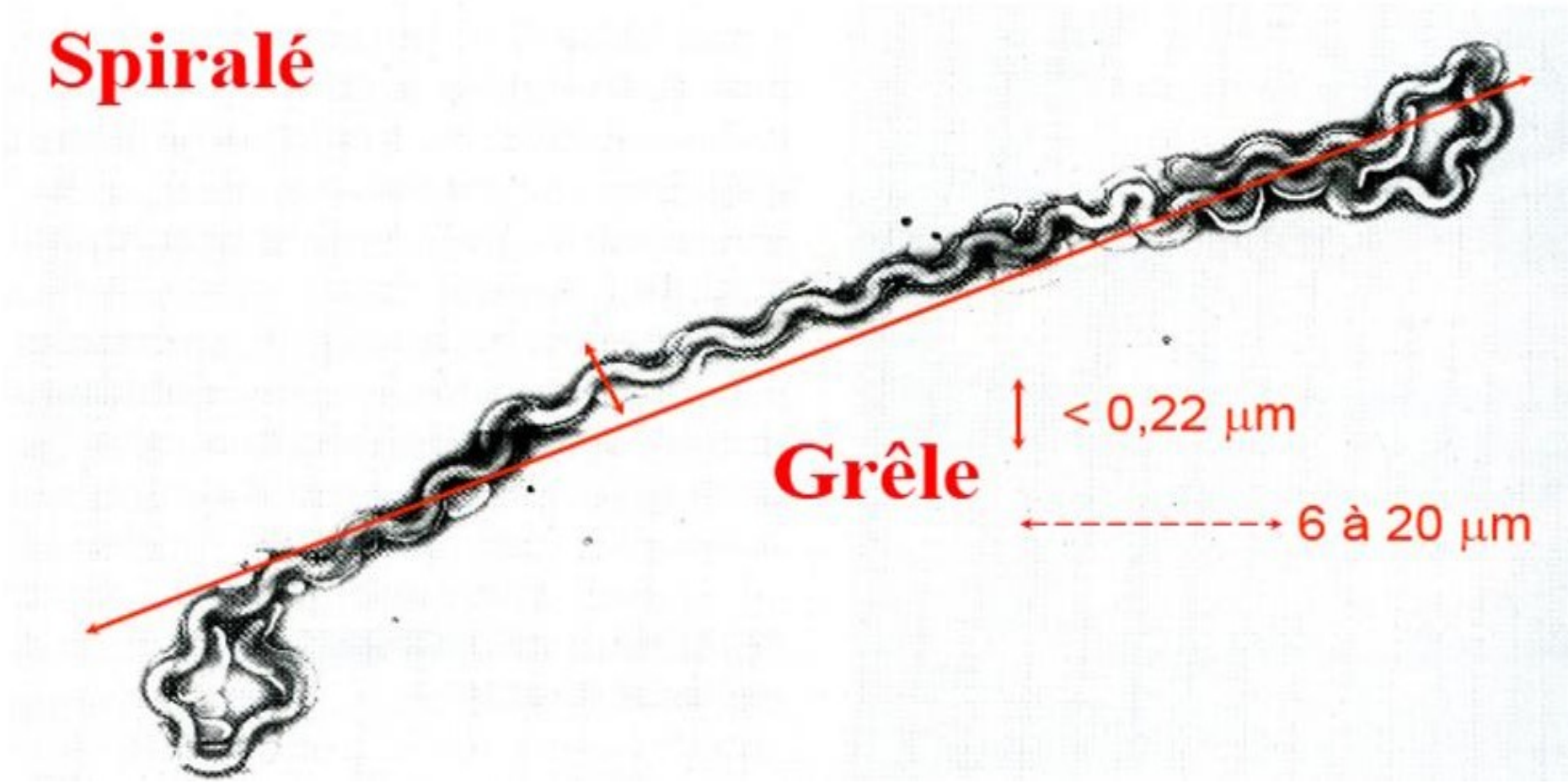
Occupational zoonosis = Moderate risk

- Significant incidence in many at-risk groups (for example swimmers, farmers, fishermen, athletes, sewer workers, etc.).
- Veterinarians.
- Essential precautions.

Etiology

Leptospirosis is caused by an infection by pathogenic spirochete bacteria of the genus ***Leptospira.***

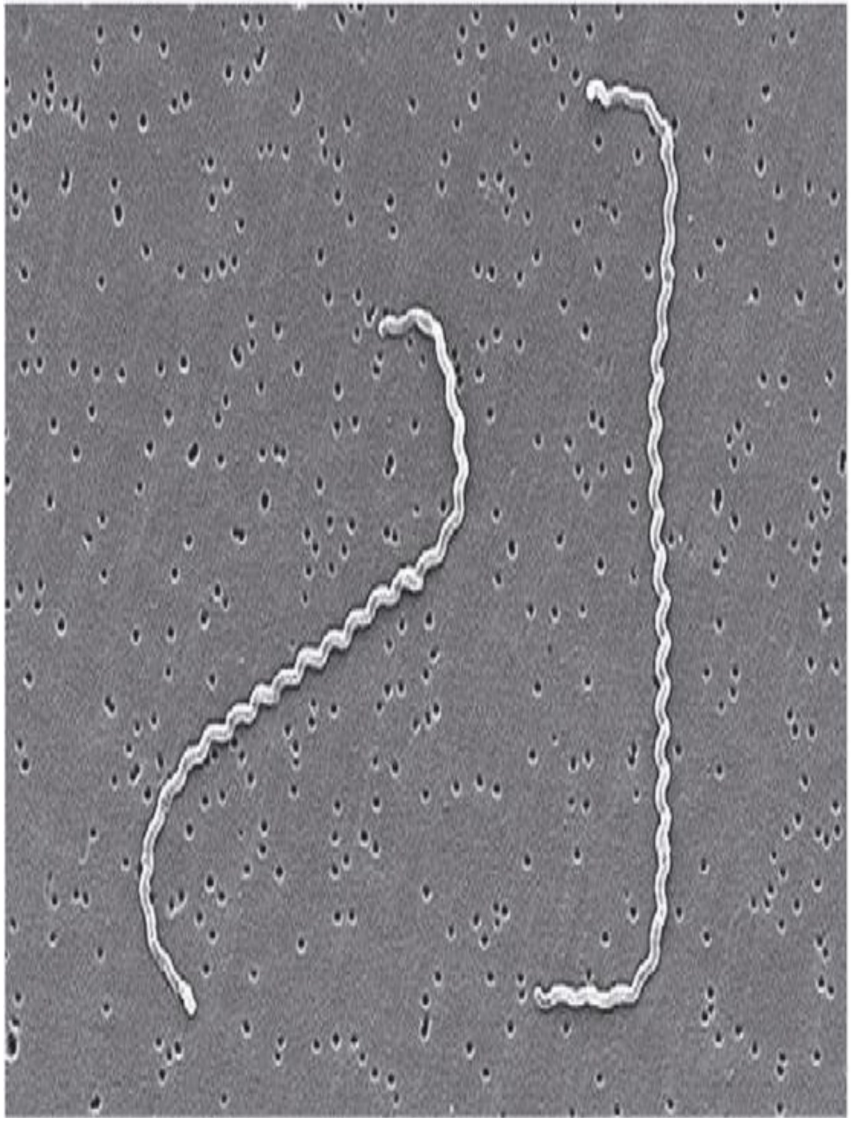
Leptospires are Gram-negative bacteria, very mobile, slender elongated and helical in shape.



Invisible under optical microscopy.

Visible: Dark field microscope; Silver impregnation; Electron microscopy.

The organism can be differentiated other from spirochetes their by distinct hook or question mark-shaped ends.



Strain of Leptospira interrogans (Electron microscopy).

- **Taxonomy = Very complex**

Most widespread serological taxonomy:

- **Order of spirochetes (3 genera: Borrelia, Treponema, Leptospira).**

- **Genus leptospira (✦ ? : "slender").**

- **2 species: Leptospira interrogans** ; Leptospira *biflexa.*

- **Concepts of serogroups and serovars.**

To understand the quite complex taxonomy of leptospires, it is useful to review the history of

typing Leptospira.

A l'origine, le genre Leptospira était divisé en 2

Espèces (phénotypiques, croissance, cultures, pathogénicité de l'organisme) :

- ***Leptospira interrogans sensu lato (souches*** pathogènes).
- ***Leprospira biflexa sensu*** lato (souches ***saprophytes, non pathogènes).***

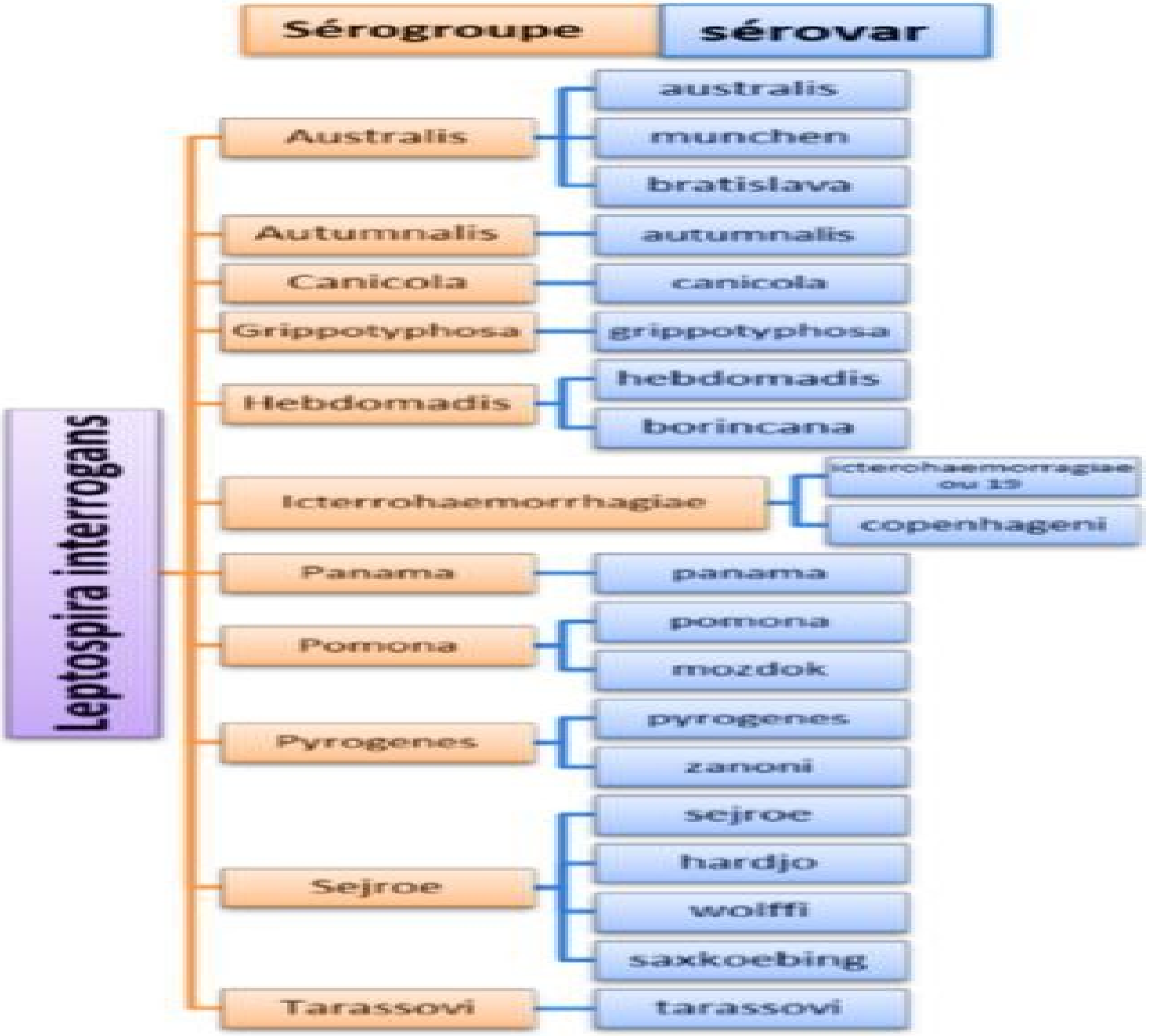
Sous classification = Sérologique

Avant le développement des méthodes de typage moléculaire, une sous-classification supplémentaire en sérovars était presque exclusivement basée sur la détermination sérologique des différences dans le composant glucidique du lipopolysaccharide leptospiral à l'aide d'antisérums spécifiques.

Antigenically related serovars have
then been grouped into serogroups. Currently,

more than 250 known pathogenic serovars have

been identified belonging to 24 serogroups.


Sérogroupe
sérovar
Leptospira interrogans
Australis
australis
munchen
bratislava
Autumnalis
autumnalis
Canicola
canicola
Grippotyphosa
grippotyphosa
Hebdomadis
hebdomadis
borincana
Icterrohaemorrhagiae
icterohaemorragiae ou 19
copenhageni
Panama
panama
Pomona
pomona
mozdok
Pyrogenes
pyrogenes
zanoni
Sejroe
sejroe
hardjo
wolffi
saxkoebing
Tarassovi
tarassovi

Species	Serogroups	Serovar	Reference strain
Panel 1 *:			
L. interrogans	Sejroe	Hardjo	Hardjo pratijno
	Pomona	Pomona	Pomona
	Canicola	Canicola	Hond Utrech IV
	Icterohaemorragiae	Icterohaemorragiae	Verdun
	Autumnalis	Autumnalis	Akiyami A

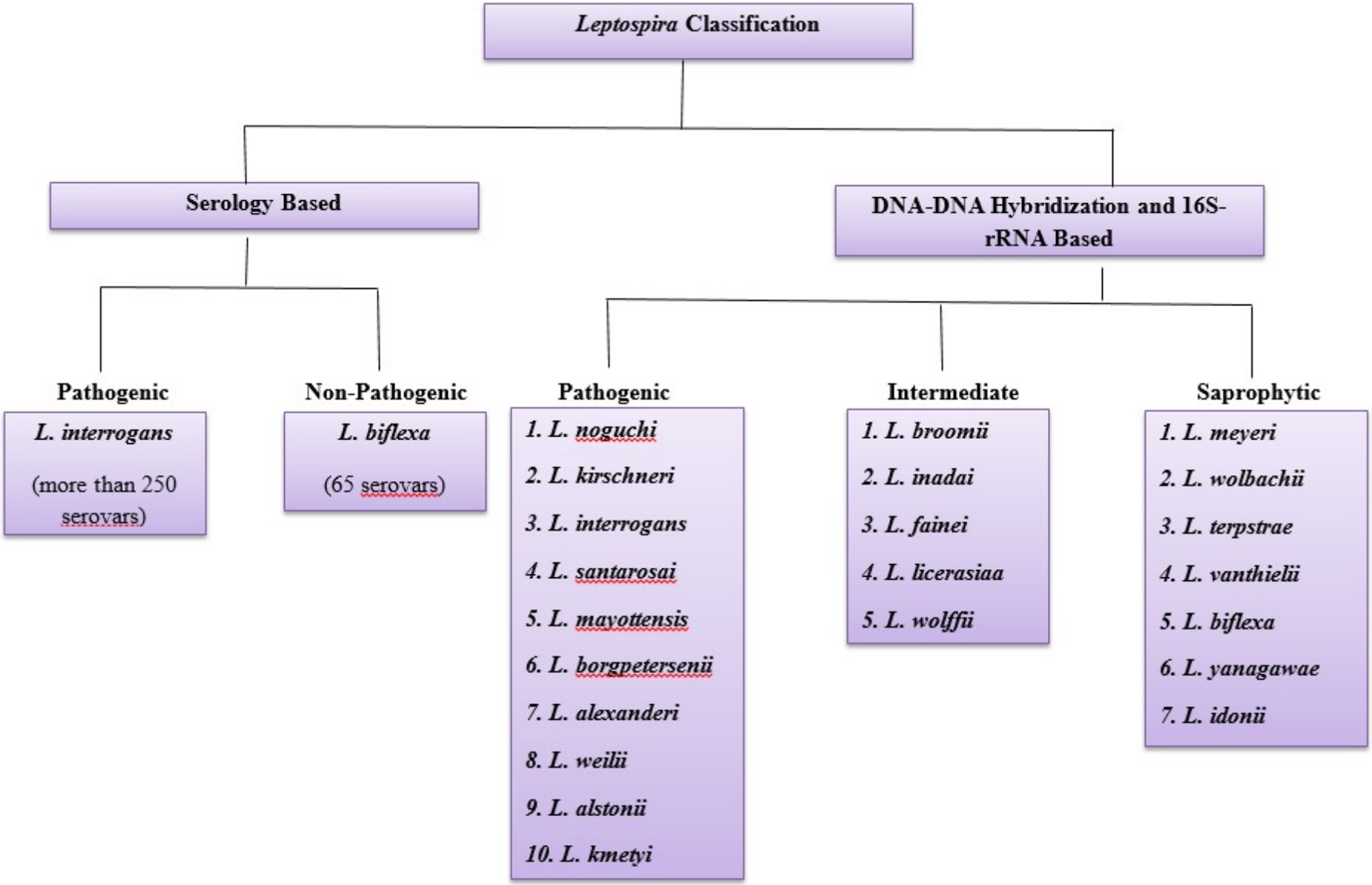
The following serogroups often affect canine species: Canicola, Icterohaemorrhagiae, Pomona, Bratislava, Grippotyphosa, Autumnalis, Batavia, Hardjo, Australis, Sejroe, and Zanoni.

More recently, a genotypic classification based on DNA hybridization has defined:

20 species of Leptospira including:

- **9 pathogenic species.**
- 6 saprophytic.
- 5 intermediate species.

New species are added as they are discovered.


Leptospira Classification
Serology Based
DNA-DNA Hybridization and 16S-rRNA Based
Pathogenic
L. interrogans
(more than 250 serovars)
Non-Pathogenic
L. biflexa
(65 serovars)
Pathogenic
1. L. noguchi
2. L. kirschneri
3. L. interrogans
4. L. santarosai
5. L. mayottensis
6. L. borgpetersenii
7. L. alexanderi
8. L. weilii
9. L. alstonii
10. L. kmetyi
Intermediate
1. L. broomii
2. L. inadai
3. L. fainei
4. L. licerasiaa
5. L. wolffii
Saprophytic
1. L. meyeri
2. L. wolbachii
3. L. terpstrae
4. L. vanthielii
5. L. biflexa
6. L. yanagawae
7. L. idonii

Unfortunately, the genetic classification of Leptospira species is not entirely correlated with serological classification as serovars from the same serogroup can belong to different genomic species.

However, serological classification is still

widely used.

Different serovars are considered to be suited to

specific reservoir hosts = Thus, their recognition is

important from an epidemiological point of view.

The accepted nomenclature:

The genus name, followed by the species name, followed by the serovar, followed by the strain.

The genus and species are italicized, with the serovar name not italicized and with an initial capital letter.

Example:

- *Leptospira interrogans serovar Australis*
- *Leptospira biflexa serovar Patoc*

➢ Bacteriological characteristics

Difficult culture (enriched media) and slow (diagnosis).

Fragile:

- Survival = humidity and pH ≈ basic.
- Destroyed by acidic pH.
- Sensitive to cold.

➢ Immunological characteristics

Protective antibodies.

Low immunogenicity = short-lived vaccine.

Protection

Epidémiologie

Les leptospires peuvent survivre pendant des mois dans l'eau et le sol humide.

Les petits rongeurs sont considérés comme les hôtes réservoirs les plus importants.

Il est probable que toutes les espèces connues de rongeurs = Souris, rat , marsupiaux et autres mammifères, y compris les humains, puissent servir des hôtes réservoirs.

Les hôtes réservoirs ne présentent

généralement aucun signe clinique = peuvent

héberger les leptospires dans leurs tubules

rénaux pendant des périodes très longues =

Excrétion de la bactérie dans l'environnement

via urine

Accidental hosts are infected:

- Either through direct contact of mucous membranes or broken skin with the urine of infected animals.
- Or through indirect contact with contaminated soil or surface waters.

= May develop severe acute forms

Maintenance hosts

Environment

Incidental hosts

Asymptomatic rodents

Soil and surface water

Wild and domestic animals

Hôte réservoir	Sérovars adaptés à l'hôte
Porc	Pomona, Tarassovi
Bovins	Hardjo, Pomona
Cheval	Bratislava
Chien	Canicola
Ovins	Hardjo
Rat	Icterohaemorrhagiae, Copenhageni
Souris	Ballum, Arborea, Bim
Chauve-souris	Cynopteri, Wolffi

Serogroups capable of infecting dogs

8 Sérogroupes	Réservoirs I.	Hôtes occasio.
Autumnalis	Souris	**Chien** - *Homme*
Bataviæ	Rat - Souris - Chien	**Chien** - *H* - *Chat*
Bratislava	Porc - Rat - Cheval	**Chien** - *Homme*
Canicola	**Chien**	**Chien** - *H* - *Chat*
Grippotyphosa	Rat - raton laveur	**Chien** - *H* - *Chat*
Hardjo	Vache	**Chien** - *H* - *Chat*
Icterohæmorrhagiæ	**Rat**	**Homme** - **Chien** **Cheval**
Pomona	Vache - Porc - raton laveur	**Chien** - *H* - *Chat*

Dogs are known to be hosts of

pathogenic leptospires.

2 main serogroups are involved in the canine

species:

- Icterohaemorrhagiae.
- Canicola.

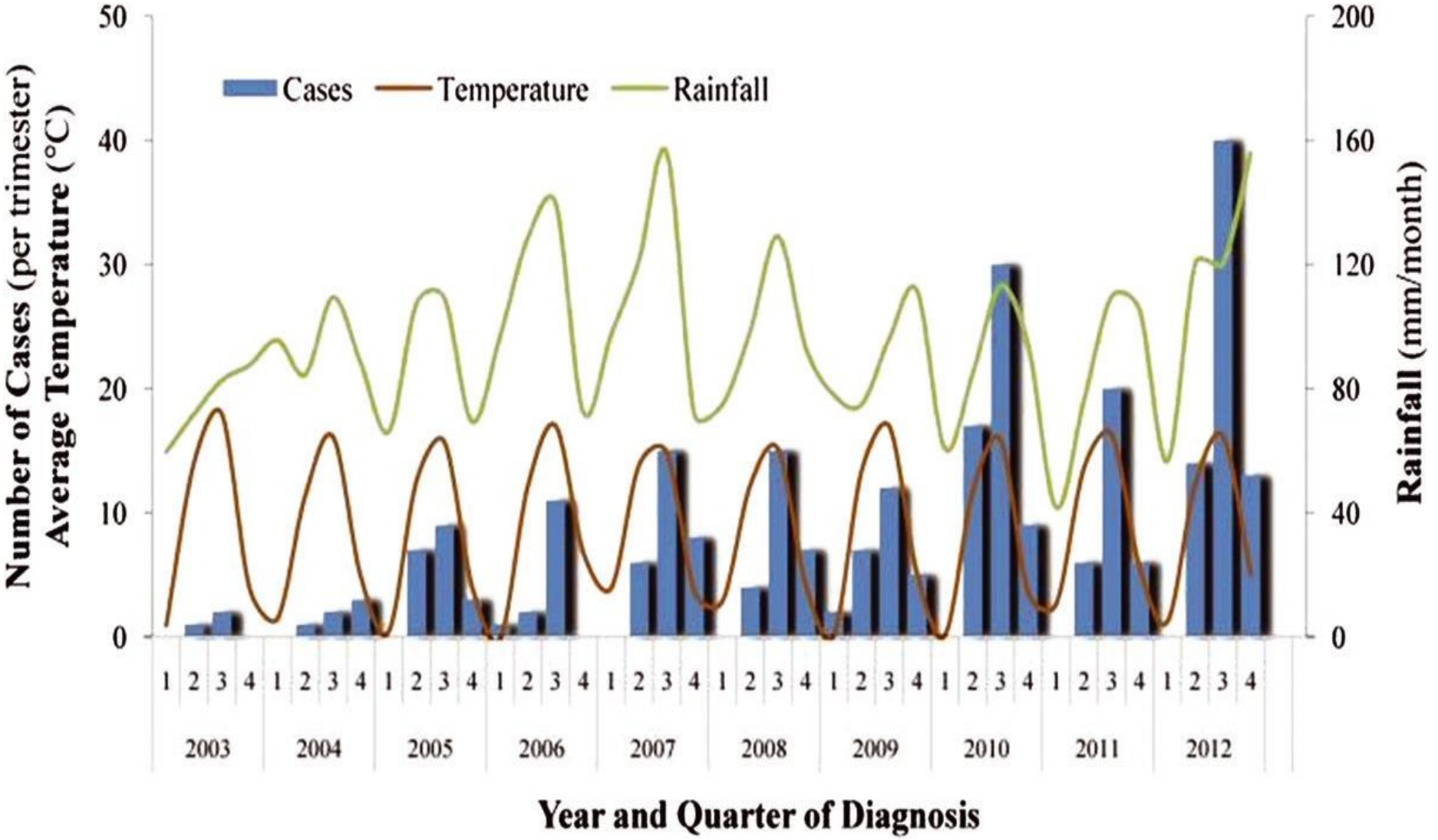
The serogroups that can infect dogs:

- Europe: Icterohaemorrhagiae, Grippotyphosa, Australis, Sejroe and Canicola.

- Grippotyphosa is common in continental Europe; seems rare in the UK and Ireland.

This could be explained by the distribution of host reservoirs.

Leptospirosis is considered a **seasonal disease, with epizootics linked to heavy rainfall or flooding.**



Distribution by quarter in 10 affected cantons (2003-2012) and the corresponding temperature and precipitation curves (Study conducted in the USA).

In cats, exposure to several serogroups has been identified:

Icterohaemorrhagiae, Canicola,

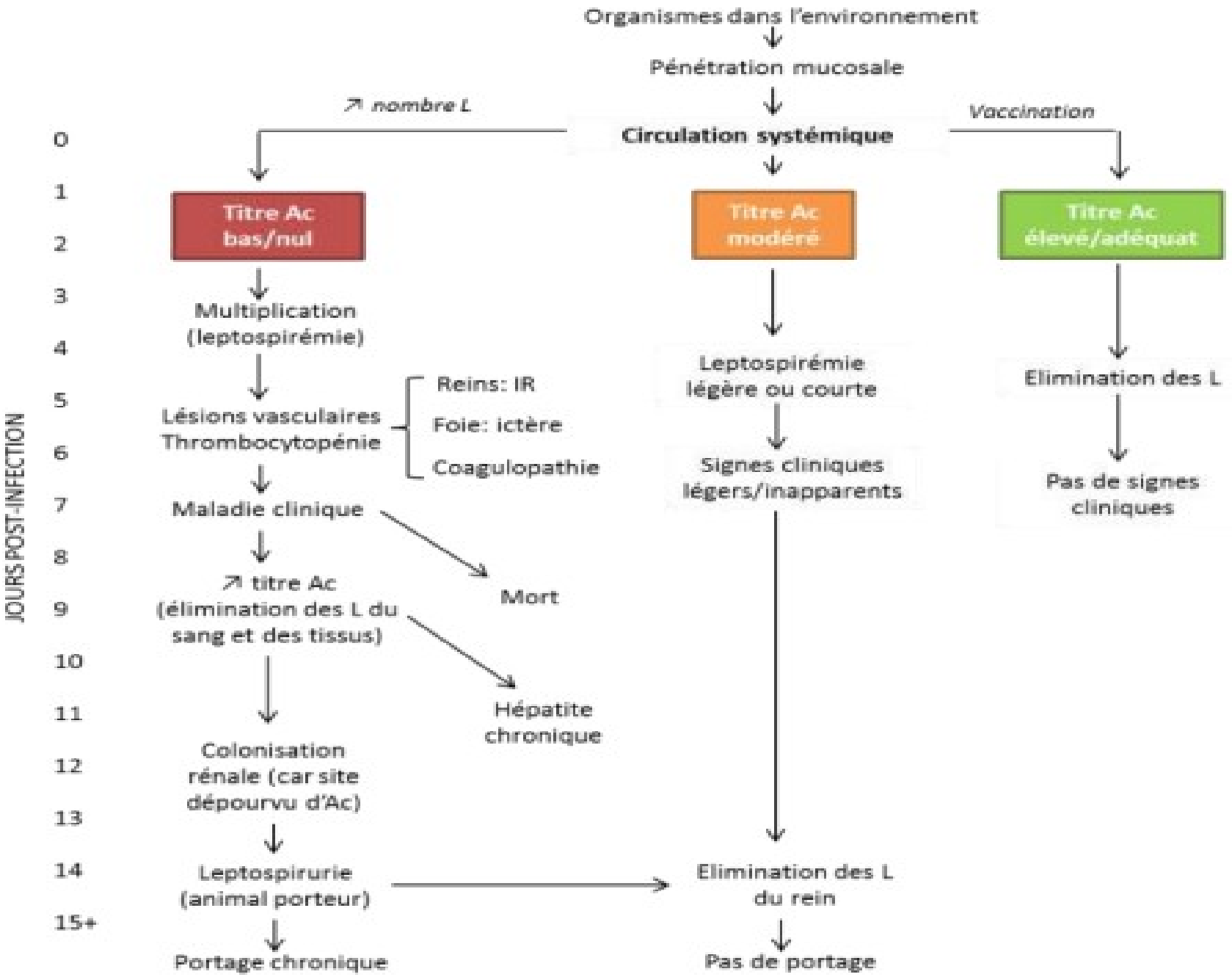
Grippotyphosa, Pomona, Hardjo,

Autumnalis, Ballum and Bratislava.

Several new studies have shown that cats can excrete leptospires in their urine and could therefore represent reservoir hosts of leptospires.

Pathogenesis

- Clinical involvement is caused by the penetration of leptospires through the mucous membranes.
- Leptospiremia.
- Dissemination and replication of leptospires in various organs: kidneys, liver, spleen, eyes, reproductive system, lungs.


Organismes dans l'environnement
Pénétration mucosale
↗ nombre L
Vaccination
Circulation systémique
Titre Ac bas/nul
Titre Ac modéré
Titre Ac élevé/adéquat
Multiplication (leptospirémie)
Leptospirémie légère ou courte
Elimination des L
Lésions vasculaires Thrombocytopénie
Reins: IR
Foie: ictère
Coagulopathie
Signes cliniques légers/inapparents
Pas de signes cliniques
Maladie clinique
Mort
↗ titre Ac (élimination des L du sang et des tissus)
Hépatite chronique
Colonisation rénale (car site dépourvu d'Ac)
Leptospirurie (animal porteur)
Elimination des L du rein
Portage chronique
Pas de portage
JOURS POST-INFECTION
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15+

NB:

Although clinical signs may be mild, death from

DIC can occur rapidly.

NB:

Renal colonization by the bacteria occurs in most infected animals.

Even after treatment and clinical recovery, leptospires can be excreted in the urine for several weeks or even months.

NB:

The elimination of leptospires begins after 7 days.

Symptoms

The disease most often affects dogs that live outdoors, including hunting dogs.

The severity of the infection varies depending on age, immune status, environment, and serotype.

Gastro-entérite hémorragique Leptospirosique (« typhus canin »

La forme ictéro-hémorragique

La forme néphritique

Formes inapparentes

Forms of evolution

Leptospirosis can take several major forms of clinical expression:

Peracute, acute, subacute or chronic, inapparent.

❖ **Peracute form**

A peracute form without characteristic symptoms can occur and cause the sudden death of the animal.

❖ Acute forms

Generally, two types of acute forms are described:

- Hemorrhagic gastroenteritis or typhus of dogs or Stuttgart disease.
- Icteric-hemorrhagic form or disease of Weil.

- **Hemorrhagic gastroenteritis or typhus of dogs or Stuttgart disease.**

Incubation, on average: 3-6 days.

Rapid evolution.

Death within 48h-72h (without treatment) due to cardiovascular shock and hypothermia.

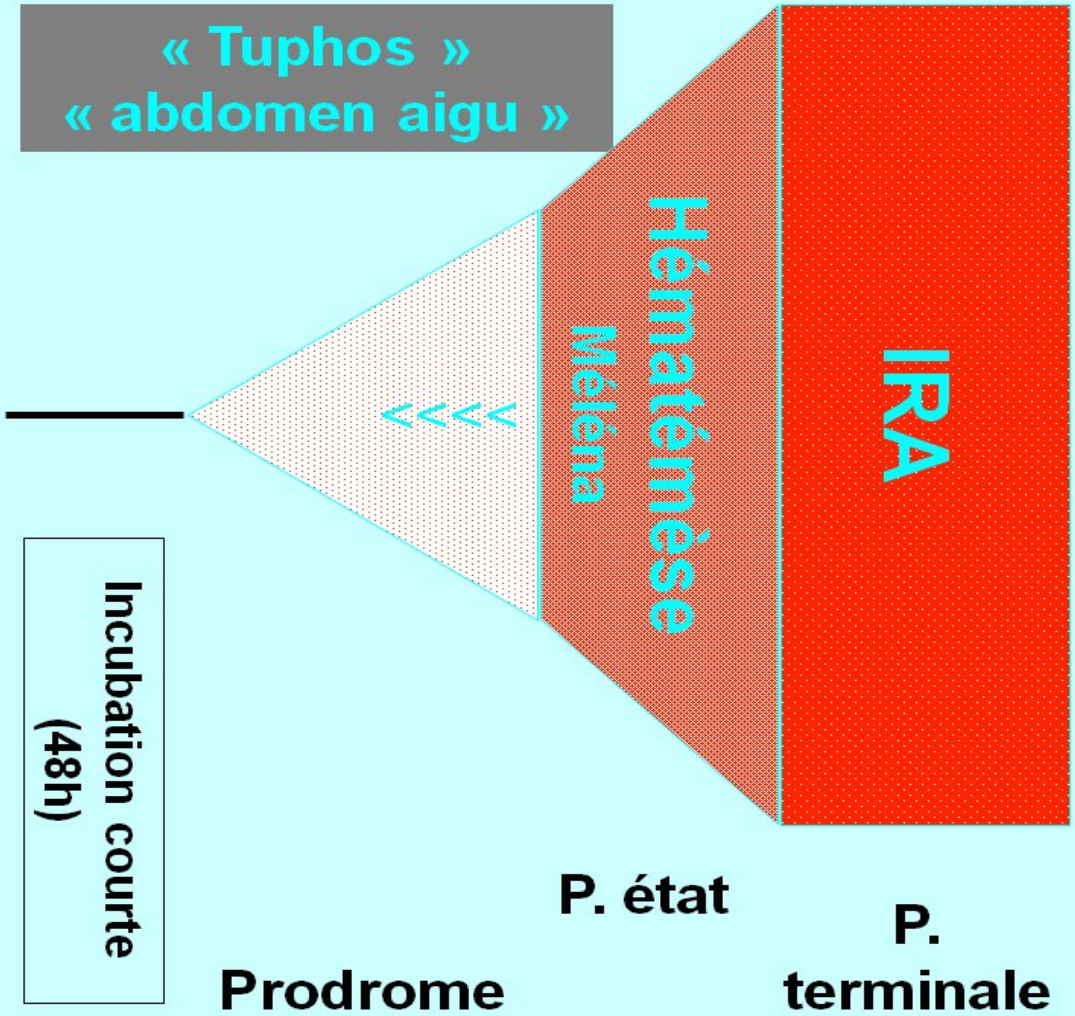
The animal presents:

- ✓ Severe hyperthermia (>40°C), state of intense prostration, anorexia, flaccidity and muscle sensitivity.
- ✓ **Hemorrhagic vomiting (hematemesis).**
- ✓ **Hemorrhagic diarrhea (hematochezia).**
- ✓ Abdominal pain.

Vomiting is common in acute cases of leptospirosis.

« le typhus canin »

Canicola



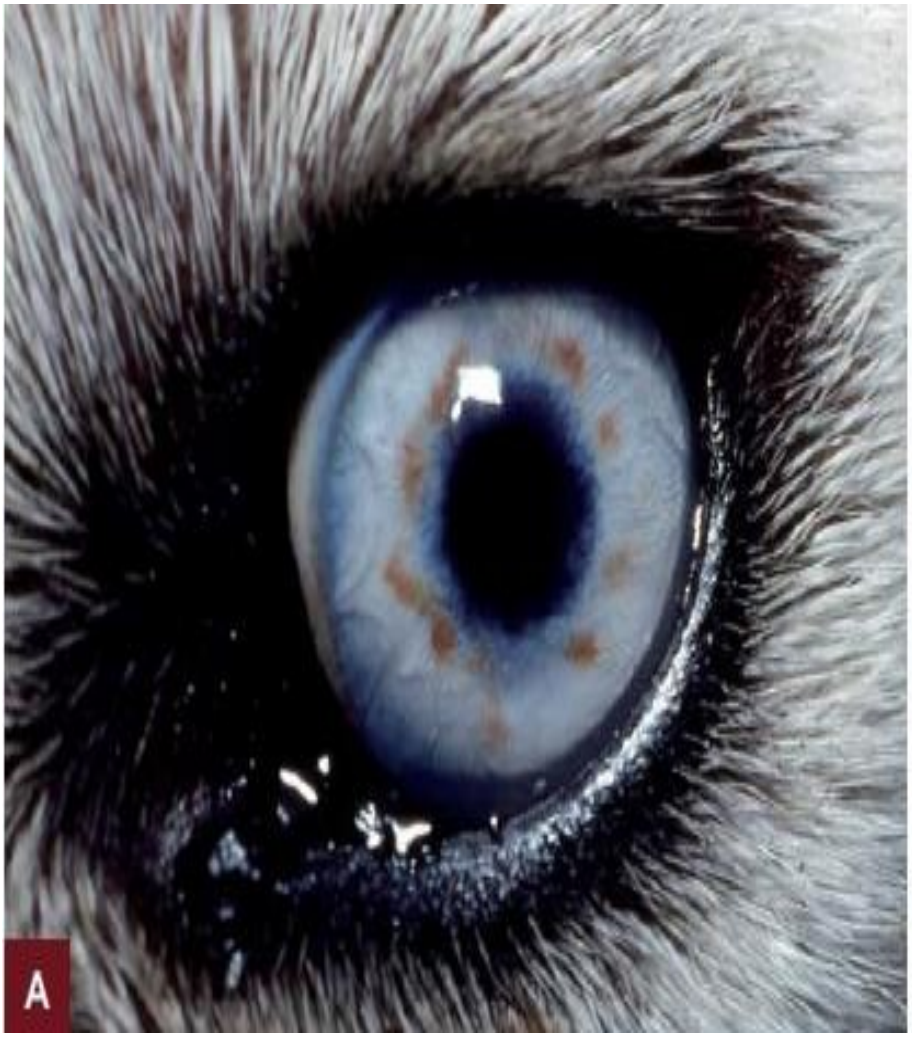
- ✓ **Acute renal failure:**

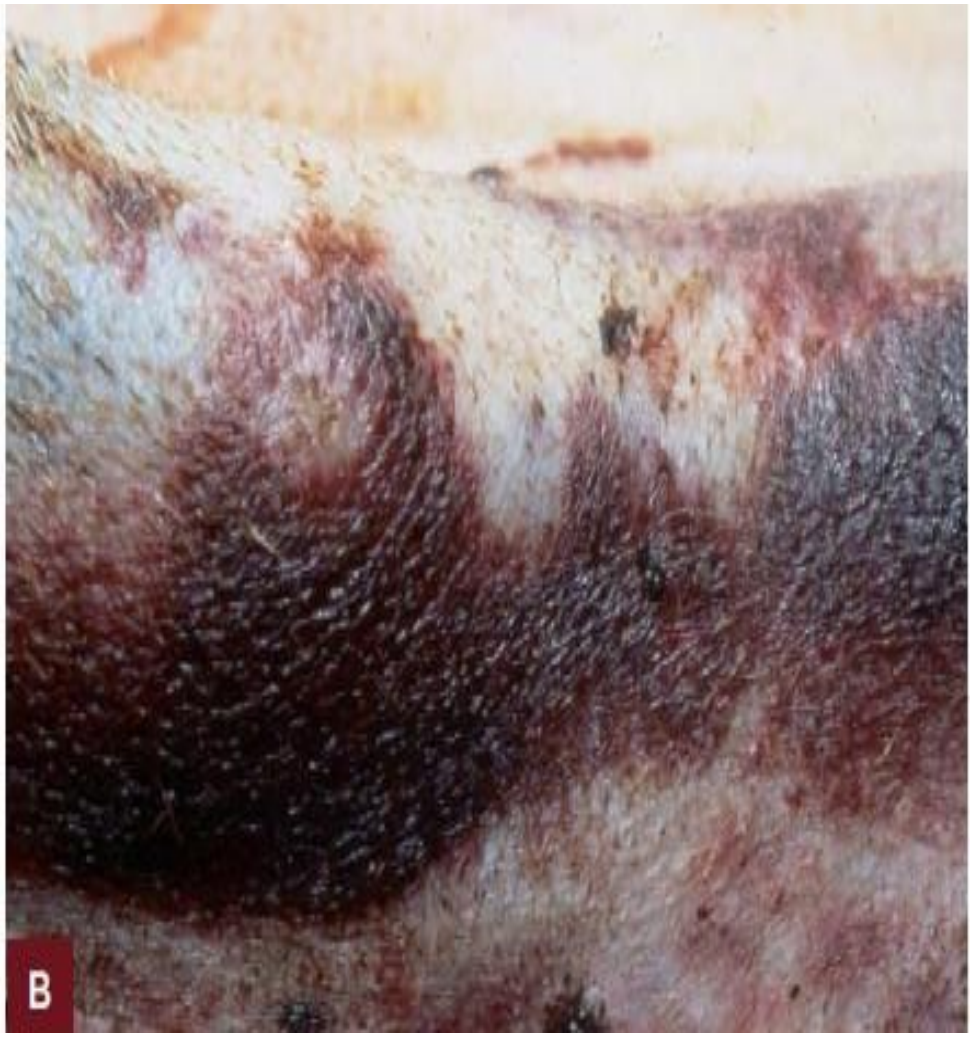
  Total kidney dysfunction leading to oliguria causing a significant increase in uremia and creatinemia.

The urine is colored and very dark.

- ✓ **Coagulopathies and signs characterizing the clinical picture of DIC: Petechiae, melena, epistaxis, and hematemesis dominate the picture of hemorrhagic symptoms.**

Hemorrhages are visible on the skin, intestinal, and retinal mucous membranes.





Petechiae (A) and ecchymoses (B) are warning signs of primary hemostasis disorders or plasma coagulation issues.

- ✓ Involvement of the cardiorespiratory system (myocarditis): Tachypnea, tachycardia, and an increased capillary refill time.

- **Icteric-hemorrhagic form or disease of WEIL**

Common agent Leptospira *icterohaemorrhagiae,* as well as other leptospires.

Less fulminant form than the previous form with a primarily hepatic tropism.

Incubation: 3-6 days.

The animal presents:

- ✓ Less severe hyperthermia and less pronounced lethargy than in the previous form.
- ✓ Uncontrollable vomiting quickly leads the dog to a state of dehydration that is often lethal, especially since renal function is greatly diminished.

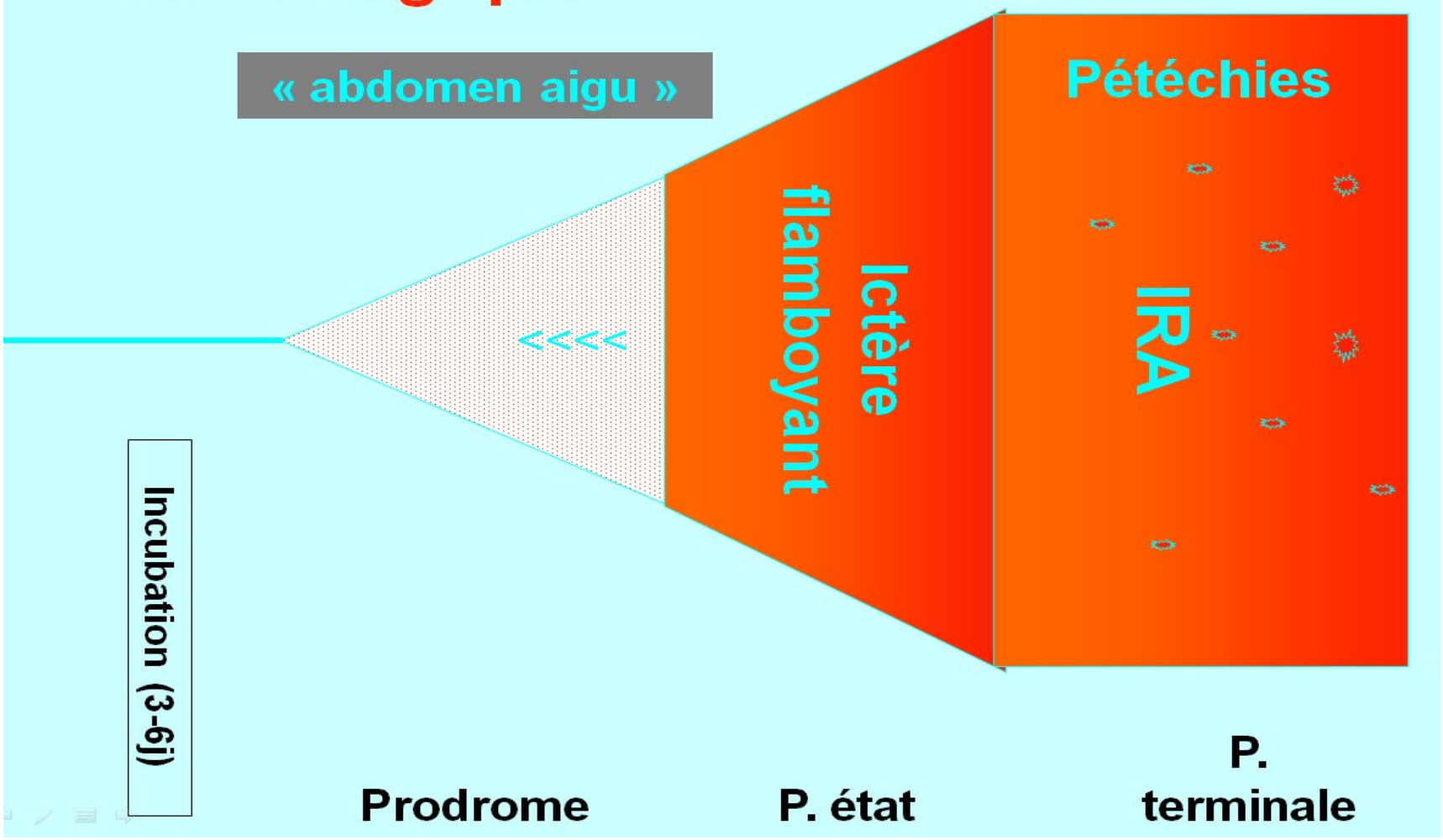
✓**Liver damage: About ten days.**

In PI, liver damage is manifested with yellow-orange jaundice (flaming jaundice). The urine produced will be very colored due to the richness in bilirubin.

- ✓ Renal damage: Acute tubular nephritis.
- ✓ In general, this form is just as fatal for the dog although it is less devastating than the previous form.
- ✓ The dog succumbs in 3-6 days once jaundice and hemorrhages have occurred.

F. Ictéro-hémorragique

Icterohæmorrhagiæ

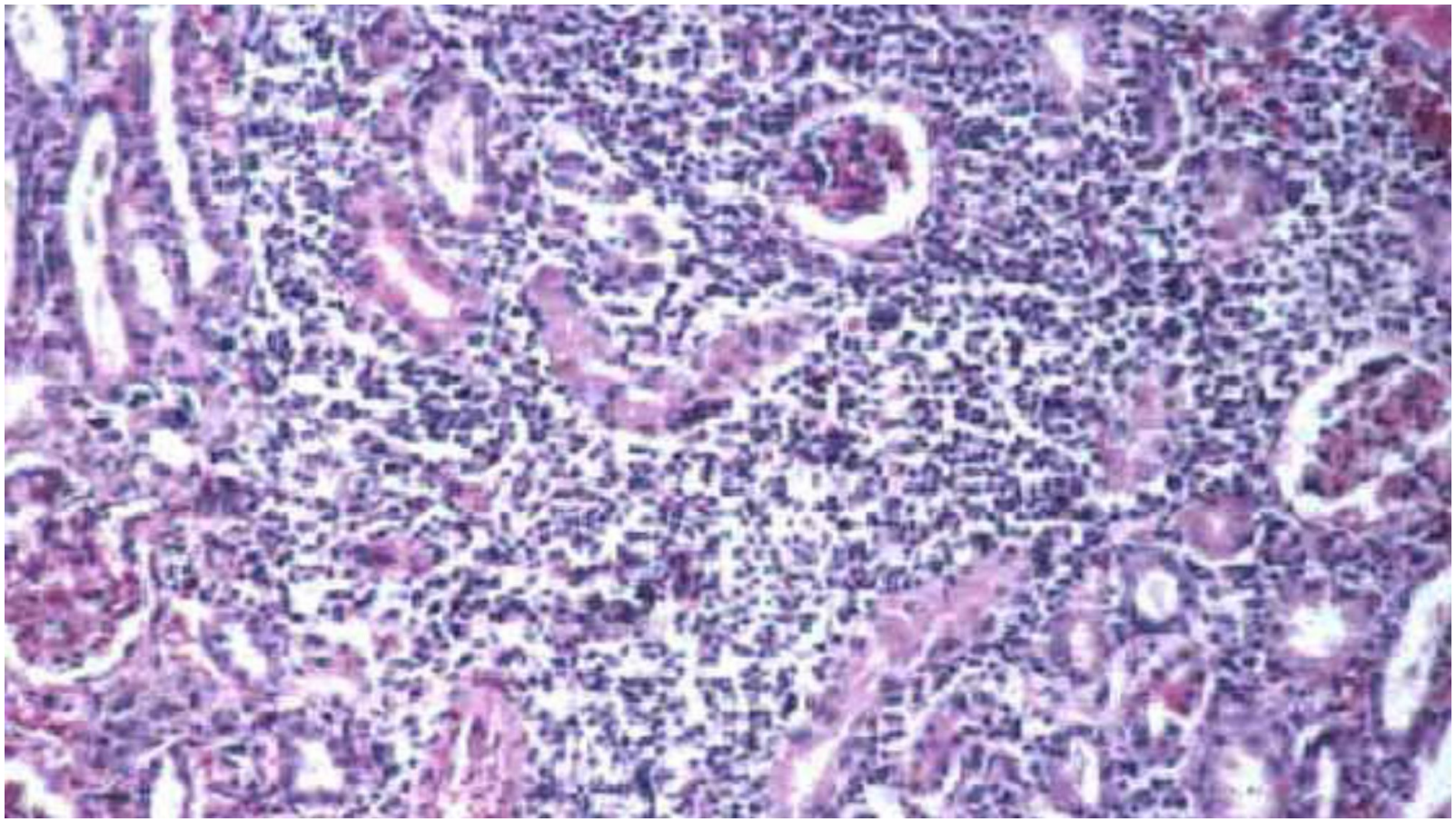


Jaundice of the sclera and oral mucous membranes in a dog suffering from leptospirosis (dog, male, 3 months).

Note:

In practice, hemorrhagic phenomena and jaundice are associated with L. icterohaemorrhagiae and nephritis with L. canicola.

Animals infected with L. pomona or grippotyphosa present with acute renal failure.



Acute-subacute interstitial nephritis; microscopic appearance. L. canicola infection (H&E stain, x25).

❖ **Subacute or chronic forms**

Generally in dogs that survive the acute forms.

The 2 main organs affected are the kidney and the liver.

❑Leptospirosis nephritides

Onset of nephritis tubulo-interstitial

chronic (chronic renal failure)

leading to a uremic syndrome.

Renal symptoms may be mild as long as at least

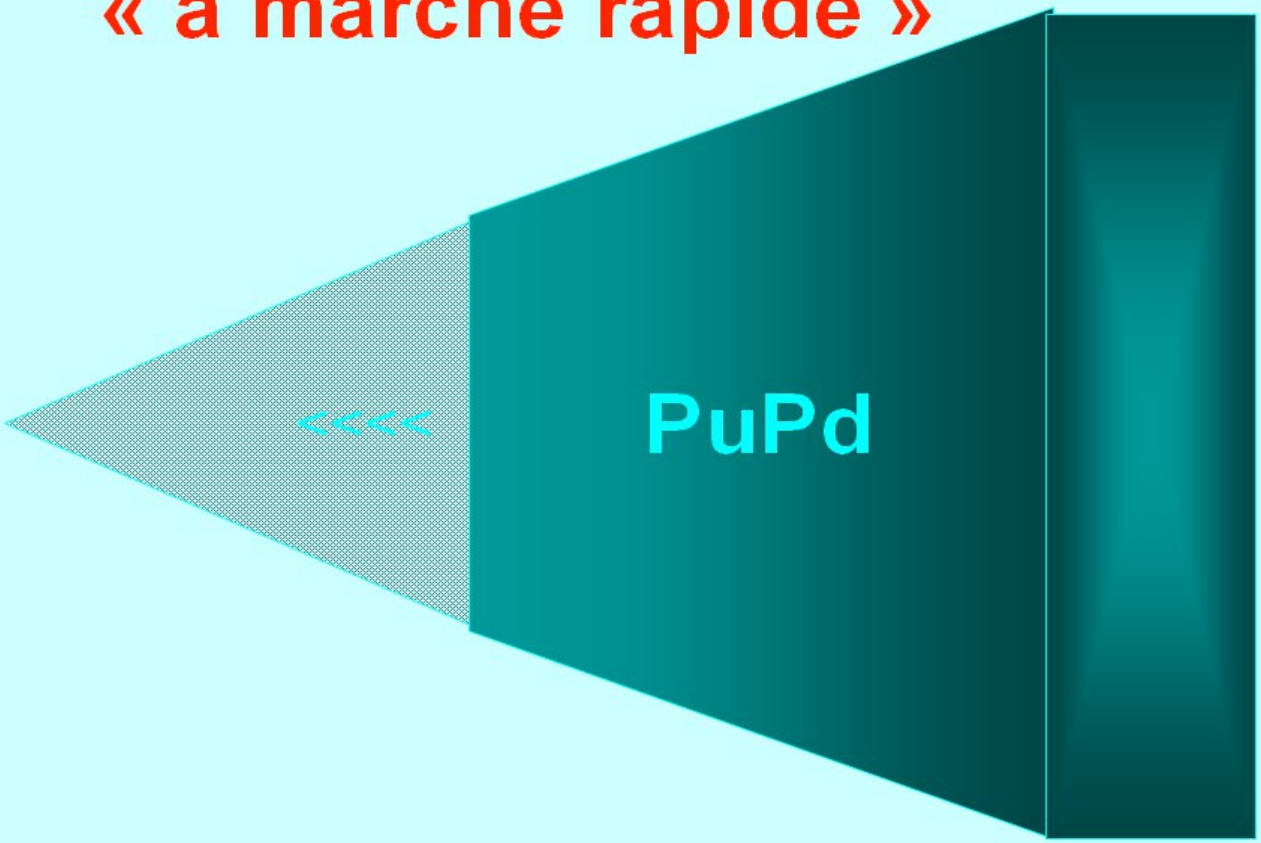
30% of the nephrons remain functional.

The first clinical signs: polyuria-polydipsia.

In advanced stages: Vomiting and diarrhea that can be fatal to the animal after the onset of uremic coma.

F. Néphritique : I.R.Subaiguë

« à marche rapide »



compensation

P. état

S. urémique

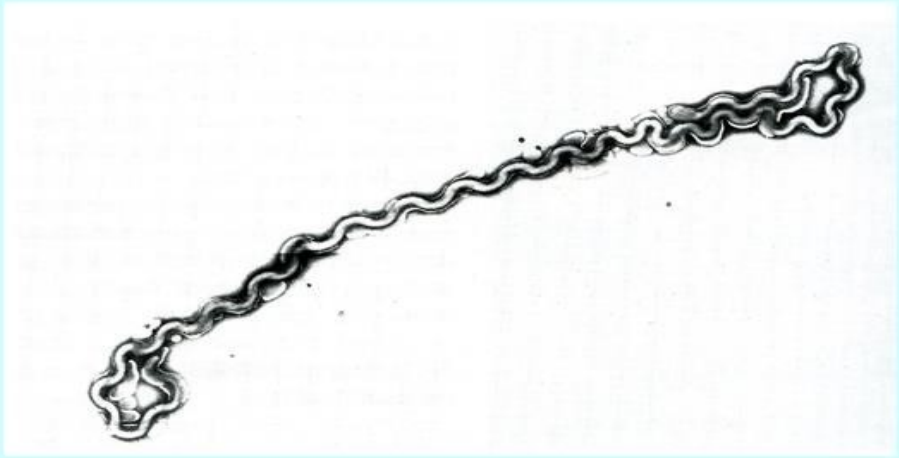
Interstitial nephritis and fibrosis resulting from chronic infection with L. canicola. Normal kidney (left), diseased kidney (right).

❑Leptospirosis hepatitis

Chronic hepatitis will progressively impair the dog's health:

Jaundice, decreased serum albumin levels, increased globulin levels, and a defect in the production of vitamin K-dependent coagulation factors (factors II, VII, IX, and X).

❖ Subclinical form



Excrétion urinaire prolongée

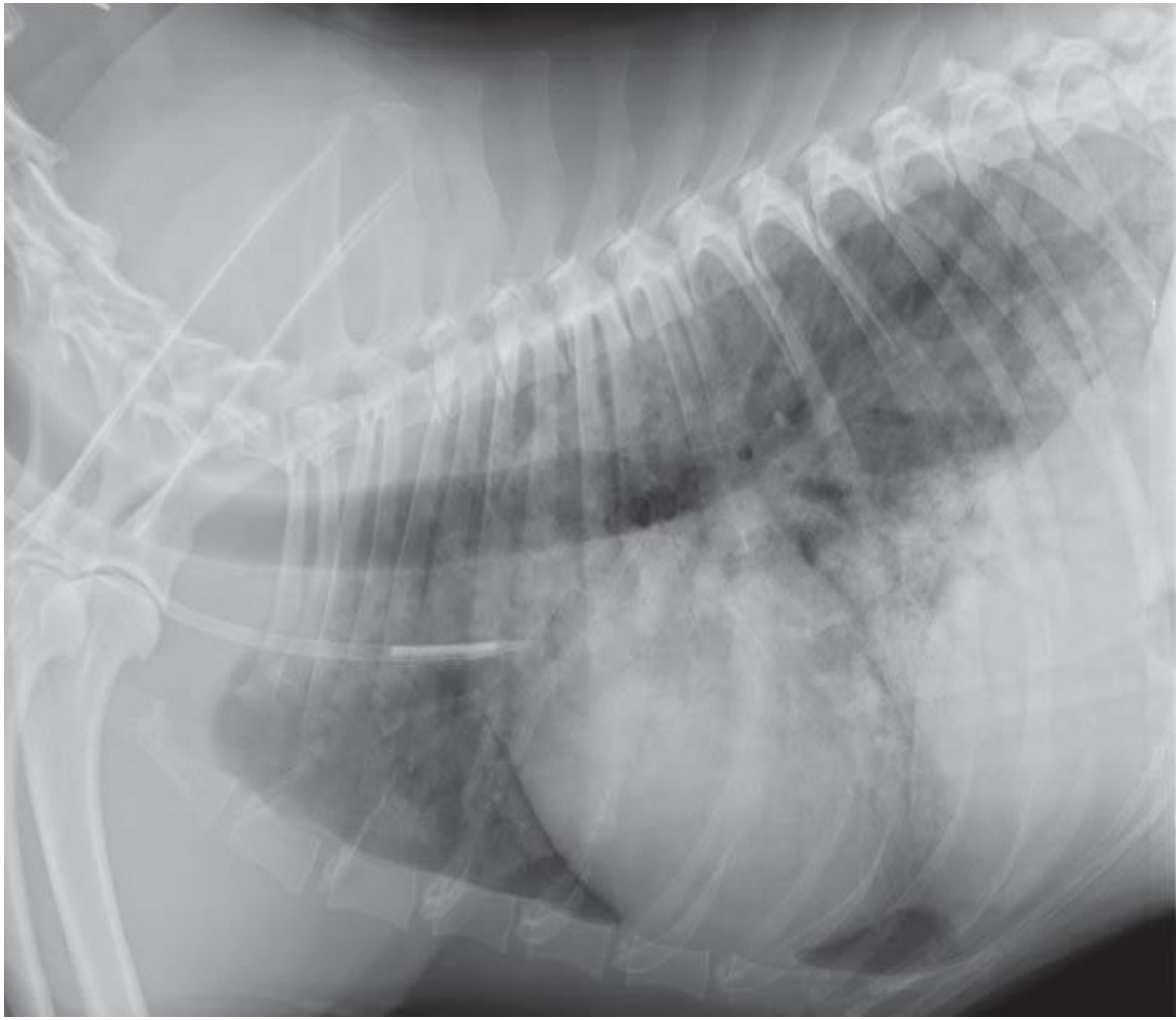
❖ Other forms

Respiratory

Pharyngitis or tonsillitis leading to symptoms of cough and dyspnea.

In some cases, these respiratory disorders can complicate into non-cardiogenic pulmonary edema, hemoptysis, or lead to secondary pneumonia (Leptospiral Pulmonary Haemorrhage Syndrome: LPHS)

Pulmonary lesions are visible radiographically.



Chest X-ray showing the typical image of pulmonary hemorrhage associated with leptospirosis

Forme pulmonaire

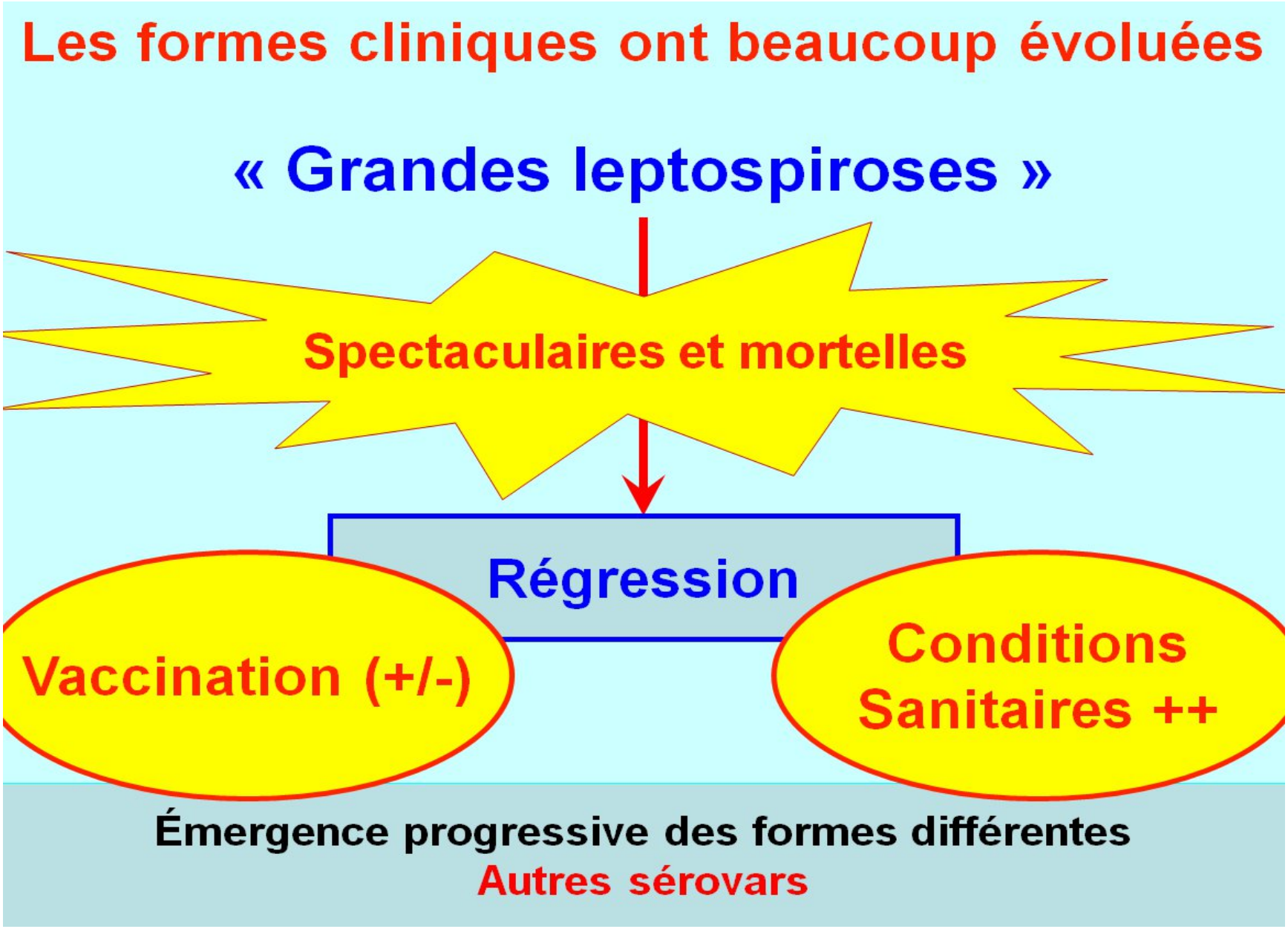
- **Ophthalmic**

The penetration of leptospires into the aqueous humor during the septicemic phase is possible. The persistence of leptospires in this part of the eye can last for months and lead to chronic uveitis.

- **Nervous**

Signs of encephalitis and meningitis.

Les formes cliniques ont beaucoup évoluées



Diagnosis

❖ **Clinical**

Difficult;

Given the non-specificity of the clinical picture, the practitioner is led to carry out complementary examinations to specify the diagnosis.

Subacute to acute forms:

Symptoms general non-specific anorexia, (lassitude, hyperthermia or Hypothermia) is generally associated with hepatic symptoms (jaundice), renal symptoms (polyuria-polydipsia, oliguria-anuria), or digestive symptoms (vomiting, diarrhea).

Atypical symptoms: respiratory (dyspnea), ocular or neurological symptoms should particularly attract the clinician's attention, just like the presence of bleeding from cutaneous, digestive, or respiratory origins.

❖ Complementary orientation examinations

Biological abnormalities:

- An elevation of alkaline phosphatases (ALP) in 50 to 80% of cases.
- An increase in alanine aminotransferases (ALT) in 30 to 75% of cases.
- An increase in creatinine in 55 to 95% of cases.

- Anemia and thrombocytopenia (50%); a consequence of hemorrhages rather than hemolysis.
- Neutrophilic leukocytosis in 30 to 80% of cases.
- Glucosuria is reported very variably (5 to 65% of cases).
- Proteinuria has been reported in 66%: which suggests glomerulopathy.

Complete Blood Count Findings at Admission in Dogs with Leptospirosis from Northern California*

Test	Reference Range	Percent Below the Reference Range	Percent Within the Reference Range	Percent Above the Reference Range	Range for Dogs with Leptospirosis	Number Tested
Hematocrit (%)	40-55	78	22	0	12-48	54
Neutrophils (cells/µL)	3000-10,500	0	35	65	3474-14,311	54
Band neutrophils (cells/µL)	Rare	0	63	37	0-2954	54
Monocytes (cells/µL)	150-1200	0	65	35	162-4594	54
Lymphocytes (cells/µL)	1000-4000	30	70	0	162-3769	54
Eosinophils (cells/µL)	0-1500	0	100	0	0-970	54
Platelets (cells/µL)	150,000-400,000	28	61	11	40,000-522,000	53

*Diagnosis based on results of acute and convalescent phase serology together with consistent clinical signs.

Serum Biochemistry Findings at Admission in Dogs with Leptospirosis from Northern California*

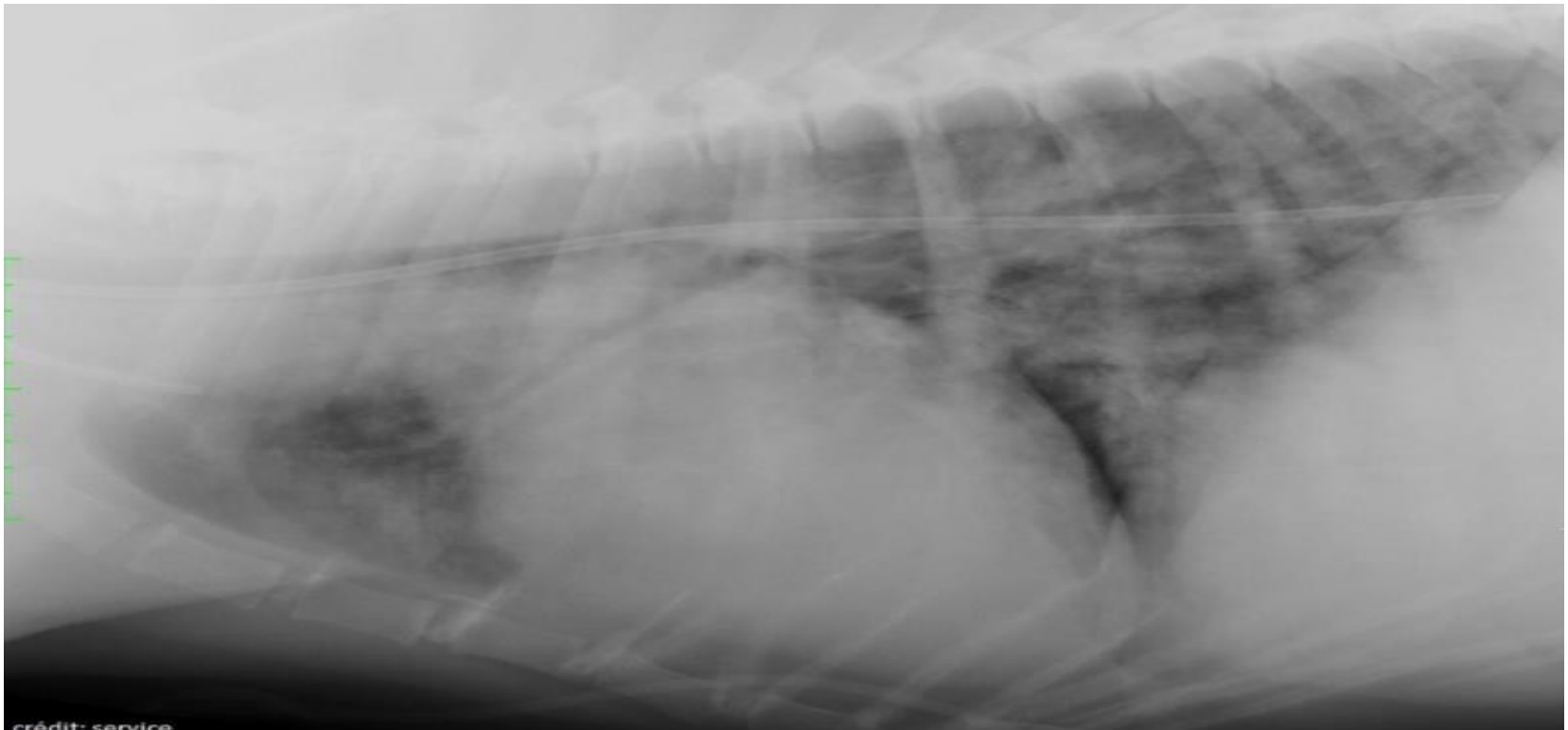
Test (Number of Dogs Tested)	Reference Range	Percent Below the Reference Range	Percent Within the Reference Range	Percent Above the Reference Range	Range for Dogs with Leptospirosis	Number of Dogs Tested
Sodium (mmol/L)	145-154	33	61	6	134-162	54
Potassium (mmol/L)	4.1-5.3	35	44	20	2.8-7.6	54
Chloride (mmol/L)	105-116	57	37	6	98-118	54
Bicarbonate (mmol/L)	16-26	33	61	6	11-28	54
Calcium (mg/dL)	9.9-11.4	39	44	17	7.2-10.9	54
Phosphorus (mg/dL)	3.0-6.2	0	9	91	2.7-13.0	54
Creatinine (mg/dL)	0.5-1.6	0	0	100	0.4-3.3	54
BUN (mg/dL)	8-31	0	2	98	8-110	54
Albumin (g/dL)	2.9-4.2	96	4	0	0.9-3.8	54
Globulin (g/dL)	2.3-4.4	9	78	13	1.6-4.7	54
Cholesterol (mg/dL)	135-345	4	91		79-408	54
Total bilirubin (mg/dL)	0-0.4	0	69	32	0-3.1	54
ALT (U/L)	19-70	0	43	48	17-1443	54
ALP (U/L)	15-127	0	67	33	29-985	54
CK (U/L)	46-320	31	8	62	5-258,720	13

*Diagnosis based on results of acute and convalescent phase serology together with consistent clinical signs.

❖ Pulmonary radiographic anomalies

Pulmonary bleeding = diffuse alveolar hemorrhage with diffuse reticular-nodular opacity is classically observed.

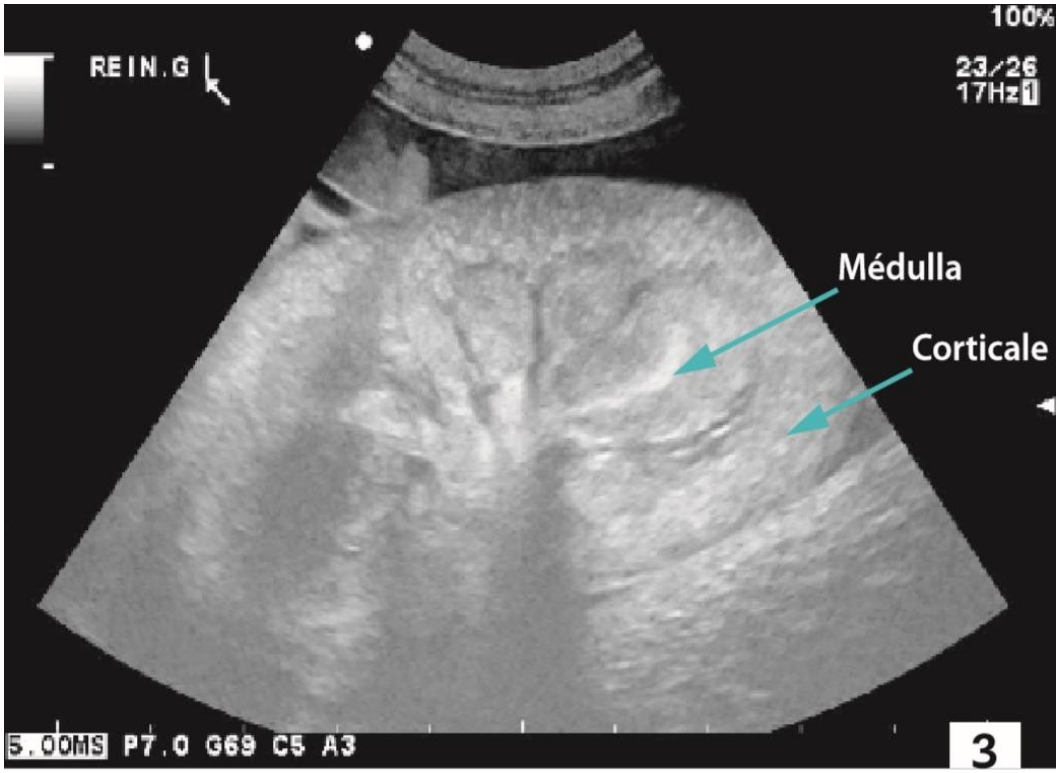
It preferentially affects the caudal lobes bilaterally.



❖ Ultrasound anomalies

Hyper-echogenicity of the renal cortices,

nephromegaly, and pyelactasis.



❖ Specific diagnosis

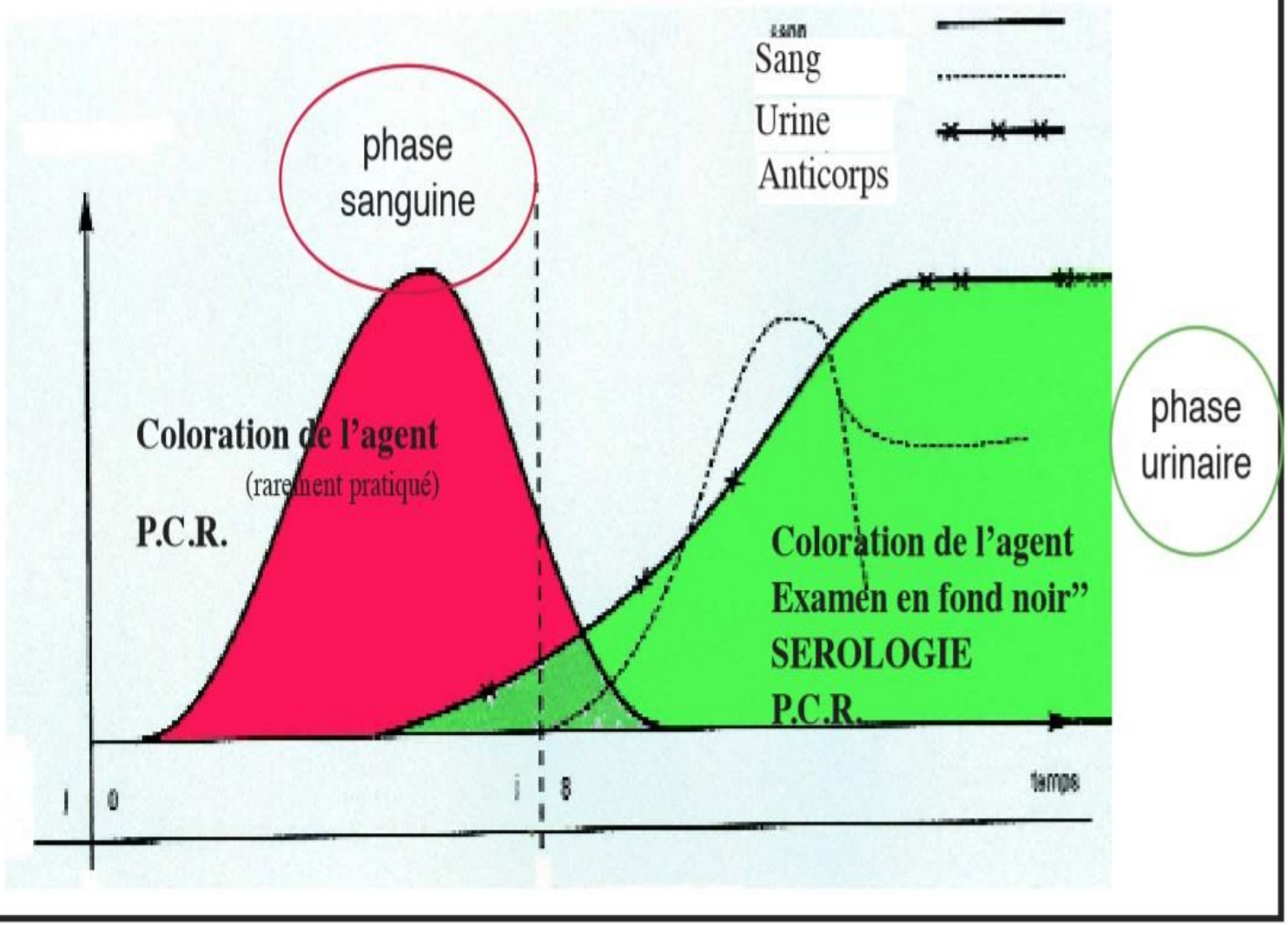
❑ Search for the germ

Difficult due to the great fragility of leptospires; this requires implementing laboratory examinations in the hours following the sampling.

The germs are found in:

The blood: before the 8th day following the onset of symptoms.

The urine: After the 8th day.


Sang
Urine
Anticorps
phase sanguine
Coloration de l'agent
(rarement pratiqué)
P.C.R.
Coloration de l'agent
Examen en fond noir"
SEROLOGIE
P.C.R.
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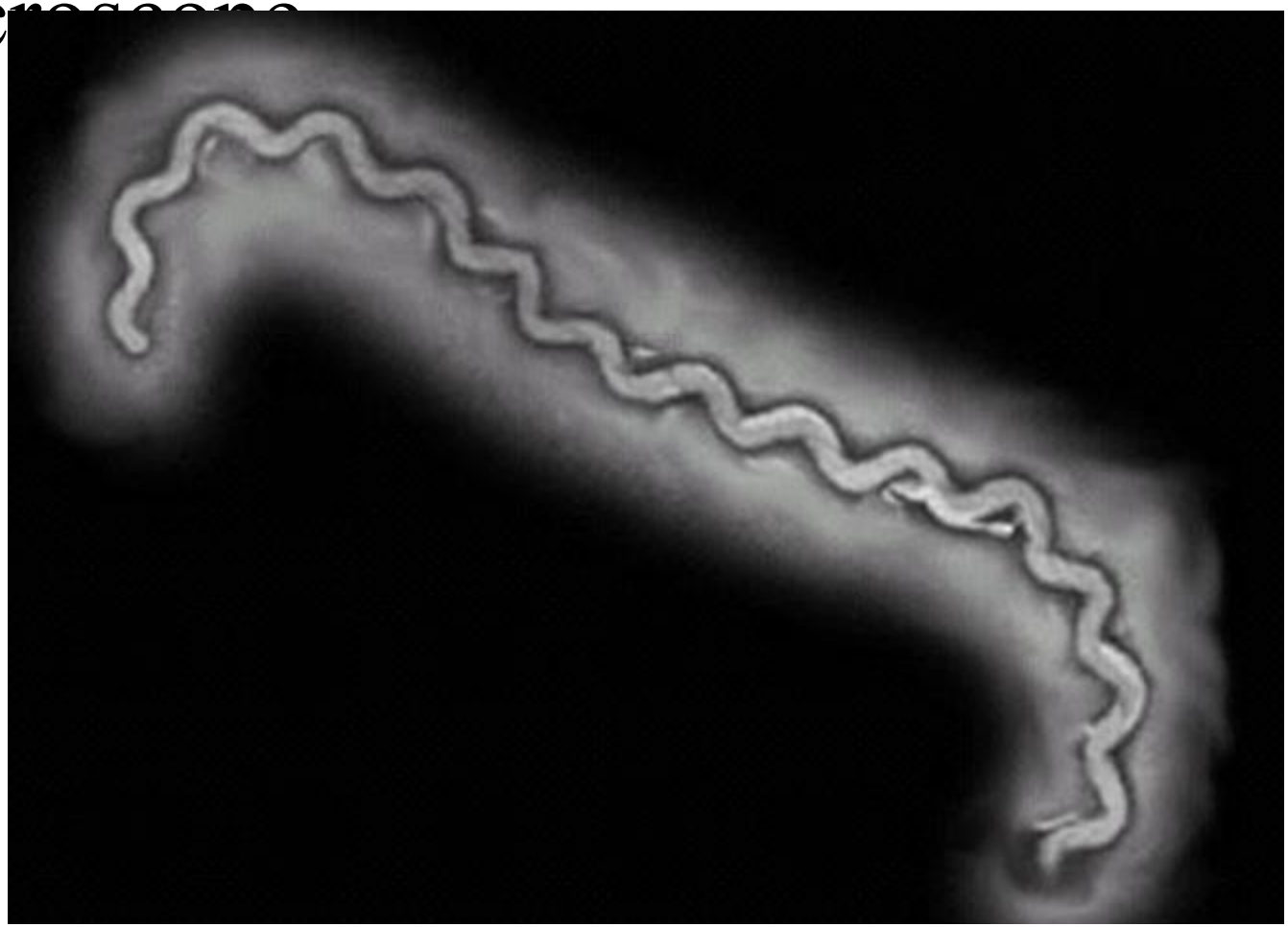
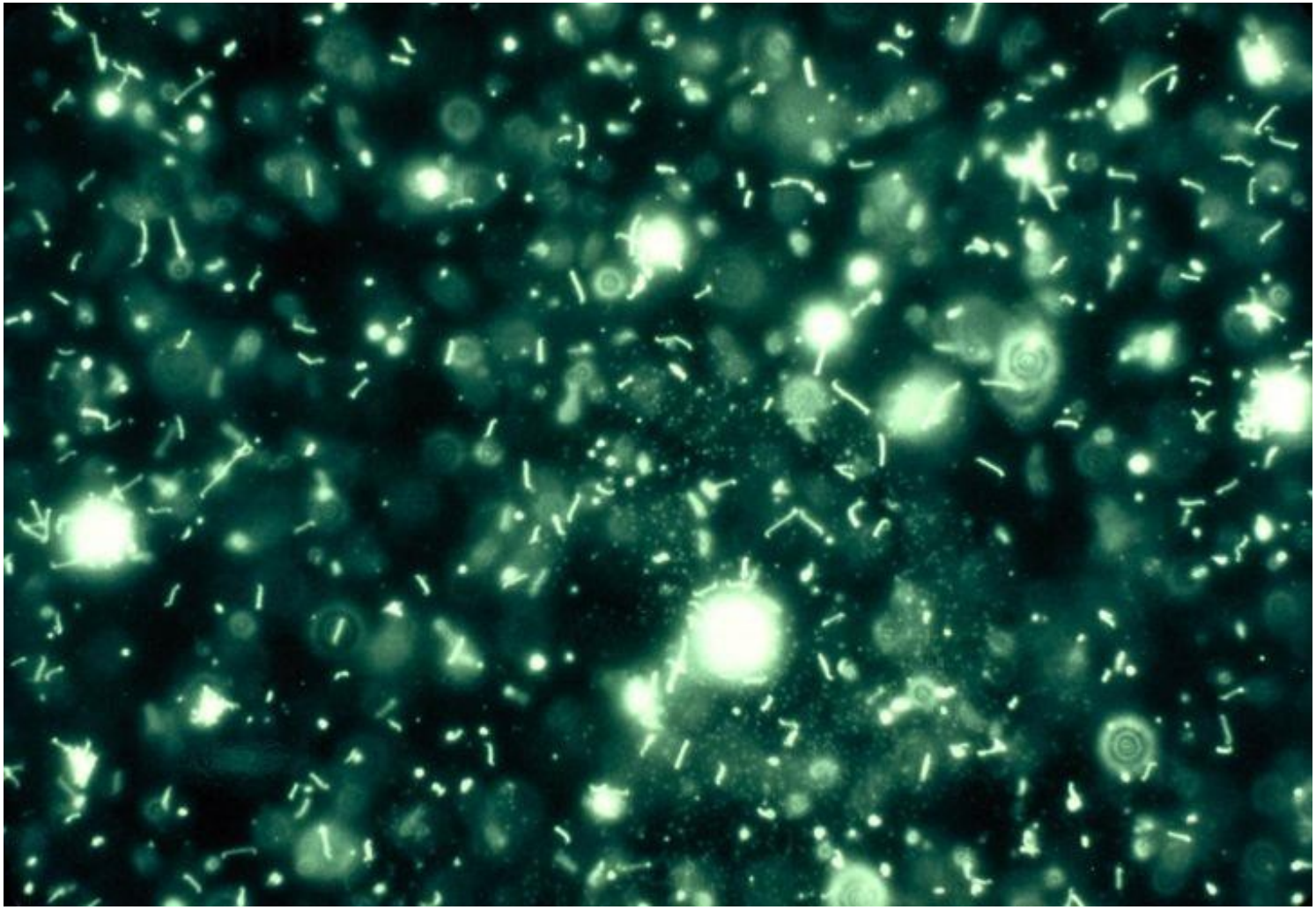
❑ Direct examination

Dark field microscope or contrast microscope



❑ Serodiagnostic

Microagglutination reaction.



❑ PCR (polymerase chain reaction)

Search for pathogenic leptospires (Leptospira interrogans sensu lato) by real-time PCR (real-time polymerase chain reaction) in blood, liver and kidneys, the fetus, etc. The following serovars are detected (non-exhaustive list): canicola, icterohaemorrhagiae, autumnalis, australis, grippotyphosa, etc.

Treatment

Often disappointing result.

- **Specific serum**

Abandoned due to being ineffective.

➢ Antibiotic therapy

The duration of hospitalization (at the beginning):

- Ampicillin-sulbactam (Unacim®): 20 to 30 mg/kg slow IV every 6-8 hours for 7 days.
- Penicillin G: 40000U/kg/3 times a day by IM or IV infusion.

Then a PO switch with:

- Doxycycline at a dose of 10 mg/kg every 24 hours for 14 days.
- Spiramycin: 15mg/kg/2 times a day orally.
- Tylosine: 5-10 mg/kg/2 times a day orally.

- **Symptomatic Treatments**

✓ **Support of renal function**

Infusion of solutions is necessary for the proper recovery of renal function when azotemia (AKI) is detected.

Placement of a permanent urinary catheter allowing quantification of diuresis.

The infusion rate will be adapted to that of diuresis (using an isotonic crystalloid solution such as Ringer's lactate or 0.9% NaCl).

- ✓ **Support of digestive function and nutritional support**

Anti-emetics, antacids, and digestive mucosal protectants are recommended in the presence of digestive signs.

The anti-emetics:

- Maropitant citrate: 1 mg/kg slow IV q24h.
- Metoclopramide: 0.3 to 0.5 mg/kg IV every 8 hours or 1 to 2 mg/kg/day in continuous infusion.

Antacids:

- Omeprazole: 0.7 to 1 mg/kg PO every 12 hours.
- Sucralfate can finally be used as a protector of the digestive mucosa (0.25 g/kg PO every 8 hours).

Nutritional support is an integral part of the medical management of dogs suffering from leptospirosis and should not be neglected:

- Enteral feeding.
- If the dog remains anorexic, it is strongly recommended to place a nasoesophageal or nasogastric refeeding tube.

✓ **Support for hemostatic function**

Tranexamic acid (Exacyl®) when bleeding is evident at a dose of 10 mg/kg by slow IV every 8 hours until disappearance of the bleeding.

In the presence of a coagulopathy such as disseminated intravascular coagulation, blood products may be used (fresh frozen plasma or whole blood).

✓ **Treatment of hepatopathy**

Leptospirosis-induced liver failure rarely manifests with severe liver failure with hepatic encephalopathy, hypoglycemic crises, or ascites.

The use of antioxidants and cholerectics has not been evaluated in dogs affected by leptospirosis.

- **Support for respiratory function**

Oxygen therapy.

Prophylaxis

Important given the danger to humans.

➢ Sanitary

- Avoid swimming or staying in contaminated ponds, lakes, or rivers.

- Encourage the extermination of rodents in kennels.

- Detect asymptomatic infected individuals and isolate them.
- Disinfect the premises (bleach).
- Collect and destroy the excretions of the sick

➢ Medical

- Inactivated vaccines:

L. canicola; L. icterohemorrhagiae.

- Primovaccination: 2 injections 15 days apart.
- Annual booster.

Guidelines for Vaccination of Individual Pet Dogs—cont'd

Vaccine	Initial Vaccination		Booster Schedule	Comments
	Age ≤ 16 Weeks	Age > 16 Weeks		
Leptospira (I, SC)	Two doses 3-4 weeks apart starting at 12 weeks of age	Two doses, 3-4 weeks apart	Annual. Revaccinate 1 month before the onset of the season if disease occurs seasonally.	*Noncore.* For dogs at risk of exposure. If available, a 4-serovar vaccine is preferred because protection is serovar-specific

A 4-serovar leptospirosis vaccine for dogs protects against four common strains: L. canicola, L. icterohaemorrhagiae, L. pomona, and L. grippotyphosa.

- **At-risk dog**

Hunting, for example.

Booster every 6