



A BRIEF FOR THE PRACTICING VETERINARIAN

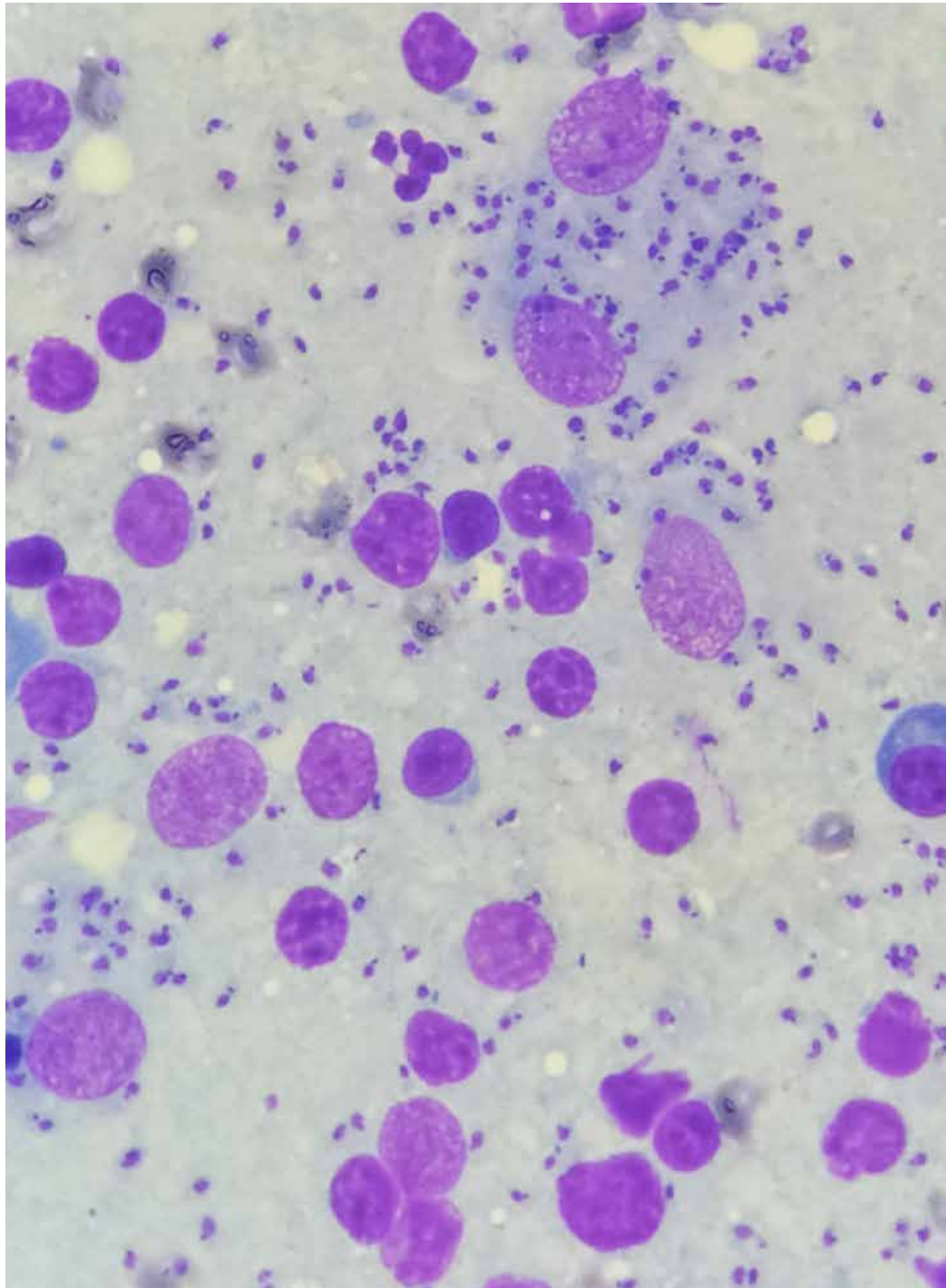
SPECIAL EDITION

**ALIVE 2**

Animal Leishmaniosis International Veterinary Event

**2024**

**CANINE LEISHMANIOSIS**



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*Leishmania infantum* amastigotes infecting macrophages from a popliteal lymphnode aspiration (Diff-Quick stain)  
(© Guadalupe Miró)





## ETIOLOGY AND EPIDEMIOLOGY (DISTRIBUTION, TRANSMISSION)

*Leishmania* infections in dogs are predominantly due to *Leishmania infantum*. However, other species of *Leishmania* may also infect dogs (most important species in dogs, their distribution and hosts are described in Table 1). Many species of *Leishmania* infect both humans and animals and are zoonotic.

The information in these guidelines is focused only on infection and disease due to *L. infantum*. This agent has a very wide distribution including the Mediterranean Basin, parts of Asia, and the Americas.

*Leishmania* spp. and more specifically *L. infantum* infection are typically transmitted by specific species of “insect vectors” belonging to the phlebotomine group (also called “sand flies”). These vectors represent the major route of transmission in endemic areas. The presence and activity of sand flies belonging to species competent for transmission defines the places where the infection or disease can be “endemic” in human and animal populations, including domestic dogs.

The vectors may transmit *Leishmania* infection to animals species other than human or dogs and a continuously increasing number and diversity of mammal species have been reported as infected including domestic (i.e. cat) or wildlife (i.e. rodents) both in rural and sylvatic environments or captive in zoos. At least some of these species are also active reservoirs with ability to be a source of infection for sand flies and consequently drive transmission of the infection to other receptive species. This results in a situation in which infected domestic dogs may represent, amongst others, a risk for human infection.

Non-vectorial transmission routes have also been demonstrated (sexual, vertical and blood transfusion). These modalities are far from being negligible and have been demonstrated in dogs. The non-vectorial transmission modalities may have a major impact in “non-endemic areas” where vectors are absent or present in very small numbers. In those areas, *Leishmania* infection may maintain mainly in and from stable foci. Non-vectorial transmission considerably extends the global distribution of the parasite and the potential concern for veterinary practitioners. As a consequence, the importation of infected animals from endemic areas may be the reason for the development of disease foci in non-endemic areas.



Female *Phlebotomus perniciosus* feeding on the muzzle of a dog (average size 3 mm)

(© Guadalupe Miró)

Table 1. The most significant species of *Leishmania* known to affect domestic dogs

Species Genus	Distribution	Hosts	Zoonotic aspects
<i>L. infantum</i>	Mediterranean Basin Middle East, South America (Brazil), parts of Asia (China, Central Asian Republics) Increasing in non-endemic countries (Europe, USA, South and Central America from Mexico to north Argentina)	Many groups of mammals found infected when looked: canids, felids, mustelids, rodents, rabbits and hares, bats, marsupials, humans, etc.	Visceral, cutaneous and mucocutaneous leishmaniosis
<i>L. major</i>	Southern Mediterranean Basin, Middle East, Arabic peninsula, central Asia to India, western/eastern Sub-Saharan Africa	Mostly wild rodents, occasional in carnivores, humans	Various forms of cutaneous leishmaniosis
<i>L. tropica</i>	North Africa, Balkan countries, Middle- East to central Asia, eastern Africa and Arabic peninsula	Humans (“anthroponotic”), rodents (hyrax in Middle East)	
<i>L. braziliensis</i>	Central and South America	Rodents, equidae, carnivores, humans	Cutaneous and mucocutaneous leishmaniosis

Several other species have been detected in dogs with still limited information on their importance (*L. amazonensis*, *L. mexicana*, *L. peruviana*, *L. panamensis*). Concerning South American species, please visit Brasileish’s group website ([www.brasileish.com.br](http://www.brasileish.com.br)).

*Leishmania donovani* infection in India and east Africa is typically anthroponotic (the disease is also called Kala Azar). The role of animals in *L. donovani* infection remains to be investigated.

Infection in the canine population in endemic areas is widespread, and the proportion of infected dogs is much higher than that of dogs with clinical leishmaniosis. Therefore, subclinical infection is common in endemic areas (clinically healthy infected dogs). Nevertheless, CanL is also often diagnosed in non-endemic countries (dogs imported from or travelling to endemic areas).

Susceptibility is related to the ability of the host to mount a protective specific immunity. A strong cellular immunity results in long term control of infection in resistant dogs. On the contrary, the development of an intense humoral response drives non-protective immunity which in return is largely responsible for clinicopathological disorders and clinical signs in susceptible dogs.





## CLINICAL MANIFESTATIONS

Table 2. Main clinical signs and clinicopathological abnormalities found in CanL due to *L. infantum*

### MAIN CLINICAL SIGNS

#### General

- ▶ Localized or generalized lymphadenomegaly
- ▶ Loss of body weight
- ▶ Decreased appetite
- ▶ Lethargy
- ▶ Pale mucous membranes
- ▶ Splenomegaly
- ▶ Polyuria and polydipsia
- ▶ Fever
- ▶ Vomiting
- ▶ Diarrhea

#### Cutaneous

- ▶ Exfoliative dermatitis with or without alopecia
- ▶ Erosive-ulcerative dermatitis
- ▶ Nodular dermatitis
- ▶ Papular dermatitis
- ▶ Pustular dermatitis
- ▶ Nails abnormalities

#### Ocular

- ▶ Blepharitis (exfoliative, ulcerative or nodular) and conjunctivitis (nodular)
- ▶ Keratoconjunctivitis, either common or sicca
- ▶ Anterior uveitis
- ▶ Endophtalmitis

#### Other

- ▶ Mucocutaneous and mucosal ulcerative or nodular lesions (oral, genital and nasal)
- ▶ Epistaxis
- ▶ Lameness (erosive or non-erosive polyarthritis, osteomyelitis and polymyositis)
- ▶ Atrophic masticatory myositis
- ▶ Vascular disorders (systemic vasculitis and arterial thromboembolism)
- ▶ Neurological disorders

### CLINICOPATHOLOGICAL ABNORMALITIES

#### CBC/Hemostasis

- ▶ Mild to moderate normocytic normochromic non-regenerative anemia
- ▶ Leukocytosis or leukopenia: lymphopenia, neutrophilia, neutropenia
- ▶ Thrombocytopenia
- ▶ Thrombocytopenia
- ▶ Impaired secondary hemostasis and fibrinolysis

#### Serum biochemical profile with proteins electrophoresis

- ▶ Hyperproteinemia
- ▶ Hyperglobulinemia (polyclonal beta and/or gammaglobulinemia)
- ▶ Hypoalbuminemia
- ▶ Decreased albumin/globulin ratio
- ▶ Renal azotemia
- ▶ Elevated liver enzyme activities
- ▶ Proteinuria

CBC: Complete blood count



Weight loss



Ulcerated papules (crater-shaped) on the dorsal part of the nose



Ulcerated nodule on one digit



Circular, large foot-pad ulcer



Uveitis, glaucoma, nasal hyperkeratosis and amyotrophy



Ulcerative dermatitis on the inner pinnae



Vasculitis



Facial exfoliative dermatitis



Nasal ulcerative dermatitis



Nasal hyperkeratosis

Pictures: © Guadalupe Miró, Gaetano Oliva and Laura Ordeix





## DIAGNOSIS

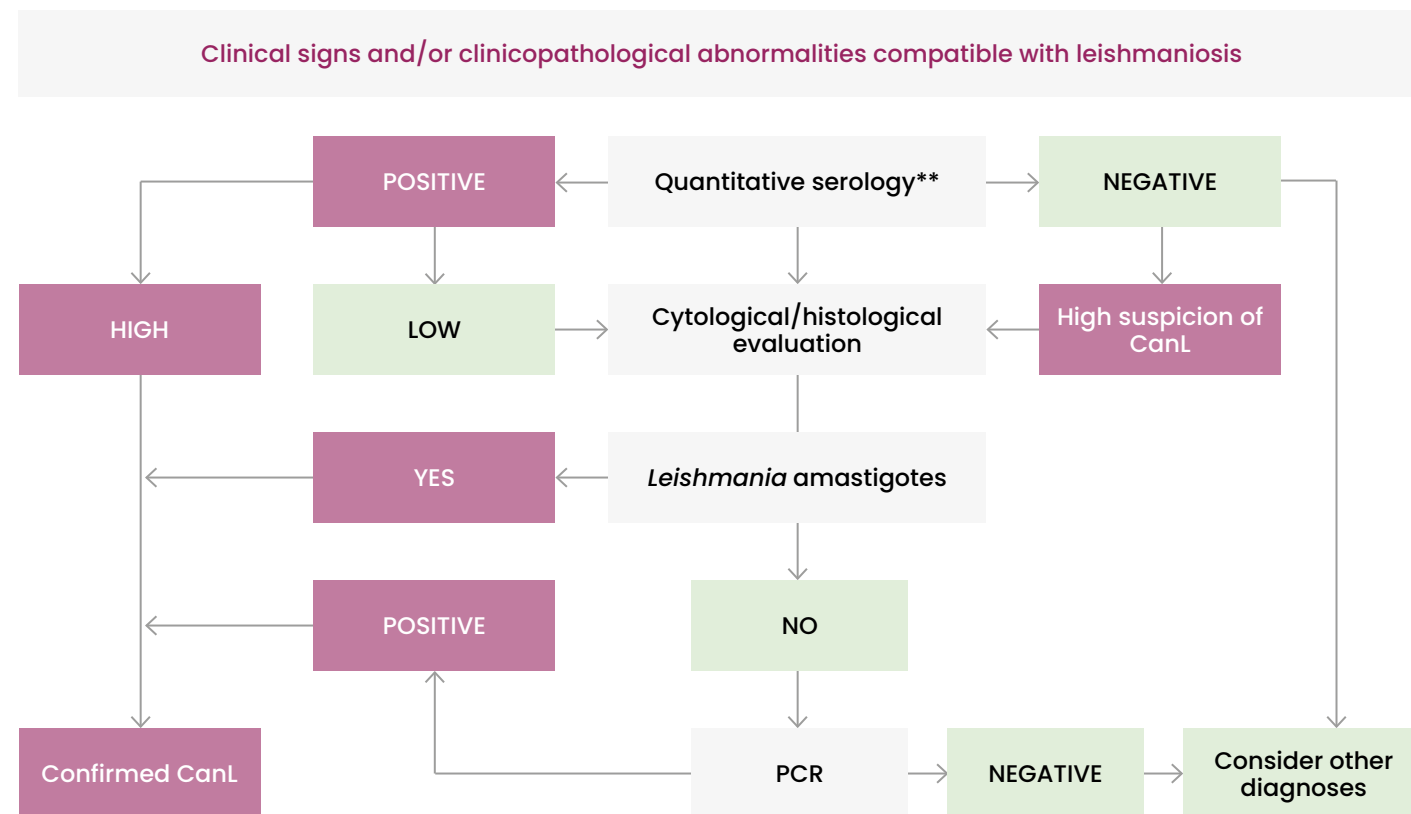
Diagnosis is based on clinical signs and/or clinicopathological abnormalities compatible with disease combined with demonstration of *L. infantum* infection, by using serological and/or molecular techniques. However, cytology and histology combined with immunohistochemistry can be used to directly correlate *Leishmania* infection with the disease.

### Main purposes for the diagnosis of *L. infantum* infection:

- Confirm the disease in a dog with clinical signs and/or clinicopathological abnormalities compatible with leishmaniosis (Table 2 and Figure 1).
- Screening of apparently healthy dogs living in or travelling from endemic areas:
  - blood donors
  - breeding dogs
  - dogs prior to vaccination against CanL
  - dogs admitted for the annual serological test for CanL
  - imported dogs (from endemic areas)

## Diagnostic approach

**Figure 1.** Flow chart for the diagnostic approach to dogs with suspected clinical signs and/or clinicopathological abnormalities compatible with leishmaniosis\*



CanL: Canine leishmaniosis – PCR: Polymerase chain reaction

\* This flow chart cannot be applied in case of recent vaccination against CanL with a vaccine known to induce cross reacting antibodies.

\*\* Cytology could be performed at the same time in any damaged tissue or biological fluid.

## Infected healthy versus infected sick dog

- ▶ Dogs with clinical leishmaniosis are those presenting compatible clinical signs and/or clinicopathological abnormalities, and having a confirmed *L. infantum* infection. It should be emphasized that a dog may be sick due to another disease with similar clinical signs and simultaneously infected by *L. infantum*. Exclusion of other differential diagnoses is recommended in infected sick dogs.
- ▶ Dogs with subclinical infection (infected but clinically healthy) are those that do not present neither clinical signs on physical examination nor clinicopathological abnormalities on routine laboratory tests (CBC, biochemical profile and urinalysis) but have a confirmed *L. infantum* infection.

## Diagnostic methods

- ▶ Parasitological: cytology, histology/immunohistochemistry and culture.
- ▶ Molecular: conventional, nested and real-time polymerase chain reaction (PCR).
- ▶ Serological: quantitative assays (IFAT and ELISA) and qualitative preliminary rapid tests.

## What samples and techniques should be used for PCR?

- ▶ Any lesional tissue or abnormal biological fluid compatible with *L. infantum* infection.
- ▶ Target organs: bone marrow, lymph node, spleen, skin.
- ▶ Less invasive samples: conjunctival swabs.
- ▶ The sensitivity of the PCR assay is much lower when performed on these samples: blood and urine.



Lymphadenomegaly  
(© Guadalupe Miró)



## CLINICAL STAGING, TREATMENT AND PROGNOSIS

Table 3. Clinical staging in CanL

	CLINICAL SIGNS	LABORATORY FINDINGS*	QUANTITATIVE SEROLOGY**	SPECIFIC THERAPY	PROGNOSIS
<b>STAGE I</b> Mild disease	Mild clinical signs such as example papular dermatitis or localized lymphadenomegaly.	No clinicopathological abnormalities observed. Normal renal profile: creatinine < 1.4 mg/dL, non-proteinuric: UPC < 0.5	Negative to low positive antibody levels.	Scientific neglected***	Usually good
<b>STAGE II</b> Moderate disease	Diffuse or symmetrical cutaneous and/or mucocutaneous lesions such as example exfoliative, ulcerative or nodular dermatitis, onychogryphosis, generalized lymphadenomegaly, loss of appetite and weight loss.	Clinicopathological abnormalities compatible with <i>L. infantum</i> infection such as example mild non-regenerative anemia, hypergammaglobulinemia and hypoalbuminemia. <b>Substage</b> a) Normal renal profile: Creatinine < 1.4 mg/dl; non-proteinuric: UPC < 0.5 b) Creatinine < 1.4 mg/dl; proteinuric (UPC= 0.5-1)	Low to high positive antibody levels.	Meglumine antimoniate + allopurinol Miltefosine + allopurinol <b>Substage b:</b> Follow IRIS Guidelines (†) for CKD	Good to guarded
<b>STAGE III</b> Severe disease	Dogs, which apart from the signs listed in stages I and II, may present signs originating due to immune-complex deposition (e.g. glomerulonephritis, uveitis).	Clinicopathological abnormalities listed in Stage II.  CKD IRIS stage 1 with proteinuria UPC > 1 or CKD IRIS stage 2 (creatinine 1.4-2.8 mg/dl)	Usually high positive antibody levels.	Meglumine antimoniate + allopurinol Miltefosine + allopurinol Follow IRIS Guidelines (†) for CKD	Guarded to poor
<b>STAGE IV</b> Very severe disease	Dogs with clinical signs listed in Stage III. Pulmonary thromboembolism, or nephrotic syndrome and end stage renal disease.	Clinicopathological abnormalities listed in stages II and III.  CKD IRIS stage 3 (creatinine 2.9-5 mg/dl) and CKD IRIS stage 4 (creatinine > 5 mg/dl) or nephrotic syndrome or marked proteinuria UPC > 5	Usually high positive antibody levels.	Specific treatment should be instituted individually. Follow IRIS Guidelines (†) for CKD	Poor

CKD: Chronic kidney disease - IRIS: International Renal Interest Society - UPC: Urinary protein:creatinine ratio

\* Full CBC, biochemical profile with serum protein electrophoresis and urinalysis with UPC.

(†) IRIS recommendations must be strictly followed in stages III and IV (<http://www.iris-kidney.com/>)

Staging is performed following canine patient diagnosis of *L. infantum* infection with clinical signs and/or clinicopathologic abnormalities to facilitate appropriate treatment and monitoring of the patient). Infected but clinically healthy dogs are not included in this staging (see below).

\*\* Infection should be confirmed via other diagnostic techniques such as cytology, histology/immunohistochemistry and PCR in dogs with negative to low positive antibody levels. High antibody levels, are conclusive of CanL.

\*\*\* Dogs in stage I (mild disease) are likely to require short treatment with one (meglumine antimoniate, miltefosine, allopurinol) or two conventional anti-*Leishmania* drugs (combination of meglumine antimoniate with allopurinol or miltefosine with allopurinol). Immune-potentiating treatments in conjunction with antileishmanial drugs or alone may be considered (domperidone, nucleotides plus AHCC). Alternatively, consider monitoring without treatment. There is limited evidence of treatment outcomes for dogs in this stage and, therefore, efficacy of these treatment options remains inconclusive.



## THERAPY

Table 4. Current treatment protocols for CanL

Drugs	Dose	Main side effects
Meglumine antimoniate <sup>A</sup>	100 mg/kg SC*, once a day or divided in two doses, for 4–6 weeks (initial reduced dosages for 2–3 days may be useful to detect any adverse events) <sup>B</sup>	<ul style="list-style-type: none"> <li>▶ Potential nephrotoxicity</li> <li>▶ Pain and inflammation at injection site</li> </ul>
Miltefosine <sup>A</sup>	2–2.5 mg/kg PO, once a day for 28 days**	<ul style="list-style-type: none"> <li>▶ Disorexia</li> <li>▶ Vomiting</li> <li>▶ Diarrhea</li> </ul>
Allopurinol	10mg/kg PO, twice a day for 6–12 months (depending on the staging and the side effects***)	<ul style="list-style-type: none"> <li>▶ Xanthine urolithiasis</li> <li>▶ Renal mineralization</li> <li>▶ Nephrolithiasis</li> </ul>
Domperidone <sup>C</sup>	0.5 mg/kg PO, once a day for 1 month and following manufacturer instructions	<ul style="list-style-type: none"> <li>▶ Galactorrhea</li> </ul>
Dietary nucleotides with AHCC <sup>C-D</sup>	Once a day, PO. Following manufacturer instructions, for 6–12 months	

- A. Registered for veterinary use in most European countries; both therapies are recommended in combination with allopurinol.
- B. There is a limited number of studies on optimal treatment regimen. Recommended dosages off-label but according to pharmacokinetic and clinical studies in dogs. Treatment may be extended by 2–3 weeks in patients stages II and III (without CKD) and with severe clinical picture or laboratory abnormalities.
- C. To be considered as monotherapy only for stage I.
- D. To be considered, as an alternative to allopurinol, in dogs with xanthinuria due to allopurinol side effects.

AHCC: Active hexose correlated compound – PO: Per os – SC: Subcutaneous

\* Injections should be administered in different skin sites.

\*\* To reduce side effect administered always with food.

\*\*\* Monitoring side effects with urinalysis and abdominal ultrasound is recommended periodically.

**Disclaimer:** Information given here on drugs and dosages are based on a consensus of clinical and scientific experience by the LeishVet members. Most recommendations have been published in scientific peer-reviewed journals. Veterinary practitioners are requested to check with product leaflets and product registrations in their related country prior to any product selection and initiation of treatment.

## MONITORING

Table 5. Recommended monitoring during and after treatment of CanL

Parameters	Frequency	
	Sick treated dogs	Clinically healthy infected dogs
<ul style="list-style-type: none"> <li>▶ Clinical history and physical examination</li> <li>▶ CBC, biochemical profile ± serum electrophoresis</li> <li>▶ Complete urinalysis ±UPC</li> </ul>	<p>After the first month of treatment and then every 3–4 months during the first year.</p> <p>Thereafter, every 6–12 months in dogs fully recovered clinically with treatment.</p>	<p>Every 3–6 months (see figure 2)</p>
<ul style="list-style-type: none"> <li>▶ Quantitative serology*</li> </ul>	<p>Not before 3 months after initial treatment and every 6–12 months.</p>	
<ul style="list-style-type: none"> <li>▶ Real-time PCR (optional)**</li> </ul>	<p>At the same time as serology.</p>	

\* Some dogs have a decrease in antibody levels (i.e. on IFAT results at least a 2–3 fold dilutions difference between monitoring samples) associated with clinical improvement within 6–12 months of therapy. An increase in antibody levels (i.e. at least 2–3 fold dilutions difference between monitoring samples) should be interpreted as a marker of disease relapse, especially following the discontinuation of treatment.

\*\* Sensitivity of PCR assays relies considerably on the type and number of tissues evaluated. Bone marrow, lymph node, spleen, and cutaneous lesions are better targets for *Leishmania* detection than whole blood. Testing two to three samples of different tissues are recommended for a more accurate diagnosis.

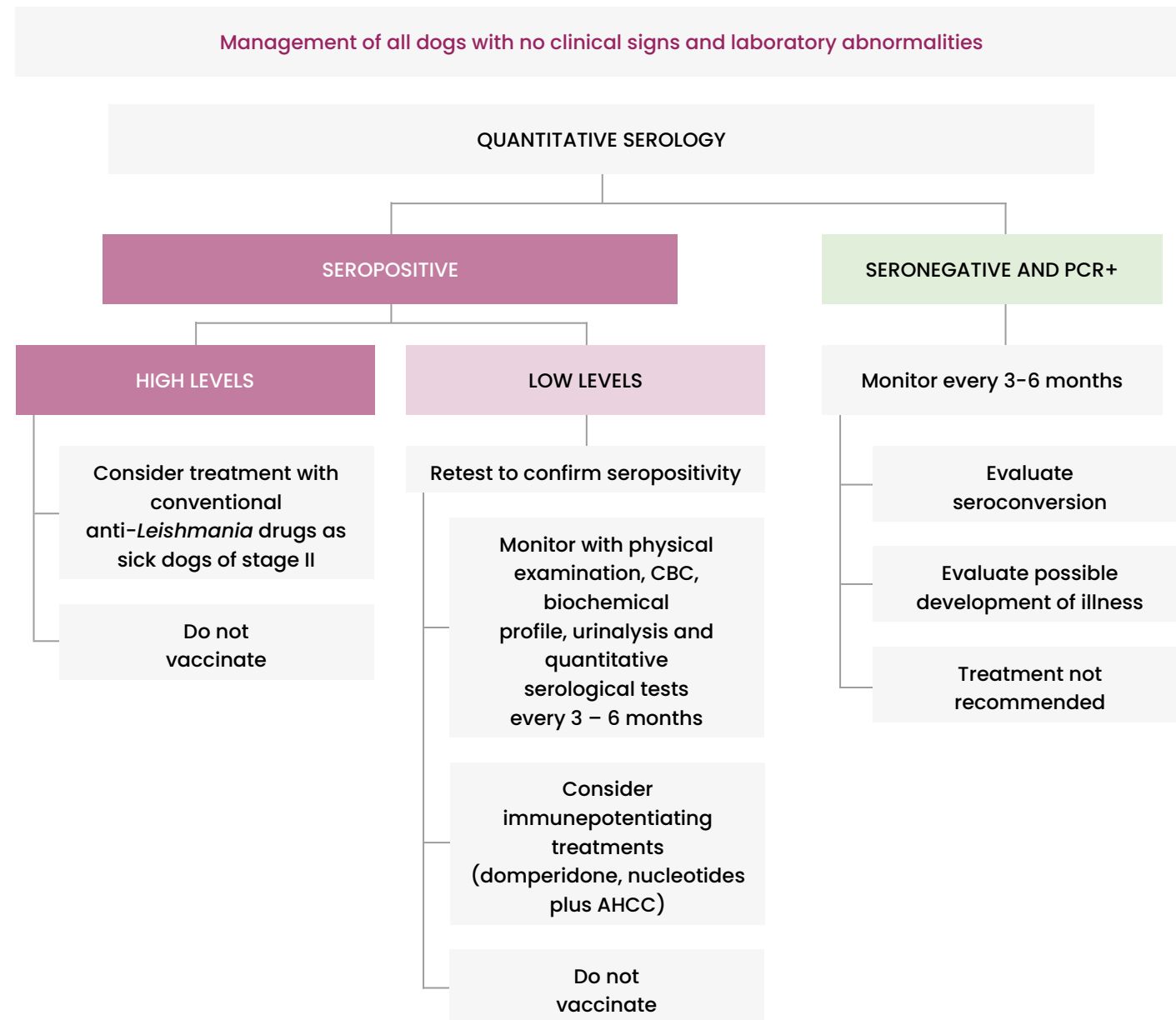


Periorbital alopecia and scaling before and after treatment (© Guadalupe Miró)





Figure 2. Management of unvaccinated infected, but apparently healthy dogs



It is recommended to use serology alone or the combination of serology with PCR for screening healthy dogs and to avoid screening clinically healthy dogs (not vaccinated) only by PCR.

## PREVENTION

Prevention for individual dogs (healthy, infected clinically healthy and sick) should always include use of a topical insecticide with proven efficacy maintained throughout the period of sand flies activity. Additionally, vaccination should be considered as a part of a multimodal approach\*.

Only insecticides that have been approved by the formal approval body should be used for the prevention of CanL.

**Topical insecticides applied to dogs living in or travelling to endemic areas should be maintained during the entire period of potential exposure to sand flies:**

### A. Spot on formulations

Treatment with permethrin spot-on formulations may provide a repellent (anti-feeding) activity against sand flies for 3-4 weeks. In the case of dogs travelling to endemic areas, the product should be applied at least 2 days before exposure.

### B. Collars

Collars impregnated with deltamethrin prevent phlebotomine sand fly bites for varying periods depending on the manufacturer, even up to 12 months for one of the products.

A flumethrin in combination with imidacloprid-containing collar, with proven repellent efficacy against sand flies, has shown in clinical field studies a reduction of the risk of infection with *L. infantum* transmitted by sand flies for up to 8 months.

All the collars should be applied at least 1-2 weeks before exposure.

\*Based on a risk-benefit assessment from endemic areas, a **multimodal approach** combining repellent use and vaccination should be considered for optimal prevention of both infection and development of clinical disease. Repellents highly reduce the risk of infection but do not prevent the appearance of clinical signs once the dog has been infected. Vaccination reduces the risk that infection would progress to disease and the probability of clinical signs developing, but it does not prevent infection.







Table 6. Preventative recommendations based on different level of risk for *L. infantum* infection

NON ENDEMIC AREAS	Level of risk (0 low - 4)	Travel history	Lifestyle	Preventative applications	Additional recommendations
	0	Local (negligible)	Any	None	Avoid breeding with or blood transfusion from dogs belonging to risk levels 3-4 and any PCR positive or seropositive dogs (and 1-2, if possible)
	1	Occasional travel to fringe or endemic areas	Any	Repellents: Cover the entire period of travelling /exposure including the delay for activity	See risk level 0 If travel once for less than 3 weeks, use topical insecticide spot-on formulations applied at least 2 days before exposure. For longer periods of travel, use repeated spot-on or collars. Test for <i>L. infantum</i> infection 6 months after travel (by quantitative serology only)
	2	Frequent/ long travel to fringe or endemic areas	Any	Repellents: Cover the period of travel including the delay for repellent activity Vaccination (optional)	See risk level 0 For long and/or frequent trips preventative and additional recommendations should be the same as for risk level 4 Test for <i>L. infantum</i> infection 6 months after last exposure (by quantitative serology). Domperidone/Nucleotides + AHCC could be considered (if not vaccinated)
	3	Re-homing from an endemic area	Any	See additional recommendations	Test for <i>L. infantum</i> infection via quantitative serology. If positive, do not breed and do not use as blood donor, consider treatment (see staging) Repellents all year round Testing of other household dogs
ENDEMIC AREAS	Serology Results (IFAT/ELISA)	Lifestyle	Preventative applications	Additional recommendations	
	Seronegative	Outdoors (high exposure)	Repellents all year round or during the known sand fly transmission season. Vaccination (strongly recommended)	Domperidone/Nucleotides + AHCC could be considered (if not vaccinated) Periodic testing (by quantitative serology) if breeding or blood donor (at least once a year)	
		Indoors (low exposure)	Repellents all year round or during the known sand fly transmission season. Vaccination (optional)	Periodic testing if breeding or blood donor Domperidone could be considered (if not vaccinated)	
	Non applicable	Seropositive (Healthy*/ Sick**)	Any	Repellents all year round	Do not use for breeding or as blood donor Staging for treatment as needed Test other household dogs

ELISA: Enzyme-linked immunosorbent assay - IFAT: Indirect Fluorescent Antibody Technique

\*Healthy: a dog without any clinical sign or clinicopathological abnormality

\*\*Sick: a dog with clinical signs and/or clinicopathological abnormalities attributed to *Leishmania*

## VACCINES

Two vaccines which were initially commercialized are not available anymore. The first one was launched in Brazil and was based on a fucose-mannose ligand enriched with glycoprotein 63 with a saponin adjuvant and the second one, the first launched in Europe, was based on purified excreted/secreted antigens of *L. infantum* combined to a saponin-like adjuvant.

The only currently available vaccine in Europe contains the active substance "protein Q", a recombinant protein containing five different antigens from *L. infantum* without an additional adjuvant. First vaccination is a single injection. Booster injections are given annually.

The vaccine available in Europe can only be injected to healthy seronegative dogs, 6 months of age or older, tested by a quantitative serological assay.

A new DNA vaccine based on the non-replicative antibiotic resistance marker-free plasmid vector pPAL which contains an encoding gene for the *L. infantum* activated protein kinase C receptor analogue (LACK) has been approved by the European Medicines Agency in 2023. This vaccine can only be administered via intranasal, to healthy dogs of 6 months of age or older.

All of these vaccines do not prevent infection but do alter disease progression and the probability of progression to clinically overt disease.

Table 7. Current anti-*Leishmania* vaccines for dogs

Commercial name (manufacturer)	Composition		Availability	Vaccine protocol	Primary outcome	Vaccine efficacy	Diagnostic interference associated with vaccine
	Antigen	Adjuvant					
Leish-Tec® (Ceva Santé Animale)*	A2	Saponin	Brazil	Three primary vaccination doses (SC), 21-day intervals; one annual booster	Parasite detection	71.4%	Yes
Letifend® (Leti Pharma laboratories)	Q-protein	None	Europe	One primary vaccination dose (SC); one annual booster	Clinical disease	72%	No
Neoleish® (CZ Vaccines S.A.U.)	DNA plasmid containing LACK gene	None	Spain	One primary vaccination dose (intranasal); one booster every 6 months	Clinical disease	-	No

\* Currently not available.



## ABOUT THE LEISHVET GROUP

**LeishVet** is a group of veterinary scientists from academic institutes in the Mediterranean Basin and North America with a primary clinical and scientific interest in canine and feline leishmaniosis. Its main goal is to improve the knowledge on different aspects of leishmaniosis in veterinary medicine and public health, including the development of consensus recommendations based on recent evidence-based literature and clinical experience that would represent the most current understanding of *Leishmania* infection in dogs, cats and other animals.

## LEISHVET MEMBERS

Gad Baneth	Hebrew University of Jerusalem, Rehovot, Israel.
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## LINKS OF INTEREST

- ▶ [www.leishvet-alive.com](http://www.leishvet-alive.com)
- ▶ [www.iris-kidney.com/guidelines/](http://www.iris-kidney.com/guidelines/)
- ▶ [www.esccap.org](http://www.esccap.org)
- ▶ [www.brasileish.com.br](http://www.brasileish.com.br)

## LIST OF ABBREVIATIONS

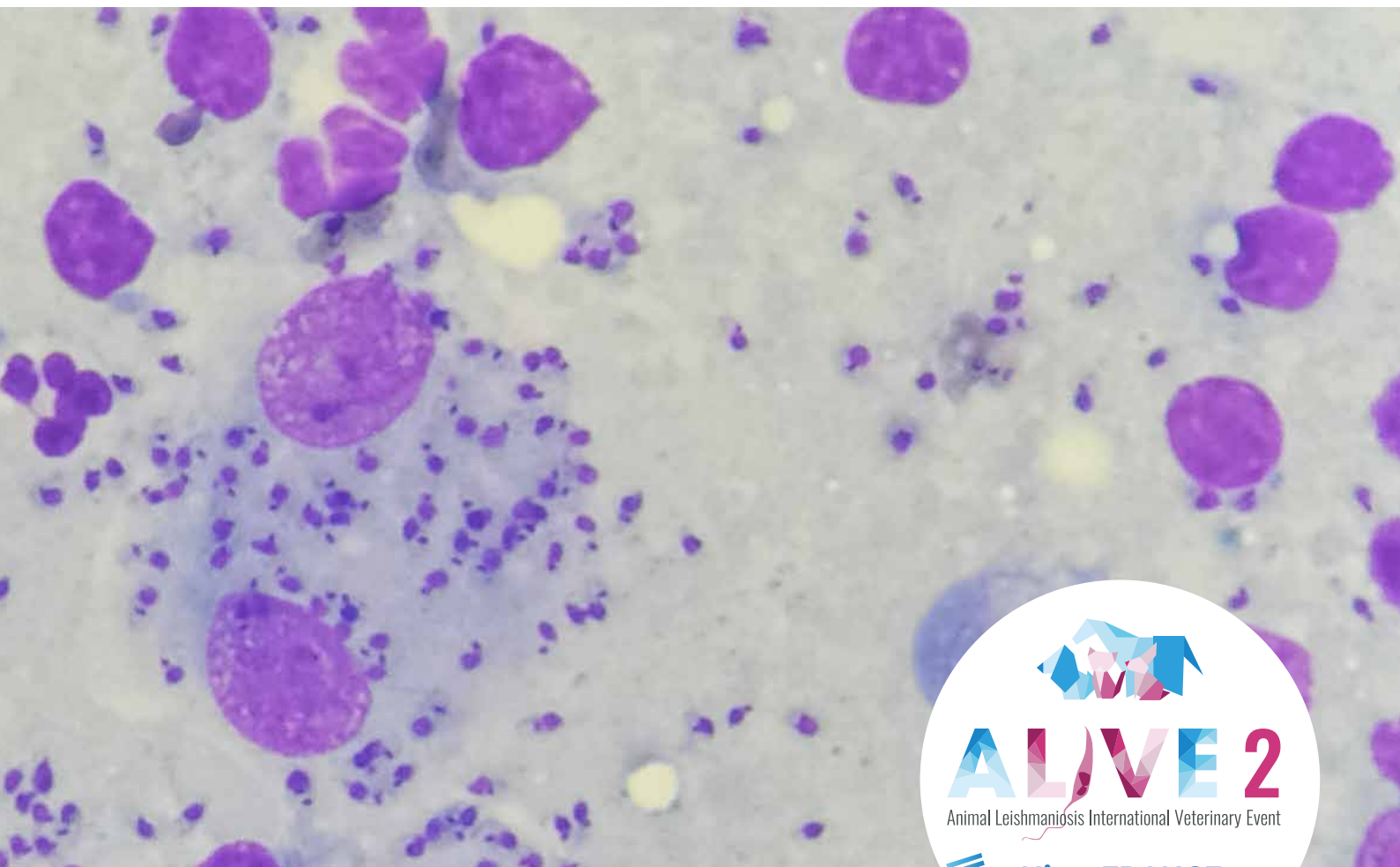
<b>AHCC</b>	Active hexose correlated compound
<b>CanL</b>	Canine leishmaniosis
<b>CBC</b>	Complete blood count
<b>CKD</b>	Chronic kidney disease
<b>ELISA</b>	Enzyme-linked immunosorbent assay
<b>IFAT</b>	Indirect Fluorescent Antibody Technique
<b>IRIS</b>	International Renal Interest Society
<b>PCR</b>	Polymerase chain reaction
<b>PO</b>	Per os
<b>SC</b>	Subcutaneous
<b>UPC</b>	Urinary protein:creatinine ratio



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