



MAILING ADDRESS

LeishVet
Veterinary Faculty
Universidad Complutense de Madrid
Av. Puerta de Hierro s/n
28040 Madrid, Spain

SPONSORSHIP



CANINE AND FELINE LEISHMANIOSIS

E-mail: leishvet@ucm.es
Web page: www.leishvet.org

4th Edition February 2018

A BRIEF FOR
THE PRACTICING
VETERINARIAN





CONTENT

| | |
|--|-----------|
| CANINE LEISHMANIOSIS (CanL) | |
| ETIOLOGY, DISTRIBUTION AND TRANSMISSION | 3 |
| CLINICAL MANIFESTATIONS | 4 |
| DIAGNOSIS | 6 |
| CLINICAL STAGING | 8 |
| THERAPY | 10 |
| MONITORING | 11 |
| PREVENTION | 13 |
| VACCINES | 15 |
| FELINE LEISHMANIOSIS (FeL) | |
| ETIOLOGY AND TRANSMISSION | 16 |
| GEOGRAPHIC DISTRIBUTION AND RISK FACTORS | 16 |
| CLINICAL PRESENTATION | 18 |
| DIAGNOSIS | 20 |
| THERAPY | 21 |
| MONITORING AND PROGNOSIS | 22 |
| PREVENTION | 23 |
| KEY POINTS | 24 |
| ABOUT LEISHVET | 25 |
| LEISHVET MEMBERS | 26 |
| REFERENCES | 27 |

ETIOLOGY, DISTRIBUTION AND TRANSMISSION

Canine *Leishmania* infections are due to a widely distributed species, *Leishmania Infantum*. However, in the new world and in the old world, other zoonotic species of *Leishmania* may infect dogs.

The information in these guidelines is related to infection and disease due to *L. infantum*.

Leishmania infantum infection is typically transmitted by a specific group of phlebotomine vectors (sand flies) which represent the main risk of transmission.

However, non vectorial modalities have also been demonstrated (venereal, vertical, dog to dog, blood transfusion.)



CANINE LEISHMANIOSIS CLINICAL MANIFESTATIONS

Table 1. Clinical manifestations and laboratory abnormalities found in CanL due to *L. infantum*.

CLINICAL MANIFESTATIONS

General

- ⊕ Generalized lymphadenomegaly
- ⊕ Loss of body weight
- ⊕ Decreased or increased appetite
- ⊕ Lethargy
- ⊕ Mucous membranes pallor
- ⊕ Splenomegaly
- ⊕ Polyuria and polydipsia
- ⊕ Fever
- ⊕ Vomiting
- ⊕ Diarrhea

Cutaneous

- ⊕ Non-pruritic exfoliative dermatitis with or without alopecia
- ⊕ Erosive-ulcerative dermatitis
- ⊕ Nodular dermatitis
- ⊕ Papular dermatitis
- ⊕ Pustular dermatitis
- ⊕ Onychogryphosis

Ocular

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

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

LABORATORY ABNORMALITIES

CBC*/Hemostasis

- ⊕ Mild to moderate non-regenerative anemia
- ⊕ Leukocytosis or leukopenia: lymphopenia, neutrophilia, neutropenia
- ⊕ 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



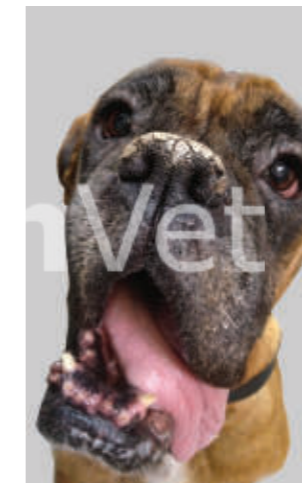
Ulcerocrusted papulo-nodular dermatitis ("inoculation sore")



Periorbital alopecia and exfoliative facial dermatitis



Periorbital alopecia and nasal hyperkeratosis



Vasculitis



Exfoliative dermatitis



Mucocutaneous ulcerative lesions



Vasculitis



Keratouveitis

Pictures: © Guadalupe Miró



DIAGNOSIS

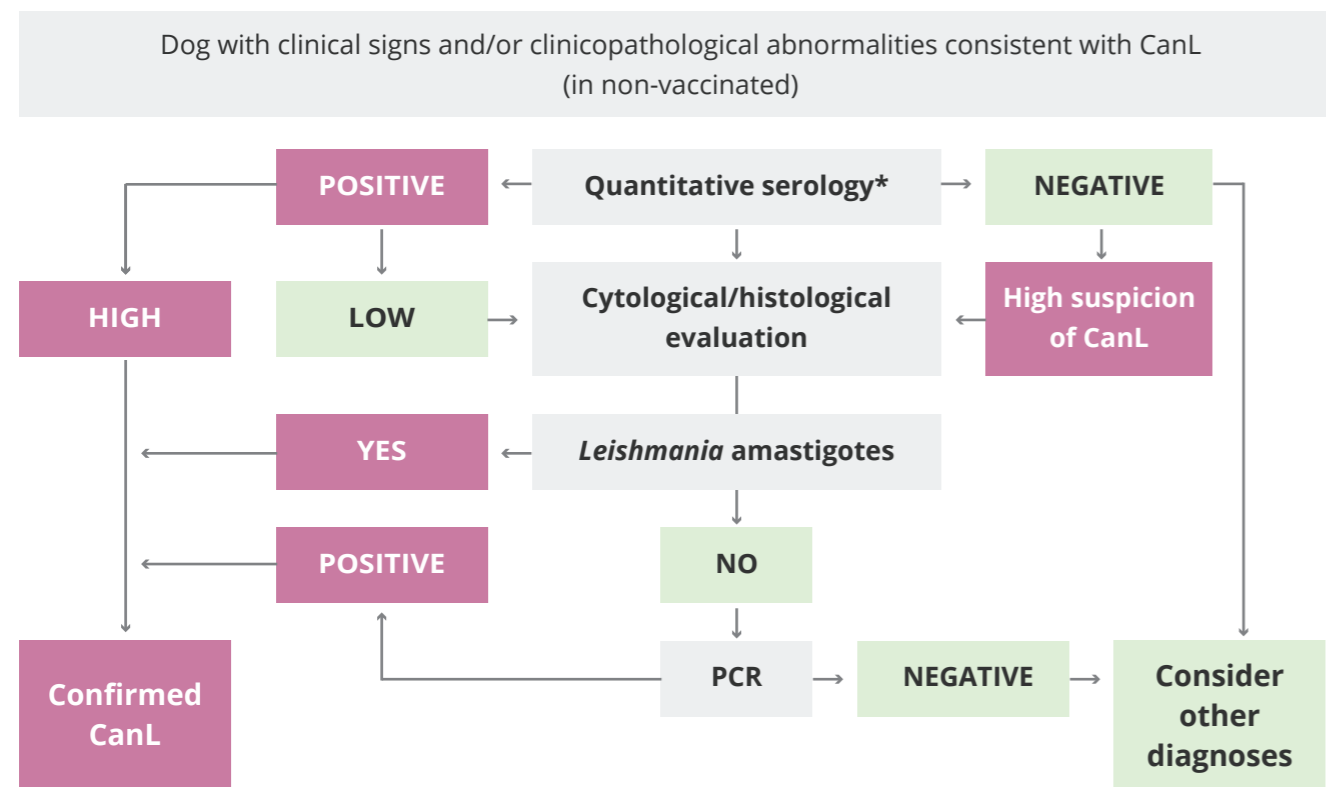
Diagnosis is based on clinical signs and/or clinicopathological abnormalities compatible with disease and by confirmation of *Leishmania infantum* infection, using mainly serological and molecular techniques.

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

- A** Confirm the disease in a dog with clinical signs and/or clinicopathological abnormalities consistent with CanL (Table 1 and Figure 1).
- B** Screening clinically healthy dogs living in or travelling to or from endemic areas:
 - a** blood donors
 - b** breeding dogs
 - c** dogs prior to leishmaniosis vaccination
 - d** imported dogs

DIAGNOSTIC APPROACH

Figure 1. Flow chart for the diagnostic approach to dogs not vaccinated against canine leishmaniosis (CanL) with suspected clinical signs and/or clinicopathological abnormalities consistent with CanL



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

Infected but healthy *versus* sick dogs

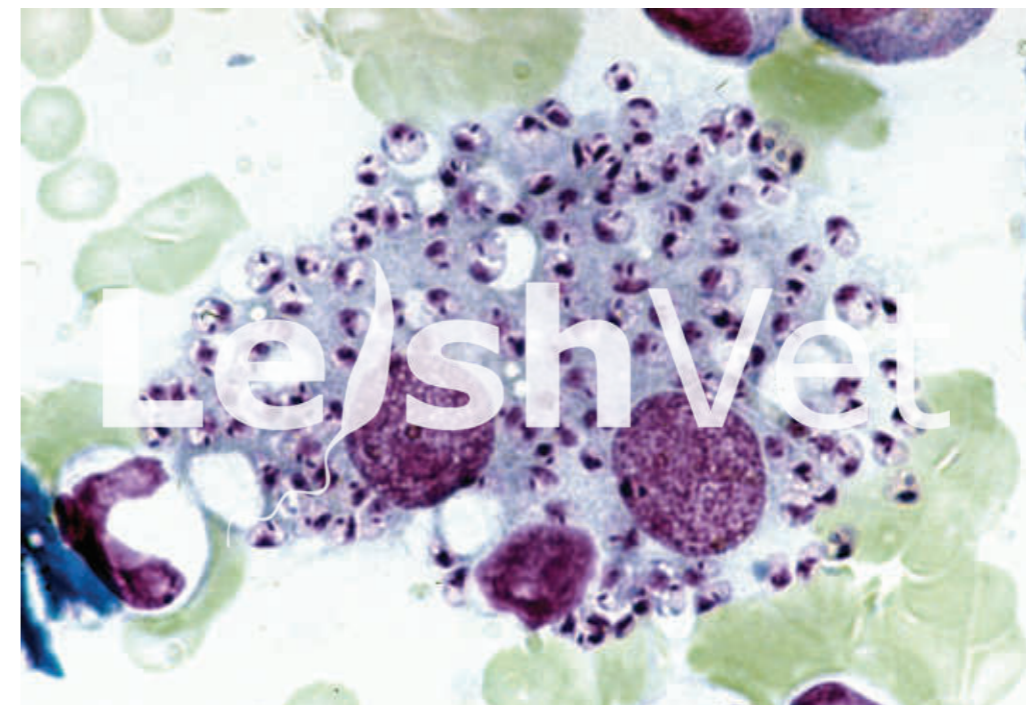
- Dogs with clinical leishmaniosis are those presenting compatible clinical signs and/or clinicopathological abnormalities, and having a confirmed *L. infantum* infection.
- Dogs with subclinical infection (infected but clinically healthy) are those that present neither clinical signs on physical examination 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 (IFAT and ELISA) and qualitative (rapid tests).

What samples and techniques should be used for PCR?

- First choice samples: bone marrow, lymph node, spleen, skin and conjunctival swabs. Less sensitive samples: blood, buffy coat and urine.
- Most sensitive technique: real-time PCR.



Leishmania infantum amastigotes in a canine macrophage
(© Torsten Naucke)



CLINICAL STAGING, TREATMENT AND PROGNOSIS

A system that classifies the disease into four stages with the goal of assisting the clinician in determining the appropriate therapy, forecasting prognosis, and implementing follow-up steps required for the management of the leishmaniosis patient.

Table 2. Clinical staging of CanL based on serological status, clinical signs, laboratory findings and type of therapy and prognosis for each clinical stage.

| CLINICAL STAGES | SEROLOGY* | CLINICAL SIGNS | LABORATORY FINDINGS | THERAPY | PROGNOSIS |
|---------------------------------|--|---|---|--|-----------------|
| STAGE I Mild disease | Negative to low positive antibody levels | Dogs with mild clinical signs such as solitary lymphadenomegaly or papular dermatitis | Usually no clinicopathological abnormalities observed. Normal renal profile: creatinine < 1.4 mg/dl; non-proteinuric: UPC < 0.2 | Scientific neglect **/ Monitoring of disease progression (see table 3) | Good |
| STAGE II Moderate disease | Low to high positive antibody levels | Dogs, which apart from the signs listed in Stage I, may present other clinical signs such as: diffuse or symmetrical cutaneous lesions such as exfoliative dermatitis/onychogryphosis, ulcerations (planum nasale, footpads, bony prominences, mucocutaneous junctions), generalized lymphadenomegaly, loss of appetite and weight loss | Clinicopathological abnormalities such as mild non-regenerative anemia, hypergammaglobulinemia, hypoalbuminemia, serum hyperviscosity syndrome. Substage a) Normal renal profile: creatinine < 1.4 mg/dl; non-proteinuric: UPC < 0.5 b) Creatinine <1.4 mg/dl; UPC= 0.5-1 | Allopurinol + meglumine antimoniate or miltefosine | Good to guarded |
| STAGE III Severe disease | Medium to high positive antibody levels | Dogs, which apart from the signs listed in Stages I and II, may present signs originating from immune-complex lesions (e.g. uveitis and glomerulonephritis) | Clinicopathological abnormalities listed in Stage II Chronic kidney disease (CKD) IRIS stage I with UPC= 1-5 or stage II (creatinine 1.4-2 mg/dl) *** | Allopurinol + meglumine antimoniate or miltefosine Follow IRIS guidelines for CKD**** | Guarded to poor |
| STAGE IV Very severe disease | Medium to high positive antibody levels | Dogs with clinical signs listed in Stage III. Pulmonary thromboembolism, or nephrotic syndrome and end stage renal disease | Clinicopathological abnormalities listed in Stage II CKD IRIS stage III (creatinine 2.1-5 mg/dl) and stage IV (creatinine > 5mg/dl)*** or Nephrotic syndrome: marked proteinuria UPC> 5 | Specific treatment should be instated individually Follow IRIS guidelines for CKD**** | Poor |

*Dogs with negative to medium positive antibody levels should be confirmed as infected with other diagnostic techniques such as cytology, histology/immunohistochemistry and PCR. High levels of antibodies are conclusive of a diagnosis of CanL and are defined as 3-4 fold increased of a well established laboratory reference cut-off.

**Dogs in Stage I (mild disease) are likely to require less prolonged treatment with one or two combined drugs (allopurinol, domperidone, meglumine antimoniate or miltefosine) or alternatively monitoring with no treatment. There is limited information on dogs in this stage and, therefore, treatment options remain to be defined.

***<http://iris-kidney.com/guidelines/staging.html>

****<http://iris-kidney.com/guidelines/recommendations.html>



THERAPY

Table 3. Current treatment protocols for CanL.

| Drugs | Dose | Main side effects |
|------------------------------------|---|---|
| Meglumine antimoniate ^a | 100 mg/kg SC, SID or divided in two doses, for 4-6 weeks (initial reduced dosages for 2-3 days may be useful to detect any adverse events) ^b | <ul style="list-style-type: none"> ⊕ Potential nephrotoxicity ⊕ Pain and inflammation at injection site |
| Miltefosine ^a | 2 mg/kg PO, once a day for 28 days | <ul style="list-style-type: none"> ⊕ Vomiting ⊕ Diarrhea |
| Allopurinol | 10 mg/kg PO, twice a day for at least 6-12 months | <ul style="list-style-type: none"> ⊕ Xanthine urolithiasis |
| Domperidone ^c | 0,5 mg/kg PO, once a day for 1 month | <ul style="list-style-type: none"> ⊕ Galactorrhea |

PO: per os; SC: subcutaneous

- a** Registered for veterinary use in most European countries; both drugs 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 prolongation by 2-3 weeks may be considered if patient improvement is insufficient.
- c** Only considered for Stage I.

Disclaimer: Information given here on drugs and dosages are based on a consensus of clinical and scientific experience by the LeishVet members. These recommendations have been published in scientific peer-reviewed scientific 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 4. Recommended monitoring during and after treatment of CanL.

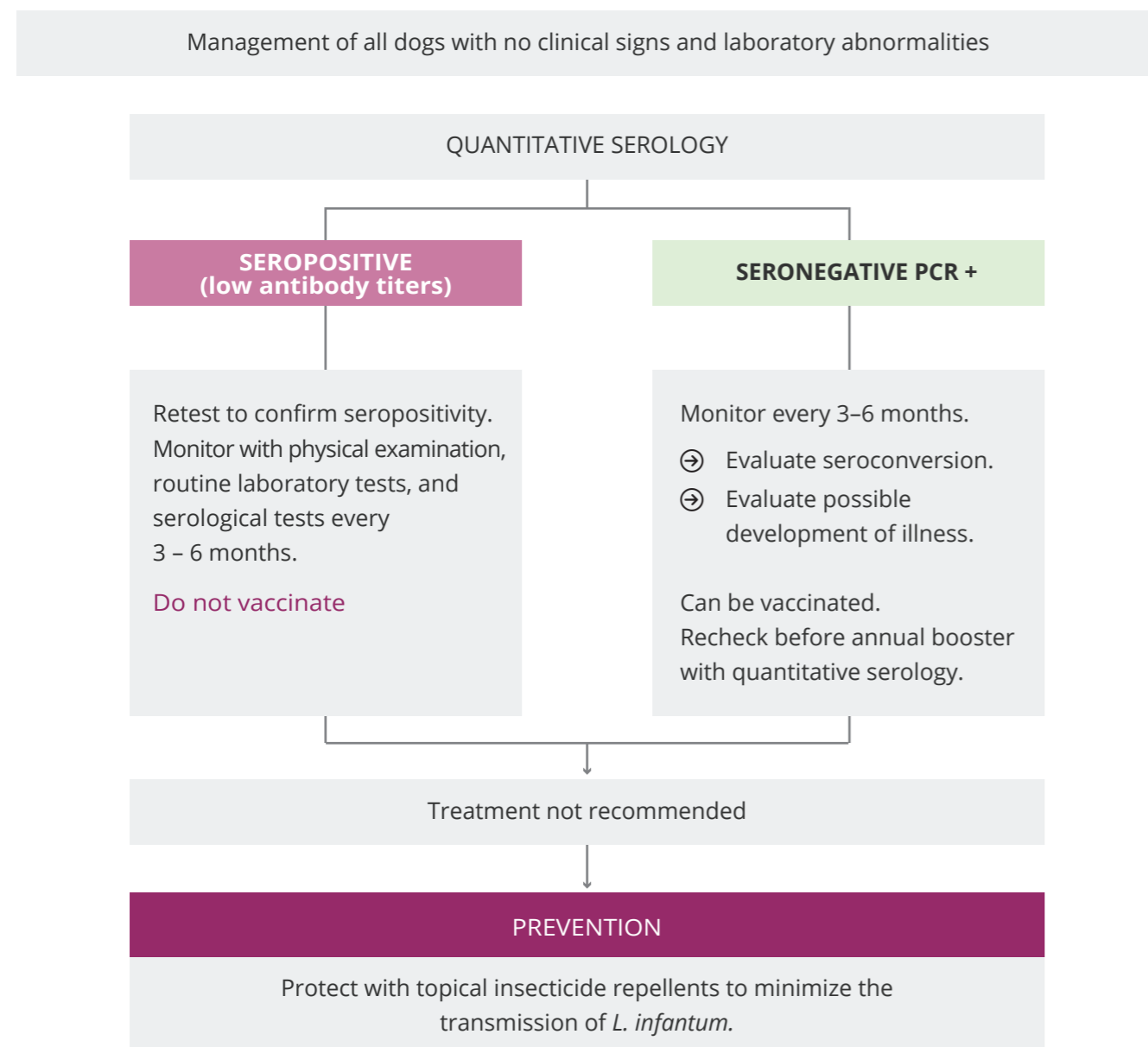
| Parameters | Frequency | |
|---|--|----------------------------------|
| | Sick treated dogs | Clinically healthy infected dogs |
| <ul style="list-style-type: none"> ⊕ Clinical history and physical examination ⊕ CBC, biochemical profile ± serum electrophoresis ⊕ Complete urinalysis ±UPC | <p>After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

CBC: complete blood count; UPC: urinary protein:creatinine ratio.

* Some dogs have a significant decrease in antibody levels (i.e. more than three two-fold dilutions difference between monitoring samples) associated with clinical improvement within 6-12 months of therapy. A marked increase in antibody levels (i.e. more than three two-fold dilutions difference between monitoring samples) should be interpreted as a marker of disease relapse, especially in dogs following the discontinuation of treatment.



Figure 2. Management of *Leishmania*-seropositive but clinically healthy dogs (not vaccinated) and of PCR-positive but seronegative 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.

Confirmed low seropositive dogs should be monitored with physical examinations, routine laboratory and serological tests on a regular basis every 3-6 months to assess the possible progression of infection towards disease.



PREVENTION

Prevention should include the application of a long-acting topical insecticide throughout the period of sand fly activity. Additionally, vaccination should be considered as a multimodal approach*.

Long-acting topical insecticides applied to dogs living in or travelling to endemic areas should be maintained during the entire period risk of potential exposure to/or activity of sand flies:

- A Spot on formulations**
Treatment with permethrin spot-on formulations provides 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 departure.
- B Collars**
Deltamethrin-impregnated collars prevent phlebotomine sand fly bites. The efficacy of this collar preventing *Leishmania* infection has been demonstrated in several field trials. The duration of efficacy of this collar is 5-6 months.
Clinical field studies performed in endemic areas using a flumethrin-containing collar indicate a significant reduction in the incidence of *L. infantum* infection. The duration of efficacy of this collar is 8 months. Collars should be applied at least 1-2 weeks before travelling.

*Based on a risk-benefit assessment (or in endemic areas), a **multimodal approach** combining the use of repellents and vaccination should be considered for an optimal prevention against both infection and development of clinical disease. Repellents reduce the risk of infection but do not prevent the appearance of clinical signs once the dog has been infected. Vaccination reduces the risk of the progression of the disease and the probability of developing clinical signs but does not prevent infection.

Table 5. Preventative recommendations based on different level of risk for *L. infantum* infection (Miró et al., 2017)

| 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 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 travelling /exposure. For longer periods of travel, use repeated spot-on or collars . Test for <i>L. infantum</i> infection 6 months post travel (via quantitative serology) |
| | 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 post last travel (via quantitative serology) |
| | 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 (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 flies season. Vaccination (strongly recommended) | Domperidone could be considered (if not vaccinated) Periodic testing (via quantitative serology) if breeding or blood donor (at least once a year) | |
| | | Indoors (low exposure) | Repellents all year round or during the known sand flies season. Vaccination (optional) | Periodic testing if breeding or blood donor | |
| | None 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 | |

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

**Sick: a dog with clinical and/or clinicopathological abnormalities

VACCINES

A vaccine based on purified excreted/secreted antigens of *L. infantum* has been licensed in Europe since 2011. This vaccine contains a saponin adjuvant.

First vaccination consists of three injections, three weeks apart. Protection is obtained one month after the third injection. Booster injections are given annually.

During 2016, a new vaccine against CanL was licensed in Europe. This new vaccine contains the active substance "protein Q", a recombinant protein made of five different antigens from *L. infantum*.

Following the European public assessment report (EPAR), this vaccine does not contain an adjuvant. Primo-vaccination includes only a single injection. Booster injections are given annually.

Both vaccines available in Europe can only be injected to healthy seronegative dogs of six months of age or older. They do not prevent the infection but the progression of the disease and reduce the probability of developing clinical signs.

Table 6. Licensed anti-*Leishmania* Vaccines.

| Commercial name (manufacturer) | Composition | | Availability | Vaccine protocol | Primary outcome | Vaccine efficacy | Diagnostic interference associated w/vaccine |
|--|-----------------------------|----------|-----------------------------|--|-------------------------------|------------------|--|
| | Antigen | Adjuvant | | | | | |
| Leishmune® (Zoetis) | Fucose-mannose ligand (FML) | QuilA | Brazil ^a | Three primary vaccination doses (SC), 21-day intervals; one annual booster | Clinical disease | 80% | Detection of vaccinal antibodies with official tests (DPP®, ELISA, IFAT). Antibodies not detected after 45 days of first annual booster by FAST or DAT |
| CaniLeish® (Virbac Santé Animale) | LiESP | QA-21 | Europe; Argentina; Paraguay | Three primary vaccination doses (SC), 21-day intervals; one annual booster | Active infection ^b | 68.4% | Detection of vaccinal antibodies with quantitative tests (ELISA, IFAT). Rare detection of vaccinal antibodies with Speed Leish K™ |
| Leish-Tec® (Hertape Calier Saúde Animal) | A2 | Saponin | Brazil | Three primary vaccination doses (SC), 21-day intervals; one annual booster | Parasite detection | 71.4% | Detection of vaccinal antibodies with official ELISA |
| Letifend® (Laboratorios Leti) | Q-protein | None | Europe | One primary vaccination dose (SC); one annual booster | Clinical disease | 72% | No detection of vaccinal antibodies by quantitative tests (IFAT, ELISA) or rapid tests |

Abbreviations: DAT, direct agglutination test; ELISA, enzyme-linked immunosorbent assay; FAST, fast agglutination screening test; IFAT, immunofluorescence antibody test; LiESP, Leishmania infantum excreted-secreted proteins; SC, subcutaneous.

^a To date not on the market.

^b Active infection was defined as the detection of parasite growth in tissue culture from PCR-positive dogs, shortly followed by the elevation of IFAT titers.



FELINE LEISHMANIOSIS ETIOLOGY AND TRANSMISSION

Feline *Leishmania* infections have been observed all over the world and are caused by endemic species also infecting humans and other animals in those areas.

Leishmania infantum is transmitted to cats by sand flies, as these have been shown to feed on cats and to be infected after feeding on naturally infected cats. **To date, non-vectorial transmission has not been described in cats but blood transfusion may be a source of infection of cats similar to humans and dogs.**



GEOGRAPHIC DISTRIBUTION AND RISK FACTORS

Most information regarding feline *L. infantum* infection has come from the cases reported within the Mediterranean basin.

The prevalence rate of *L. infantum* infection in cats, as evaluated in many studies (Table 7), is not negligible; however, it is commonly lower than the prevalence of canine infection.

Table 7. Prevalence of *L. infantum* in Mediterranean countries (diverse serological or blood PCR techniques) according to studies performed in cats (1982 – 2017).

| Prevalence | SEROLOGY (1982-2017) | | BLOOD-BASED PCR (2000-2017) | |
|------------|----------------------|---|-----------------------------|---------------------------------------|
| | Studies (n) | Countries | Studies (n) | Countries |
| < 5% | 16 | Albania-Cyprus-Egypt-Greece Italy-Portugal-Spain | 9 | Cyprus-Italy-Portugal-Spain Turkey |
| 5-25% | 11 | Egypt-France-Greece-Israel Italy-Portugal-Spain-Turkey | 7 | Greece-Italy-Portugal-Spain |
| >25% | 7 | Italy-Spain | 5 | Italy-Portugal-Spain |

Clinical feline leishmaniosis (FeL) remains rare, even in areas where the disease is common in dogs. It is postulated that cats are therefore more resistant than dogs to *L. infantum* infection, but it cannot be excluded that the disease is underdiagnosed because it is unknown to most practitioners and masked by concurrent diseases, and feline medicine is still underdeveloped in many areas as compared to canine medicine.



Considering that cats may be a source of infection for sand flies and that cats may suffer from chronic infection, LeishVet postulates that **infected cats may represent an additional domestic reservoir for *L. infantum*.**

Approximately 100 clinical cases were reported in Europe during the last 25 years (Italy, Spain, France, Portugal) with some cases diagnosed (Switzerland) in cats imported from endemic regions.

Host factors predisposing to susceptibility may exist, as roughly half of the reported clinical cases have been observed in cats that could have had an impaired immune system secondary to feline immunodeficiency virus (FIV) or feline leukemia virus (FeLV) infections, immune-suppressive therapies or debilitating concomitant diseases.

Geographic distribution of feline *Leishmania* spp. infection is summarized in Table 8.

Table 8. *Leishmania* spp. detected in cats and countries where infection and/or disease cases were reported (1982-2017).

| <i>Leishmania</i> species | Old World Countries | New World Countries |
|---------------------------|---|---|
| <i>L. infantum</i> | Cyprus - France - Greece - Iran - Israel Italy - Portugal - Spain - Switzerland* Turkey | Brazil - Mexico |
| <i>L. braziliensis</i> | --- | Brazil - France (French Guiana) Mexico |
| <i>L. mexicana</i> | --- | Mexico - USA (Texas) |
| <i>L. venezuelensis</i> | --- | Venezuela |
| <i>L. amazonensis</i> | --- | Brazil |
| <i>L. tropica</i> | Turkey | --- |
| <i>L. major</i> | Turkey | --- |

*Cats rehomed from Spain



CLINICAL PRESENTATION

Feline leishmaniosis is a chronic disease with clinical signs and clinicopathological abnormalities similar to those found in dogs (Table 9).

The most common muco-cutaneous lesions described are ulcerative and nodular dermatitis mostly distributed on the head or symmetrically on distal limbs (Figures 3 and 4). Uveitis is the most important ocular lesion (Figure 5). Oral lesions consist of nodules (tongue and/or gingival mucosa) or chronic stomatitis (Figure 6).

Complete blood count, biochemical profile and urinalysis are required in any suspected case to identify hyperglobulinemia, non-regenerative anemia, renal disease or other less common laboratory abnormalities associated with leishmaniosis.

FIV and FeLV testing are recommended in case of risk of exposure, as well as investigation of other concurrent diseases that alter feline immunocompetence.



Figure 3: Nodular conjunctivitis (upper eyelid) and ulcerative dermatitis



Figure 4: Ulcerative dermatitis on distal limb



Figure 5: Bilateral uveitis with bleeding in the anterior chamber (hyphema)



Figure 6: Stomatitis and glossitis involving the cheeks and margin of the tongue

Table 9. Frequency of clinical and clinicopathological abnormalities reported in FeL

*: present in around 50% of cases

** : present in around 30% of cases

***: present in less than 25% of cases and listed in descending order of frequency

| Clinical and clinicopathological abnormalities reported in feline leishmaniosis | | |
|---|--|--|
| Reported frequently* | Uncommon** | Rare*** |
| <ul style="list-style-type: none"> ⊕ Skin and/or muco-cutaneous nodules and ulcers ⊕ Lymphadenomegaly | <ul style="list-style-type: none"> ⊕ Ocular lesions ⊕ Oral lesions ⊕ Pale mucous membranes ⊕ Weight loss - Anorexia - Lethargy | <ul style="list-style-type: none"> ⊕ Icterus ⊕ Hepatomegaly - Splenomegaly ⊕ Cachexia - Fever ⊕ Vomiting - Diarrhea ⊕ Polyuria/Polydipsia ⊕ Dehydration ⊕ Chronic nasal discharge ⊕ Dyspnoea - Wheezing ⊕ Abortion ⊕ Hypothermia |
| <ul style="list-style-type: none"> ⊕ Hypergammaglobulinemia | <ul style="list-style-type: none"> ⊕ Proteinuria ⊕ Mild to moderate non-regenerative anemia | <ul style="list-style-type: none"> ⊕ Azotemia - Hypoalbuminemia ⊕ Monocytosis - Neutrophilia ⊕ Pancytopenia |



DIAGNOSIS

Table 10. Diagnostic methods used for FeL.

| IMMUNOLOGICAL | PARASITOLOGICAL |
|--|--|
| Antibody detection ⊕ IFAT (cut off: 1:80) ⊕ ELISA (lab. validated cut-off values) ⊕ DAT (cut-off: 1/800) ⊕ Western blot (detection of 18 KDa band) | ⊕ Cytological evaluation of skin, mucosal or mucocutaneous lesion, lymph node and bone marrow smears (Figure 7) ⊕ Histological evaluation of skin, mucosal or muco-cutaneous biopsied lesions (± IHC and/or PCR) ⊕ PCR from skin, mucosal or muco-cutaneous lesion, lymph node, bone marrow, blood, conjunctival and oral swabs ⊕ Culture of skin, mucosal or mucocutaneous lesion, lymph node, bone marrow and blood samples |

DAT: direct agglutination test; ELISA: enzyme-linked immunosorbent assay; IFAT: indirect fluorescence antibody test; IHC: immunohistochemistry; PCR: polymerase chain reaction.

To confirm diagnosis, a quantitative serological test or Western blot should be performed in sera from cats with clinical signs or clinicopathological abnormalities compatible with FeL. However, in case of negative or low-positive antibody titers, a parasitological technique should be used to identify infection (cytology, histology, PCR or culture), before discharging diagnosis.

Evaluation of *Leishmania*-specific serology and PCR techniques (blood, lymph nodes or conjunctival swabs) are recommended in the following special situations in endemic areas:

- ➔ Blood donors
- ➔ Cats requiring immunosuppressive therapies
- ➔ Before re-homing cats to non-endemic areas

THERAPY

- ➔ There are no published controlled studies of FeL therapy.
- ➔ In the absence of evidence indicating otherwise, empirical treatment giving the same drugs recommended for dogs is usually considered effective and apparently safe. **Allopurinol** (10 mg/kg 12 h or 20 mg/kg 24 h P.O., for at least 6 months) has been more frequently used than meglumine antimoniate (20-50 mg/kg 24 h S.C., for 30 days). These two drugs have also been given in combination.
- ➔ Cats under therapy with allopurinol or meglumine antimoniate should be carefully monitored for any adverse effects.

Disclaimer: Information given here on drugs and dosages are based on a consensus of clinical and scientific experience by the LeishVet members. These recommendations have been published in scientific peer-reviewed scientific 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.

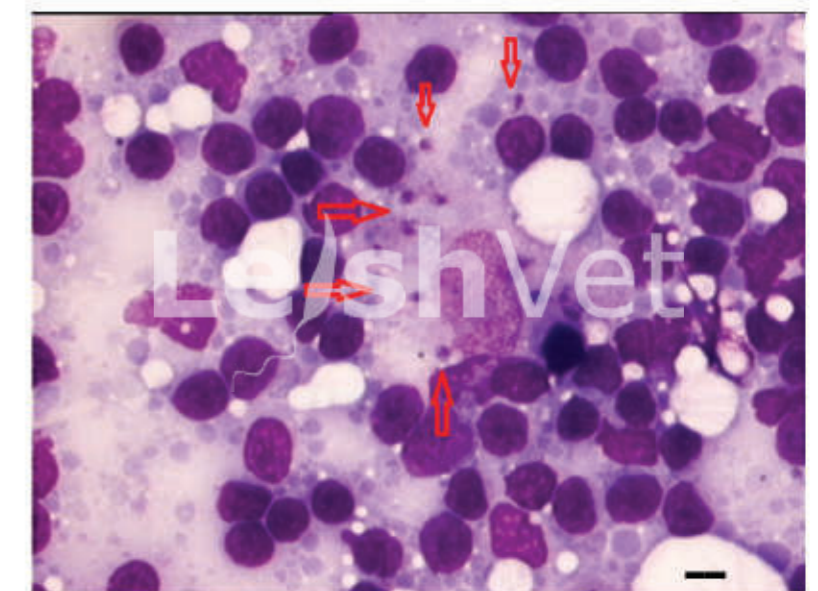


Figure 7: Fine needle aspirate of a reactive lymph node: lymphoid hyperplasia and a macrophage with *L. infantum* amastigotes (red arrows). May-Grünwald-Giemsa stain, scale bar = 20 µm (© Maria Grazia Pennisi)



MONITORING AND PROGNOSIS

→ Recurrence of clinical signs may occur; careful monitoring after the end of anti-*Leishmania* treatment should include physical examination, CBC, biochemical profile, urinalysis and quantitative serology at the frequencies indicated below (Table 11).

→ The life expectancy of cats with FeL is usually good (years) unless concurrent conditions (neoplasia, FIV/FelV infections) or complications (renal disease) occur.

Table 11. Follow-up regimen.

| ACTION | FREQUENCY |
|---|--|
| Physical examination CBC* | → At least weekly (meglumine antimoniate) or fortnightly (allopurinol) during the first month of therapy |
| Biochemical profile Urinalysis including UPC** | → Every 3 months in the first year or after stopping therapy → Every 6 months after the first year |
| Quantitative serology | → Every 3 months in the first year or after stopping therapy → Every 6 months after the first year |

* CBC: complete blood count.

** UPC: urinary protein: creatinine ratio.

PREVENTION

→ It is advised to protect (in endemic areas):

- Individual cats from the risk of developing infection and clinical disease.
- Feline population to improve the control of *L. infantum* infection in the vector.
- General prevention of sand fly bites is based on the same procedures as for dogs.
- Topical insecticides
Insecticides currently available for cats have no demonstrated effect in preventing the bites of sandflies.
- Most pyrethroids are toxic for cats. Flumethrin collar is at present the only pyrethroid formulation licensed for cats and it was able to reduce the incidence of *L. infantum* in cats in a field study
- Test blood donors by antibody detection and blood PCR



Female *Phlebotomus perniciosus* unfed



KEY POINTS

- ➔ *Leishmania infantum* is most likely transmitted to cats by sandflies although blood transfusion may be a non-vectorial route of transmission.
- ➔ The prevalence of *L. infantum* infection in cats is commonly lower than that of canine infection in endemic areas but often not negligible.
- ➔ Cats seem to be more resistant than dogs to *L. infantum* infection and subclinical feline infections are common in areas endemic for canine leishmaniosis while clinical illness in cats is rare.
- ➔ Skin lesions, lymph node enlargement and hypergammaglobulinemia are the most common clinical findings, followed by ocular and oral lesions, proteinuria, non-regenerative anemia.
- ➔ Infected cats may represent an additional domestic reservoir for *L. infantum* infection.
- ➔ Diagnosis is based on serological and parasitological techniques.
- ➔ Currently, treatment is empirically based on some drugs used also for dogs.
- ➔ Most pyrethroids are toxic for cats and only flumethrin collars are safe to be used.



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 CanL. 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.



Female *Phlebotomus perniciosus* feeding on the muzzle of a dog
(© Guadalupe Miró)



LEISHVET MEMBERS

| | |
|-----------------------------|--|
| Gad Baneth | Hebrew University of Jerusalem, Rehovot, Israel. |
| Patrick Bourdeau | Ecole Nationale Vétérinaire, Agroalimentaire et de l'Alimentation, Nantes-Atlantique (ONIRIS), Nantes, France. |
| Luís Cardoso | Universidade de Trás-os-Montes e Alto Douro, Vila Real, Portugal. |
| Lluís Ferrer | Universitat Autònoma de Barcelona, Bellaterra, Cerdanyola del Vallès (Barcelona), Spain. |
| Guadalupe Miró | Universidad Complutense de Madrid, Madrid, Spain. |
| Gaetano Oliva | Università di Napoli Federico II, Napoli, Italy. |
| Maria Grazia Pennisi | Università di Messina, Messina, Italy. |
| Christine Petersen | University of Iowa, College of Public Health, USA. |
| Laia Solano-Gallego | Universitat Autònoma de Barcelona, Bellaterra, Cerdanyola del Vallès (Barcelona), Spain. |

LEISHVET HONORARY MEMBERS

Alek F. Koutinas Aristotle University of Thessaloniki, Thessaloniki, Greece.



REFERENCES

- Baneth G, Koutinas AF, Solano-Gallego L, Bourdeau P, Ferrer L: Canine leishmaniosis – new concepts and insights on an expanding zoonosis: part one. Trends Parasitol 2008; 24:324–330.
- Miró G, Cardoso L, Pennisi MG, Oliva G, Baneth G: Canine leishmaniosis – new concepts and insights on an expanding zoonosis: part two. Trends Parasitol 2008; 24(8):371–377.
- Pennisi MG, Cardoso L, Baneth G, Bourdeau P, Koutinas A, Miró G, Oliva G, Solano-Gallego L. 2015. Leishvet update and recommendations on feline leishmaniosis. Parasites & Vectors 2015; 2: 302.
- Solano-Gallego L, Koutinas AF, Miro G, Cardoso L, Pennisi MG, Ferrer L, Bourdeau P, Oliva G, Baneth G: Directions for the diagnosis, clinical staging, treatment and prevention of canine leishmaniosis. Vet Parasitol 2009; 165:1–18.
- Solano-Gallego L, Miró G, Koutinas AF, Cardoso L, Pennisi MG, Ferrer L, Bourdeau P, Oliva G, Baneth G: LeishVet guidelines for the practical management of canine leishmaniosis. Parasites & Vectors 2011; 4:86.
- Miró G, Petersen Ch, Cardoso L, Bourdeau P, Baneth G, Solano-Gallego L, Pennisi MG, Ferrer LI, Oliva G. Novel areas for prevention and control of canine leishmaniosis. Trends in Parasitology 33(9): 718-730. 2017.
- Solano Gallego L, Cardoso L, Pennisi MG, Petersen Ch, Bourdeau P, Oliva G, Miró G, Ferrer LI, Baneth G. Diagnostic challenges in the era of canine Leishmania infantum vaccines. Trends in Parasitology 33(9): 706-717. 2017.
- www.leishvet.org
- www.iris-kidney.com/guidelines/
- www.esccap.com

Front cover images: Dog © Justin Veenema | Cat © Luis Mezquita

Black and white images: Dog © Andy Mabbett | Cat © Ian Livesey