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SOCIETA' VETERINARI PIEMONTESI
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ASSOCIAZIONE FEDERATA A.N.M.V.I.

scivac

con il patrocinio dell'Ordine dei Medici Veterinari della Provincia di Torino

FEDERAZIONE INTERREGIONALE
ORDINI MEDICI VETERINARI
PIEMONTE E VALLE D' AOSTA

CONF PROFESSIONI
confederazione italiana libere professioni

Leishmaniosi canina: apparentemente semplice, maledettamente complicata

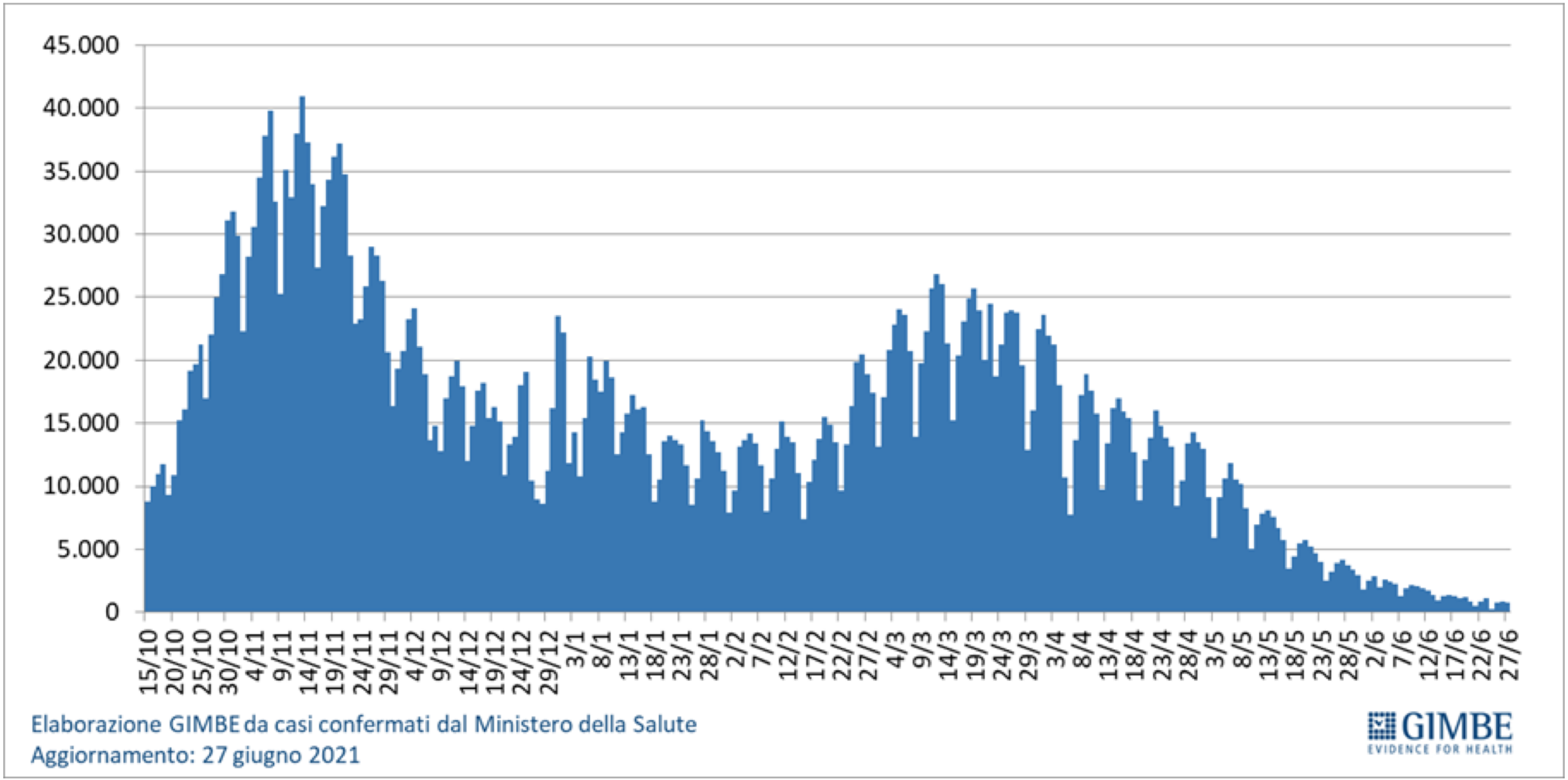
Prof. Gaetano Oliva

Dipartimento
Medicina Veterinaria
Produzioni Animali

INFEZIONE E MALATTIA:
COME ESEGUIRE UNA CORRETTA DIAGNOSI

Nuovi casi giornalieri di COVID-19

Il grafico illustra, in numero assoluto, il trend dei nuovi casi giornalieri positivi al SARS-CoV-2 a partire dal 15 ottobre 2020



1910
Napoli, 18 Luglio

N. 29
Anno XXVI

LA RIFORMA MEDICA

Abb. annuo { Italia L. 20,50 / Estero „ 35,50

L' abbonamento non disdetto 15 giorni prima della scadenza s' intende rinnovato.

DIRETTORE Comm. G. RUMMO
Professore di clinica medica nella R. Università di Napoli.

Redattore-Capo: Prof. LUIGI FERRANNINI.

GIORNALE SETTIMANALE
NAPOLI

Gli abbonamenti si ricevono in tutti gli ufficii postali e decorrono dal 1° gennaio e dal 1° luglio.

Indirizzare manoscritti, opere, memorie, giornali, esclusivamente al Prof. G. RUMMO - Napoli.

Iemma, Di Cristina e Cannata. Infezione sperimentale da " Leishmania infantum „ nei cani.

Dai risultati dei vari esperimenti si può venire alla conclusione che non tutti i cani iniettati vanno incontro alla infezione, sia che l'innesto si faccia per la via peritoneale sia che si segna la via sanguigna. Quando l'animale contrae l'infezione diventa cachettico e diminuisce di peso; ha lievi oscillazioni di temperatura e alterazioni della crasi sanguigna Nei cani riferiti nella pubblicazione e in quelli che sono ancora in osservazione hanno notato, come prima manifestazione dell'avvenuta infezione, un dimagrimento progressivo che si protrae di tanto che l'animale non può più reggersi in piedi. Eccezionalmente in due cani, nei quali l'infezione è stata constatata positiva, non vi è stata alcuna alterazione delle condizioni generali. L'infezione che contrae il cane sembra

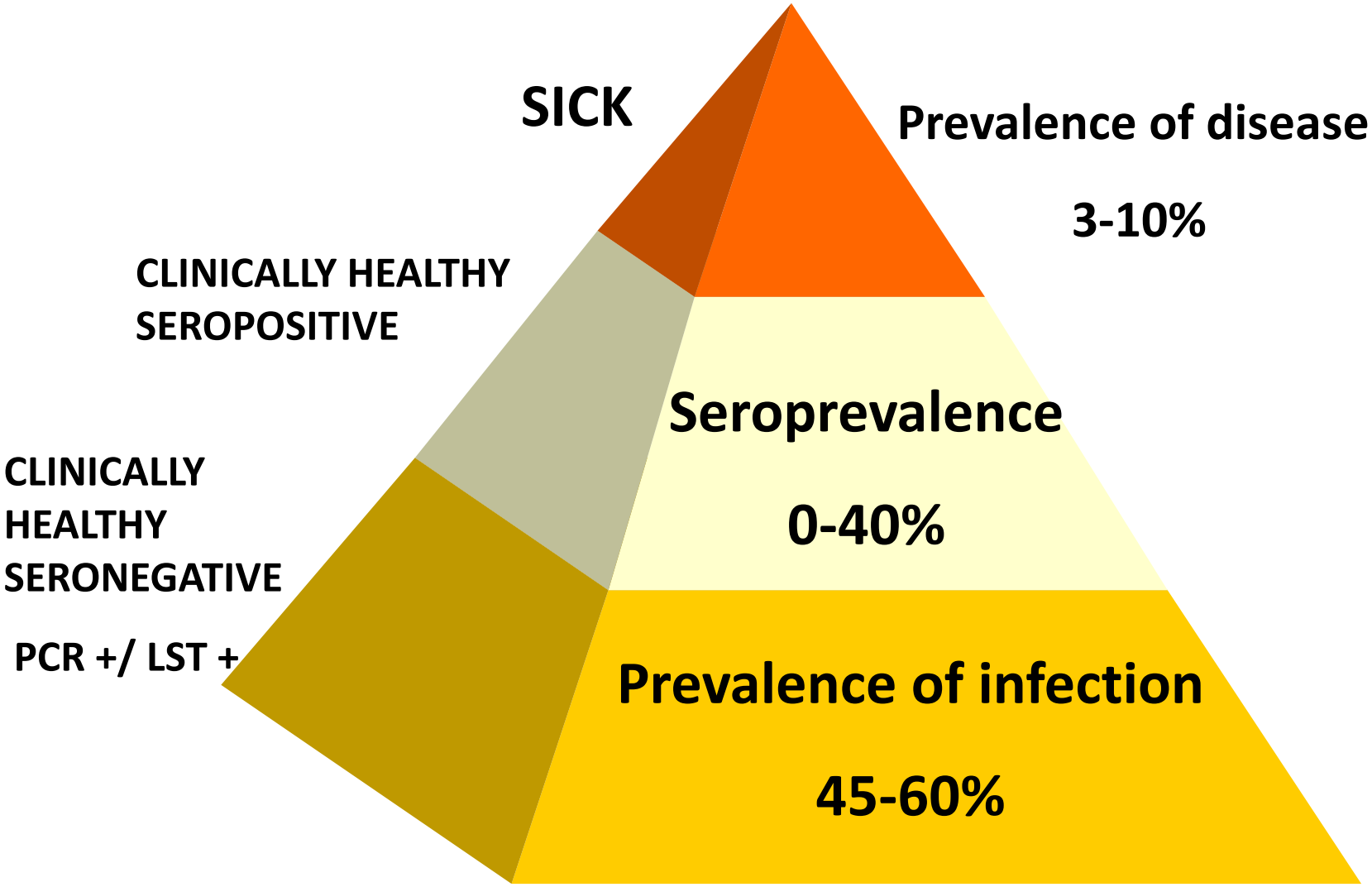

NON INFETTO


ESPOSTO/INFETTO SUBPATENTE
NEGATIVE/TRANSIENT
/LOW SEROLOGY


INFEZIONE PROGRESSIVA
SEROLOGY INCREASES
DURING THE TIME


MALATO

Leishmania infantum infection in dogs from endemic areas



Berrahal et al. (1996). *Am J Trop Med Hyg*, 55: 273-277
Cabral et al. (1998). *Vet Parasitol*, 76: 173-180
Cardoso et al . (1998). *Vet Parasitol*, 79: 213-220
Solano-Gallego et al. (2000). *Vet. Parasitol.*, 383**,** 787-793
Solano-Gallego et al. (2001). *J Clin Microb*, 39: 560-563
Baneth et al. (2008). Trends in Parasitol.

Months	BM Nested PCR	BM RT PCR	Lymph node Culture	IFAT	ELISA	Haemato Biochemical parameters	Clinical examination	STATUS
M9	neg	neg	neg	<1/40	Neg.	normal	Mild weight loss	Negative
M15	pos	4.9	pos	1/320	1/2000	PLT↓	Asymptomatic	Progressive infection
M18	pos	6.5	pos	1/5120	5000	RBC↓ PLT↓ < A/G ratio	Lymphoadenopathy (popliteal)	SICK
M21	pos	6.7	pos	1/20480	5000	RBC↓ < A/G ratio	Pale mucosae Loss of weight Muscle atrophy	SICK

Months	BM Nested PCR	BM RT PCR	Lymph node Culture	IFAT	ELISA	Haemato Biochemical parameters	Clinical examination	STATUS
M9	neg		neg	<1/40		PLT↓	prescapular enlarged	negative
M15	Pos		neg	<1/40	(-)	TP↓	asymptomatic	Subpatent infection
M18	neg		neg	<1/40		WBC↑	asymptomatic	Healthy negative
M21	neg		neg	<1/40		RBC↓ TP↓	asymptomatic	Healthy negative
M24	Pos	2.9	neg	1/160	1/200	normal	asymptomatic	Subpatent infection
M 30	neg		neg	<1/40		normal	asymptomatic	negative
M33	neg		neg	<1/40		RBC↓ TP↓	asymptomatic	negative

Lady (mail del

Cane femmina, meticcio pelo raso, nero, 12 kg, 5- 6 anni (anno di nascita presunto 2014-2015)

Trovata in provincia di Cosenza, randagia e gravida nel 2016, ha partorito 8 cuccioli. Rimane in rifugio fino a dicembre 2017 quando arriva in Lombardia.

In Calabria non ha avuto sintomi, **quando è arrivata aveva 2 piccole cicatrici sul dorso del naso tra la cute e il tartufo**.

Dal rifugio mi hanno riferito test IC leishmania negativo. Nella primavera 2018 test rapido ELISA (IDEXX) negativo.

A gennaio 2020 esami di screening tra cui anche test ELISA Leishmania positivo 7,6 U (IR <7 U)

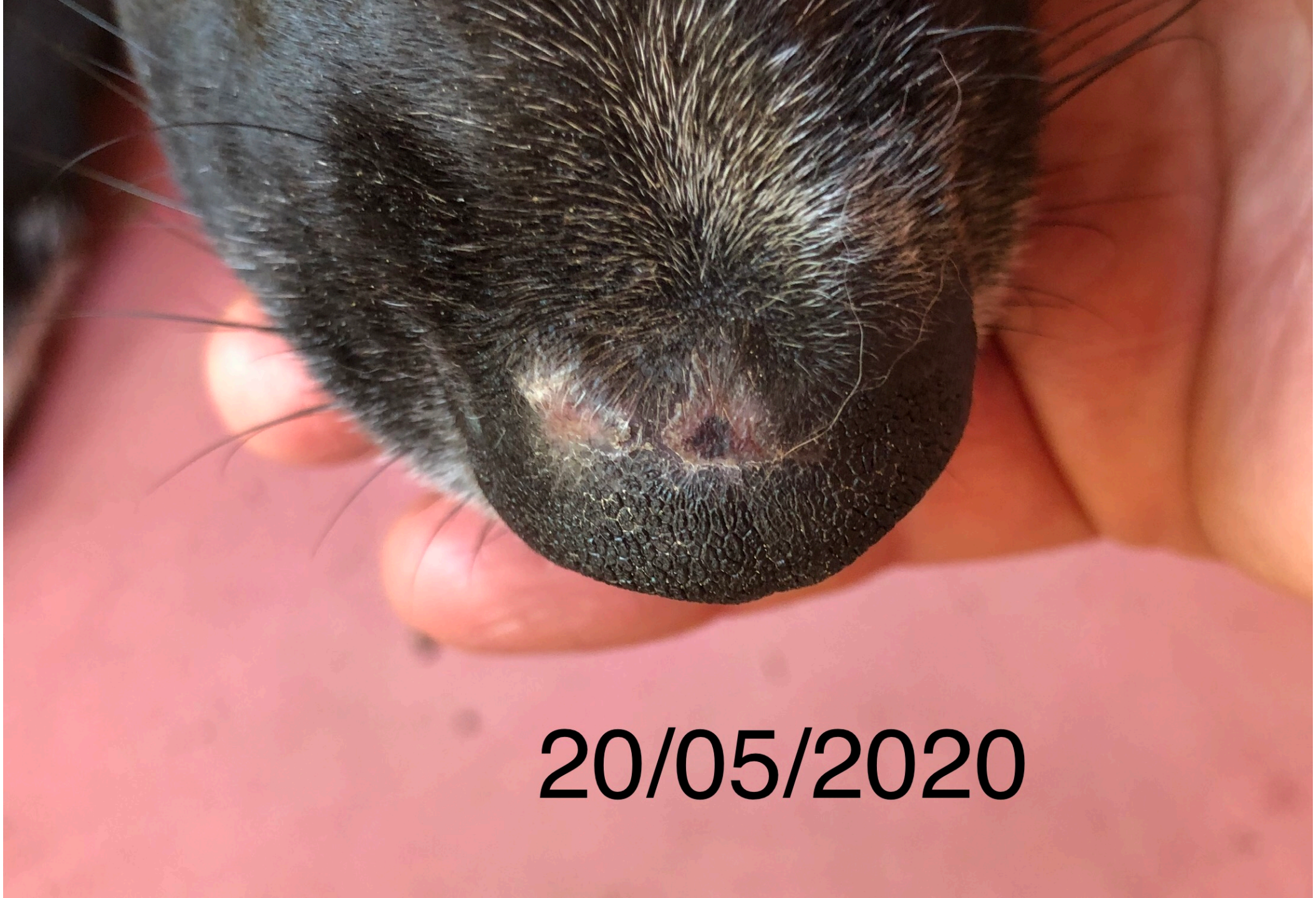
Le lesioni sul naso si sono evolute in lieve erosione che talvolta sanguina, nel giro di una settimana si forma una crosta.

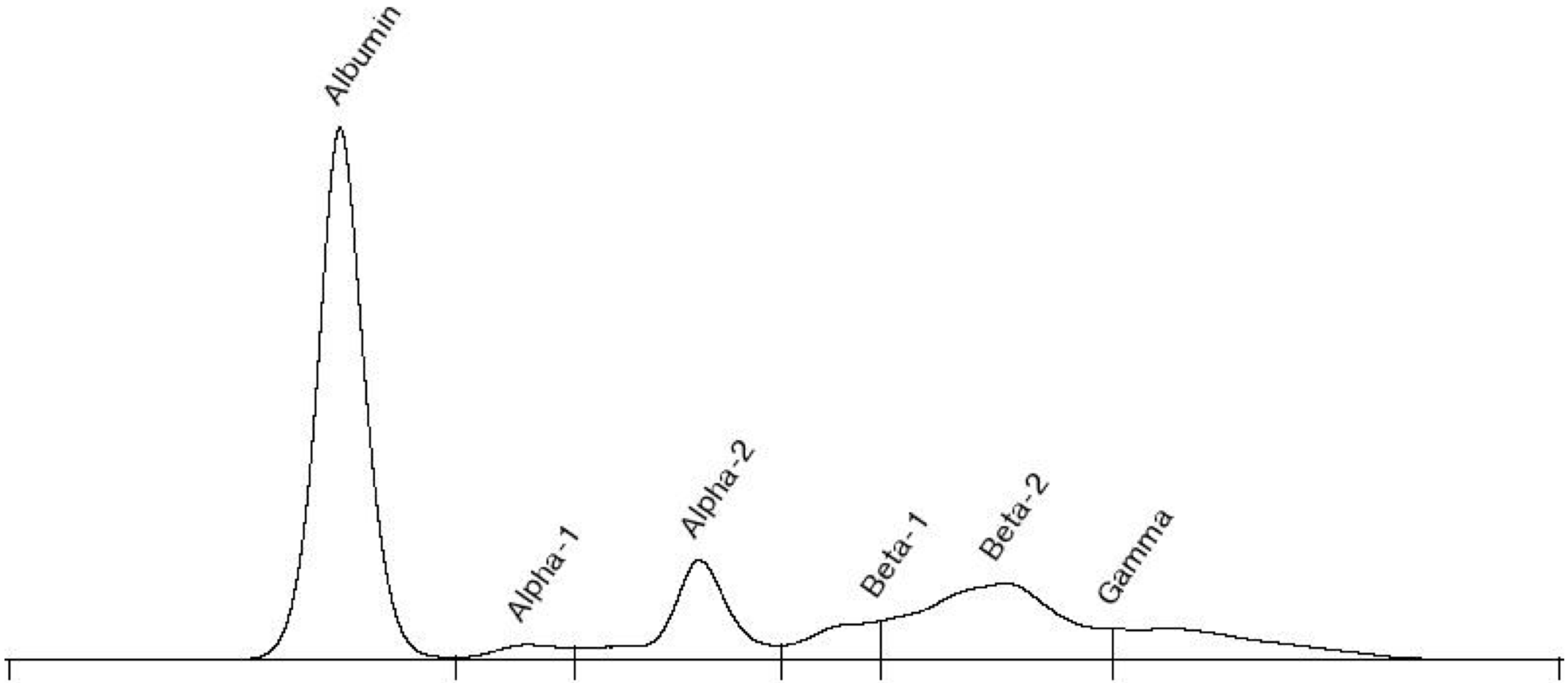
A fine aprile ripeto gli esami Leishmania ELISA 37,9 e elettroforesi (in allegato)

Le lesioni sono asciutte e arrossate

Ai primi di maggio ripeto elettroforesi e faccio esame urine. Tutti gli esami e le immagini delle lesioni sono in allegato

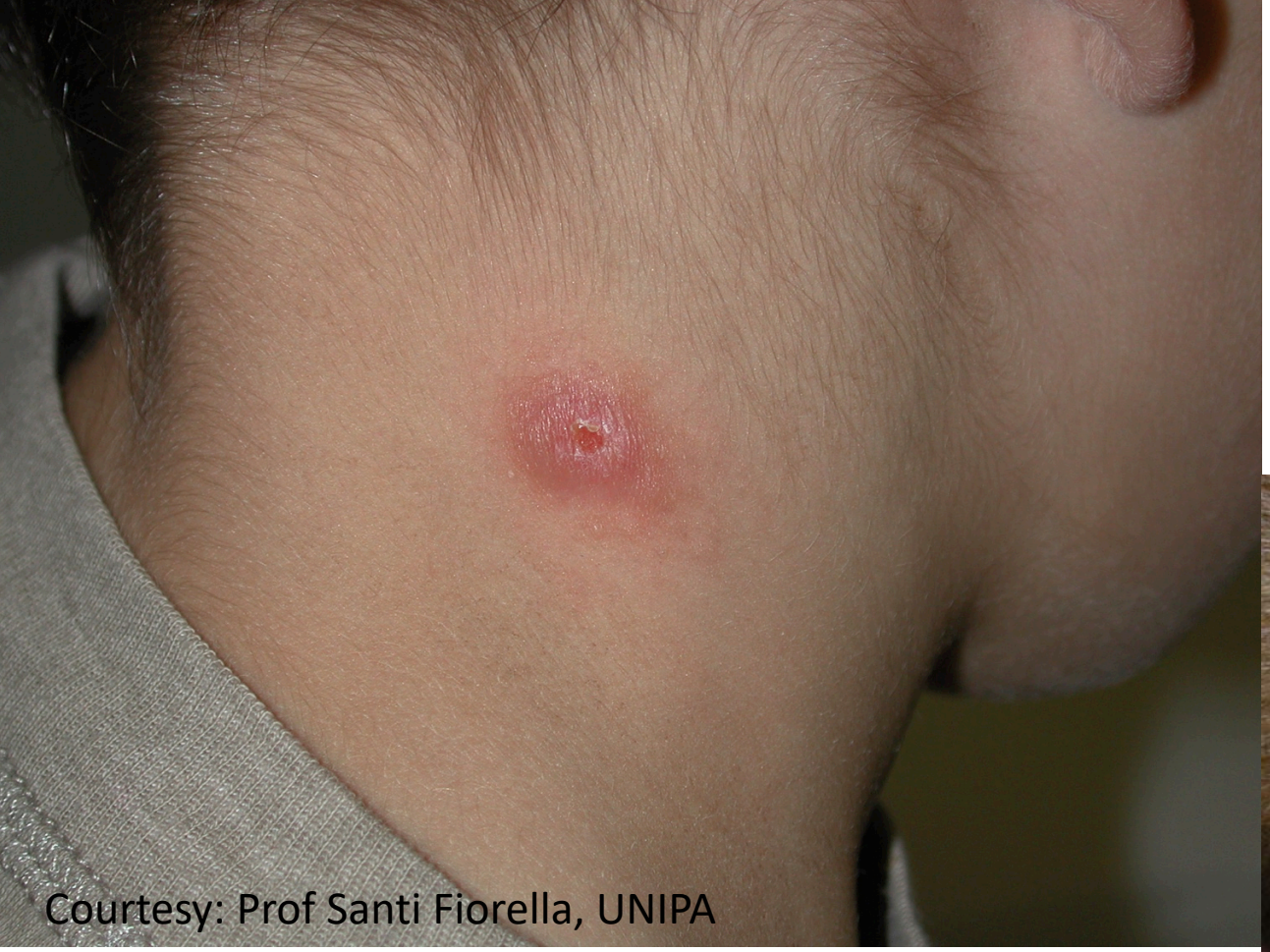
Il cane (da quando è con me, dicembre 2017) non ha mai avuto sintomi sistemici apparenti, i linfonodi sono di volume normale, solo i prescapolari si potrebbero definire lievemente aumentati.

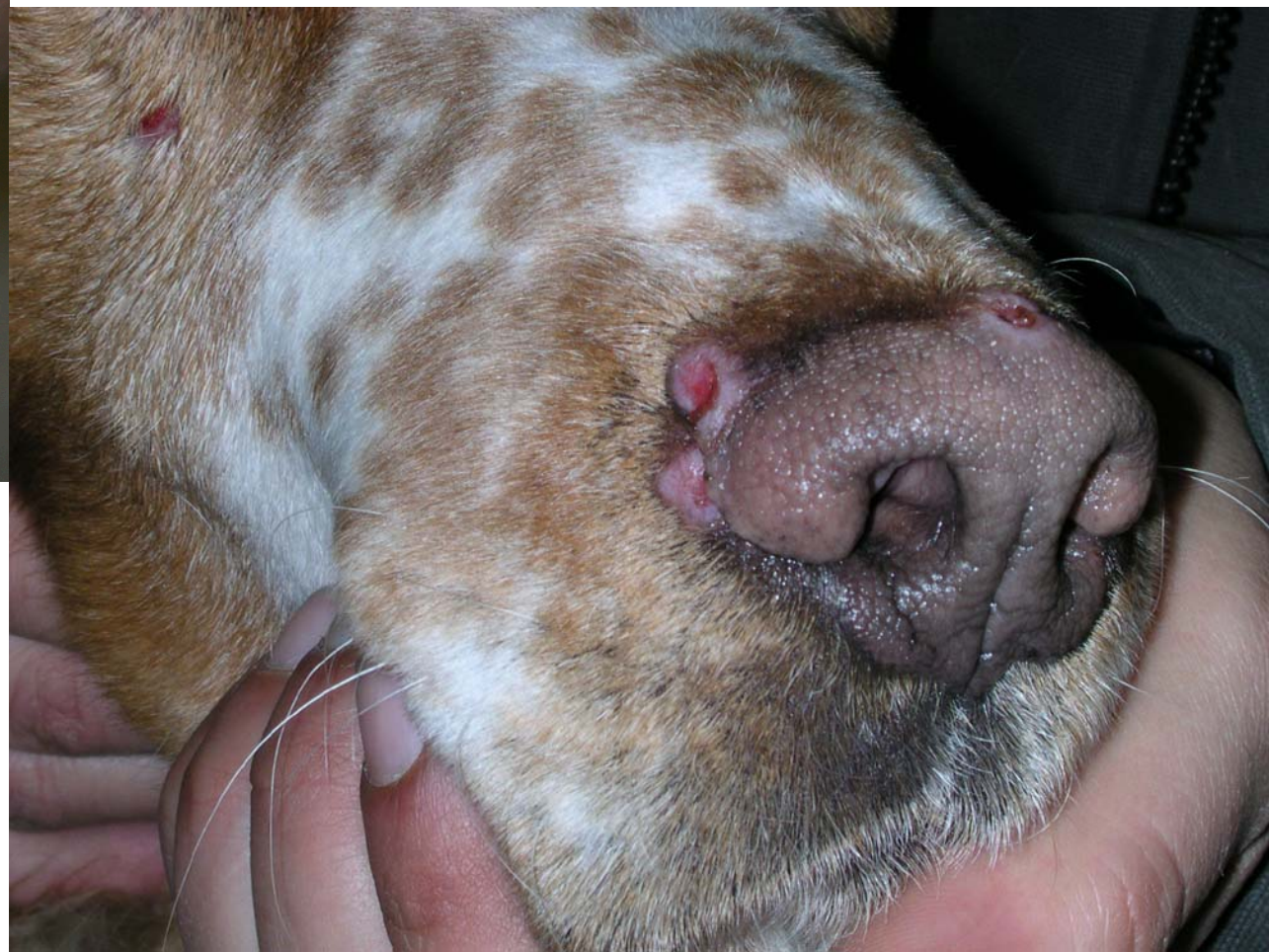

20/05/2020


Albumin
Alpha-1
Alpha-2
Beta-1
Beta-2
Gamma

Risposta: visto il titolo anticorpale che si è quadruplicato (e più) in pochi mesi, è presupponibile che l'immunità cellula-mediata che il cane aveva sviluppato nei confronti del parassita, con confinamento dello stesso solo a livello delle ulcere nasali, stia switchando verso un'immunità umorale (deleteria per il soggetto).
In questi casi è consigliabile il trattamento. Allo stesso tempo, però, eseguirei un citologico e PCR per Leishmania dalle lesioni nasali (per ulteriore conferma) e una PCR dal linfonodo e o midollo. Quest'ultima ti permetterà di capire lo spread del parassita, se cioè è in atto (o è già avvenuta) la sua "visceralizzazione" o se, al contrario, il parassita è ancora confinato a livello cutaneo.

RISULTATO: RT-PCR MIDOLLO positiva
Citologico linfonodo popliteo: positivo


Courtesy: Prof Santi Fiorella, UNIPA



PERCHE’ PROGREDISCE:

ETA’
RAZZA
STILI DI VITA (OUTDOOR)
FATTORI GENETICI

STIMOLAZIONI ANTIGENICHE CONTINUE

INFEZIONI/MALATTIE CONCOMITANTI

Razze più suscettibili

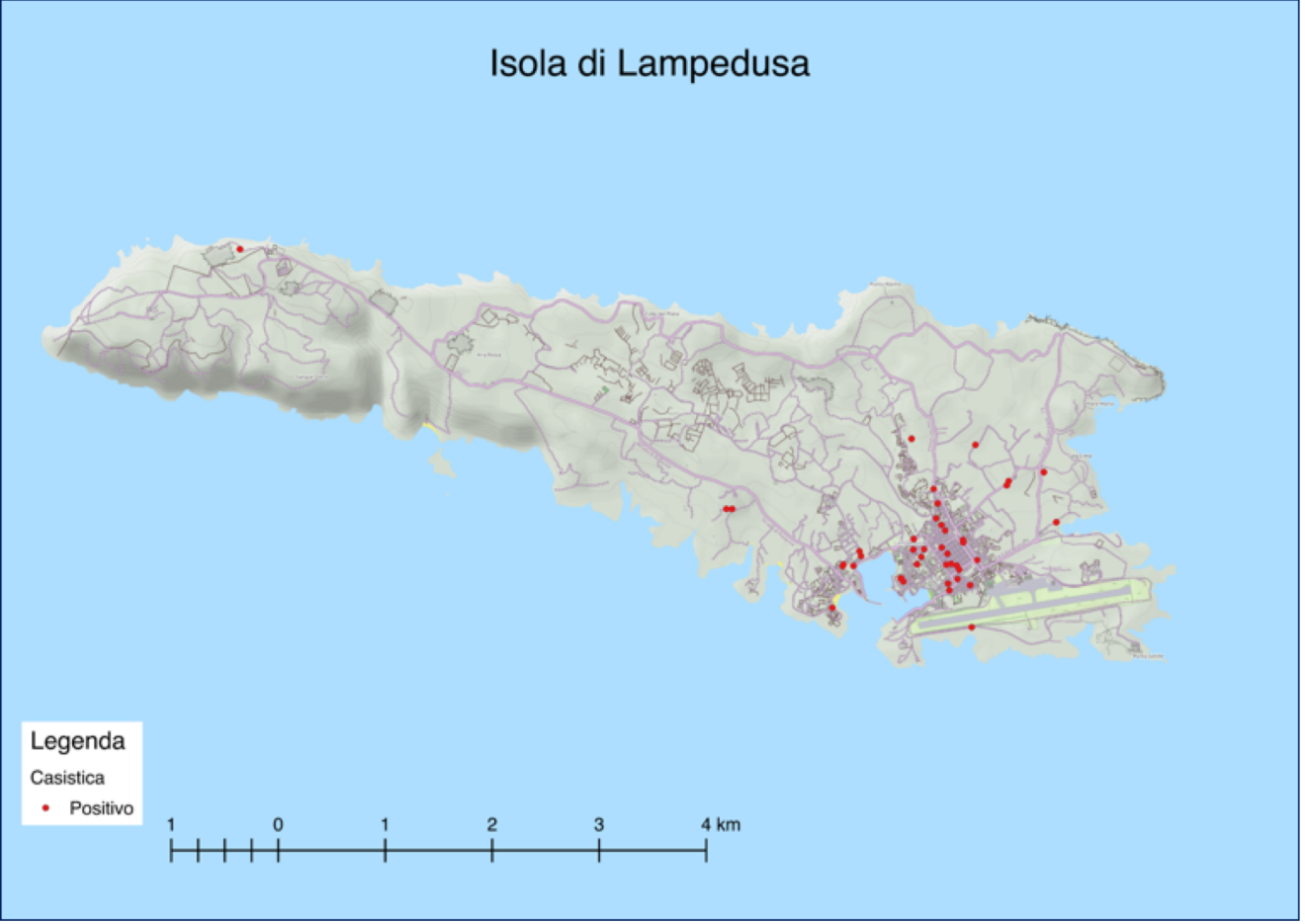
German shepherd

Boxer

Rottweiler

Razza più resistente (Ibizan hound)

Solano Gallego et al., 2000. Veterinary Parasitology



n. dogs	271	%
NEGATIVE	101	37,2
EXPOSED	77	28.4
POSITIVE	93	34,3

POSITIVE + EXPOSED

62,7%

Foglia Manzillo et al. BMC Veterinary Research (2018) 14:286
https://doi.org/10.1186/s12917-018-1606-x

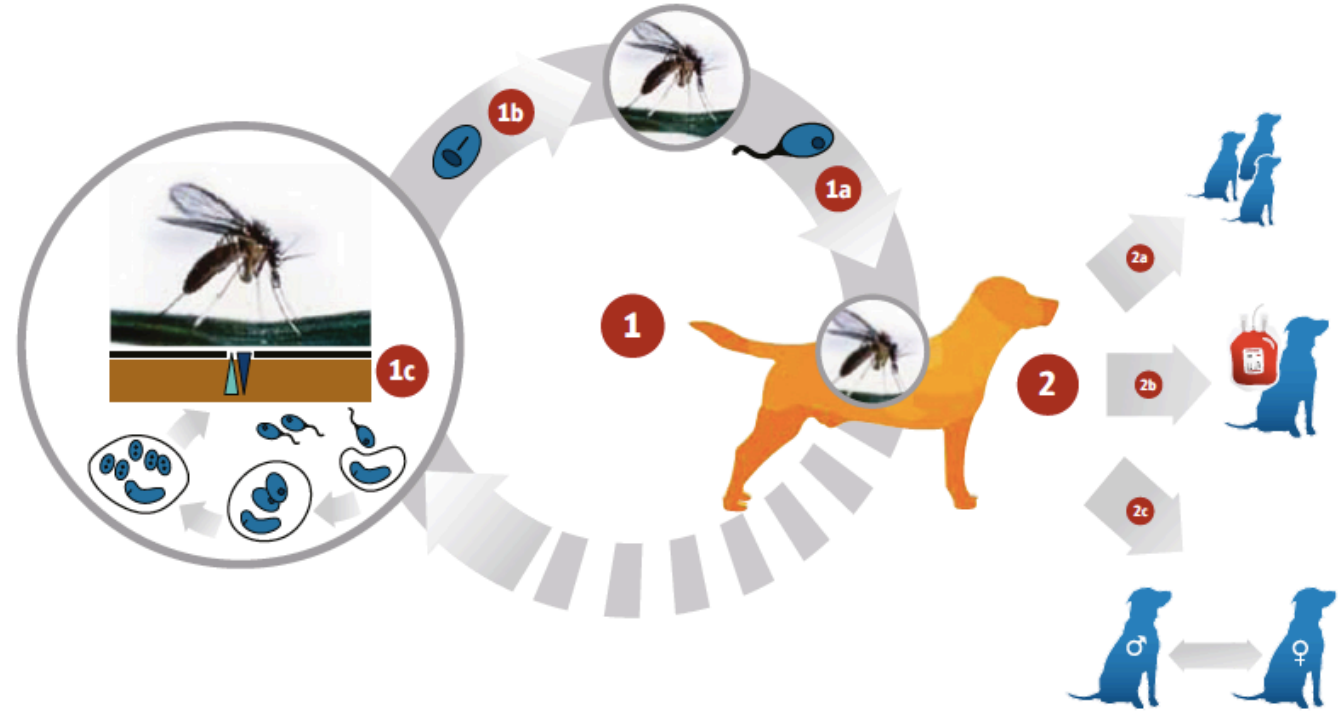
BMC Veterinary Research

RESEARCH ARTICLE Open Access

Serological and entomological survey of canine leishmaniasis in Lampedusa island, Italy

Valentina Foglia Manzillo [1], Manuela Gizzarelli [1*], Fabrizio Vitale [2], Serena Montagnaro [1], Alessandra Torina [2], Salvo Sotera [3] and Gaetano Oliva [1]

Local episodes of dog-to-dog *Leishmania* transmission by non-vectorial routes, including sexual, vertical or blood transfusion-borne infections, should not be attributable to an endemic status of the area in the absence of the specific vector



RESEARCH Open Access

Leishmania infantum and *Dirofilaria immitis* infections in Italy, 2009–2019: changing distribution patterns

Jairo Mendoza-Roldan[1], Giovanni Benelli[2], Rossella Panarese[1], Roberta Iatta[1], Tommaso Furlanello[3], Frederic Beugnet[4], Andrea Zatelli[1] and Domenico Otranto[1,5*]

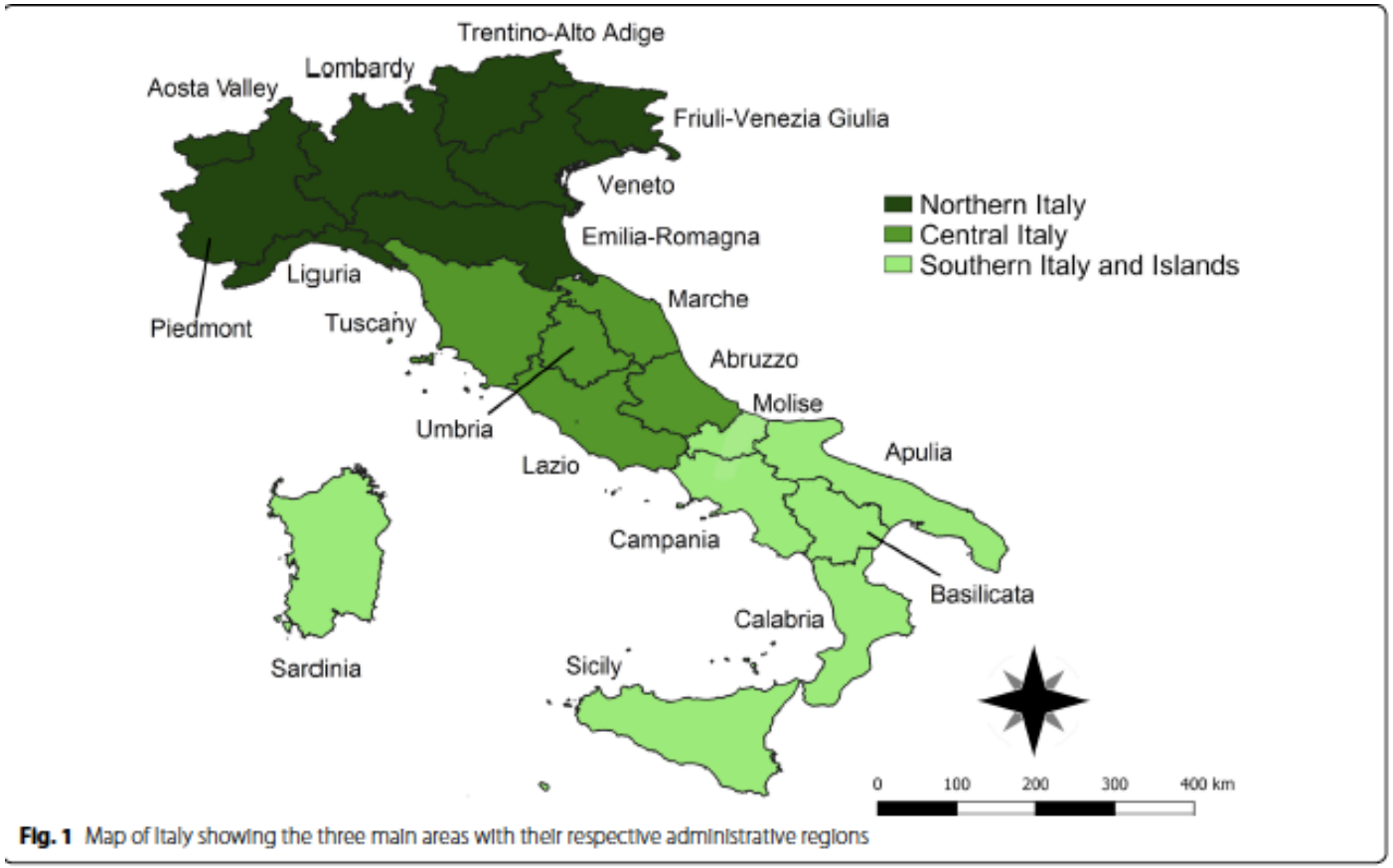


Fig. 1 Map of Italy showing the three main areas with their respective administrative regions

Table 1 Number (*n*) and percentage of serological tests positive for canine leishmaniosis and hearthworm disease in three main macroareas of Italy

Species	North *n* (%)	Centre *n* (%)	South and Islands *n* (%)
Leishmania infantum	4664 (21.6) (Total: 21,545)	7801 (29.6) (Total: 26,128)	9208 (28.2) (Total: 32,610)
Dirofilaria immitis	151 (2.8) (Total: 5335)	243 (7.8) (Total: 3119)	93 (4.9) (Total: 1866)

Kostopoulou et al. Parasites Vectors (2020) 13:282
https://doi.org/10.1186/s13071-020-04153-8

Parasites & Vectors

RESEARCH Open Access

Mapping the canine vector-borne disease risk in a Mediterranean area

Despoina Kostopoulou[1†], Manuela Gizzarelli[2†], Panagiota Ligda[1†], Valentina Foglia Manzillo[2], Katerina Saratsi[1], Serena Montagnaro[2], Bettina Schunack[3], Annette Boegel[3], Matthias Pollmeier[3], Gaetano Oliva[2*] and Smaragda Sotiraki[1*]

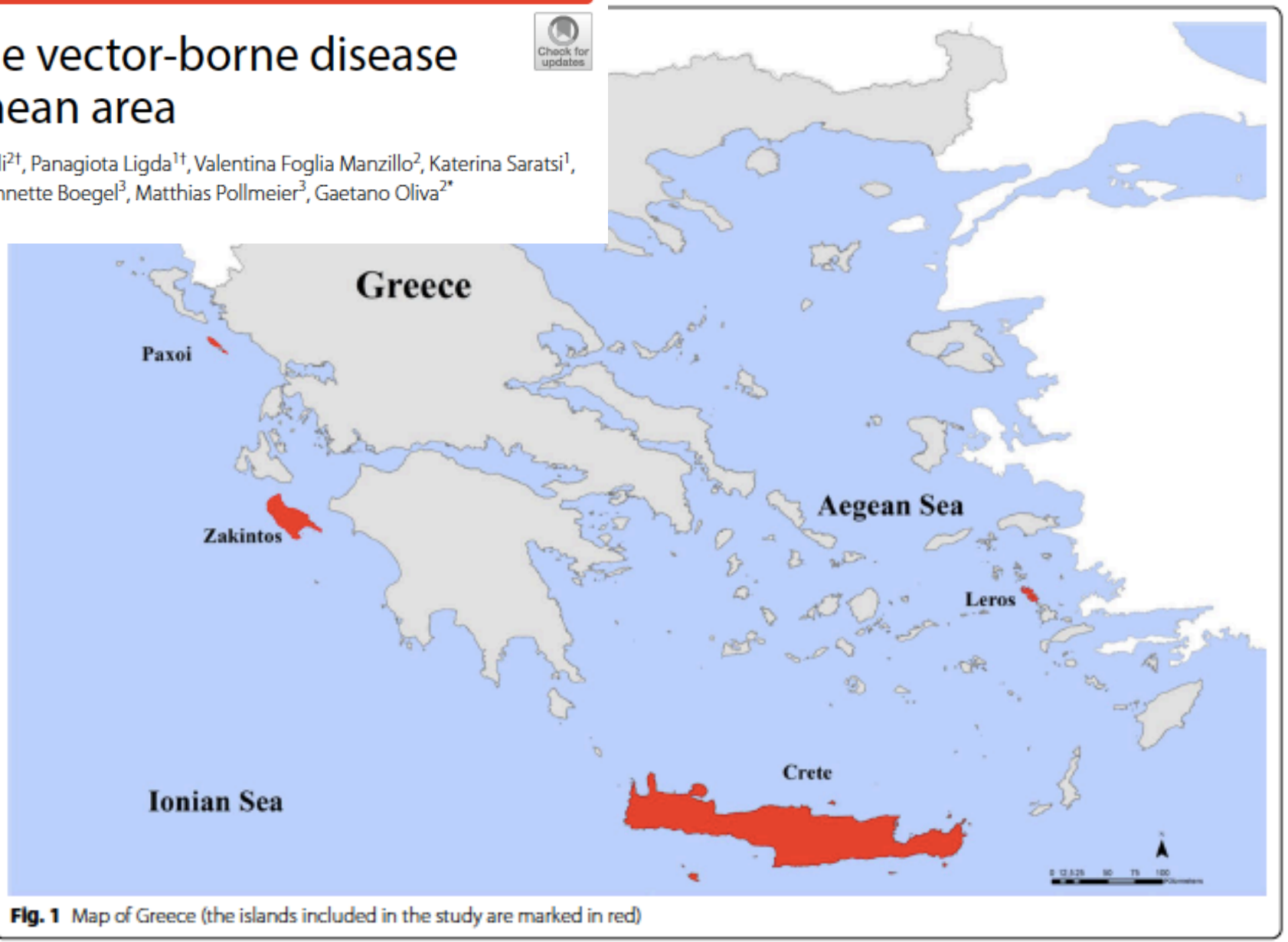


Fig. 1 Map of Greece (the islands included in the study are marked in red)

Does co-infection with vector-borne pathogens play a role in clinical canine leishmaniosis?

Marta Baxarias[1], Alejandra Álvarez-Fernández[1], Pamela Martínez-Orellana[1], Sara Montserrat-Sangrà[1], Laura Ordeix[1,2], Alicia Rojas[3], Yaarit Nachum-Biala[3], Gad Baneth[3] and Laia Solano-Gallego[1*]

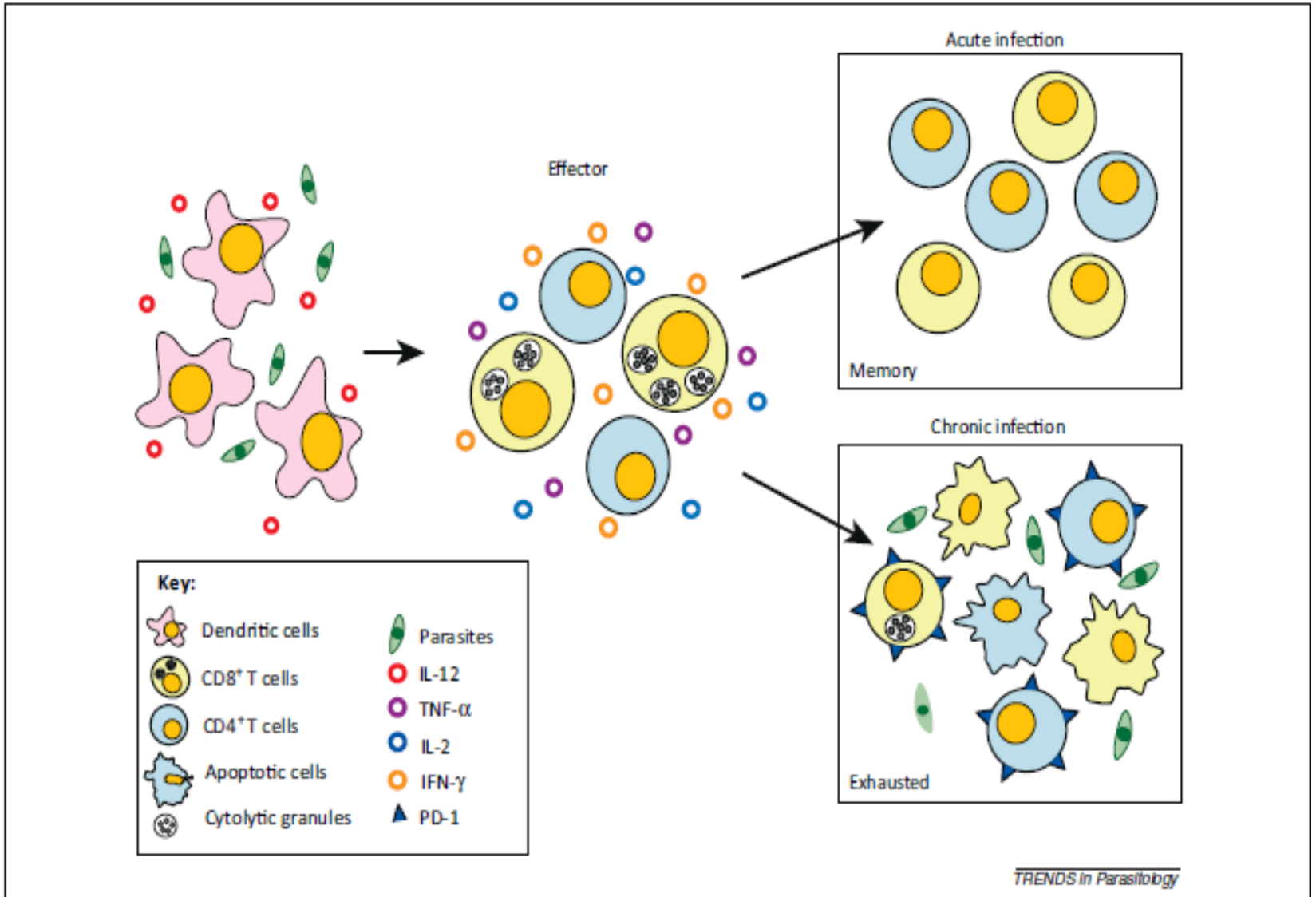
Comorbid infections induce progression of visceral leishmaniasis

Angela J. Toepp[1,2], Glória R. G. Monteiro[3], José F. V. Coutinho[3], Adam Leal Lima[1,2], Mandy Larson[1,2], Geneva Wilson[1,2], Tara Grinnage-Pulley[1,2], Carolyne Bennett[1,2], Kurayi Mahachi[1,2], Bryan Anderson[1,2], Marie V. Ozanne[4], Michael Anderson[1,2], Hallie Fowler[1,5], Molly Parrish[1,2], Kelsey Willardson[1,2], Jill Saucier[6], Phyllis Tyrell[6], Zachary Palmer[7], Jesse Buch[6], Ramaswamy Chandrashekar[6], Grant D. Brown[4], Jacob J. Oleson[4], Selma M. B. Jeronimo[3] and Christine A. Petersen[1,2,5*]

Ehrlichia canis and *Leishmania infantum* co-infection: a 3-year longitudinal study in naturally exposed dogs

Y. Mekuzas[1], L. Gradoni[2], G. Oliva[3], V. Foglia Manzillo[3] and G. Baneth[1]

T cell exhaustion *(Boggiatto, 2010)*



- 2/10/2019
- prof oliva sono…… medico veterinario di Mottola (TA) .ho letto abstract del suo lavoro su caso di leishmaniosi e linfoma nel cane.
- vorrei mostrarvi alcuni quadri citologici linfonadali prescapolari da me prodotti in ambulatorio su jack r. maschio di 7 anni, trattato l'anno scorso per leishmaniosi a prevalenza cutanea. il cane ha risposto benissimo al trattamento che per difficoltà di gestione del proprietario ha richiesto Milteforan - allopurinolo.
- a distanza di un anno mi portano il cane con un ingrossamento linfonodale (prescapolare-retrofaringeo) rapido a dire del proprietario. procedo con aspirato dal destro circa 5 cm indicativamente e esaminandolo mi ritrovo un quadro simil linfomatoso in assenza di amastigoti. Se disponibili proprietari procedo con ulteriori indagini. le invio citologico. il cane non mostra altri segni clinici e i linfonodi poplitei sono nella norma.
- grazie per l'attenzione mi sarebbe di grande supporto un vostro parere sul caso.
- saluti

Clinically healthy but infected

Th1 like response

Low serology

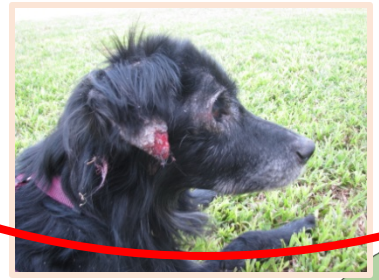
Predominant cellular immunity

Low parasite load (control infection)

L. infantum clinical manifestation

Self-limiting disease

Severe non self-limiting disease



Th2 like response

High serology

Decrease cellular immunity

High parasite load (dissemination of infection)

Solano-Gallego et al., 2011. Parasites and Vectors

ORIGINAL RESEARCH ARTICLE

Front. Vet. Sci., 19 May 2020 | https://doi.org/10.3389/fvets.2020.00273 (https://doi.org/10.3389/fvets.2020.00273)

Assessment of Circulating Immune Complexes During Natural and Experimental Canine Leishmaniasis

Manuela Gizzarelli (https://www.frontiersin.org/people/u/794567)[1], Eleonora Fiorentino (https://www.frontiersin.org/people/u/894158)[2], Nour El Houda Ben Fayala (https://www.frontiersin.org/people/u/753070)[1], Serena Montagnaro[1], Raquel Torras (https://www.frontiersin.org/people/u/894153)[3], Luigi Gradoni (https://www.frontiersin.org/people/u/600037)[2], Gaetano Oliva (https://www.frontiersin.org/people/u/755558)[1*] and Valentina Foglia Manzillo (https://www.frontiersin.org/people/u/750041)[1]

[1]Department of Veterinary Medicine and Animal Production, University of Naples Federico II, Naples, Italy

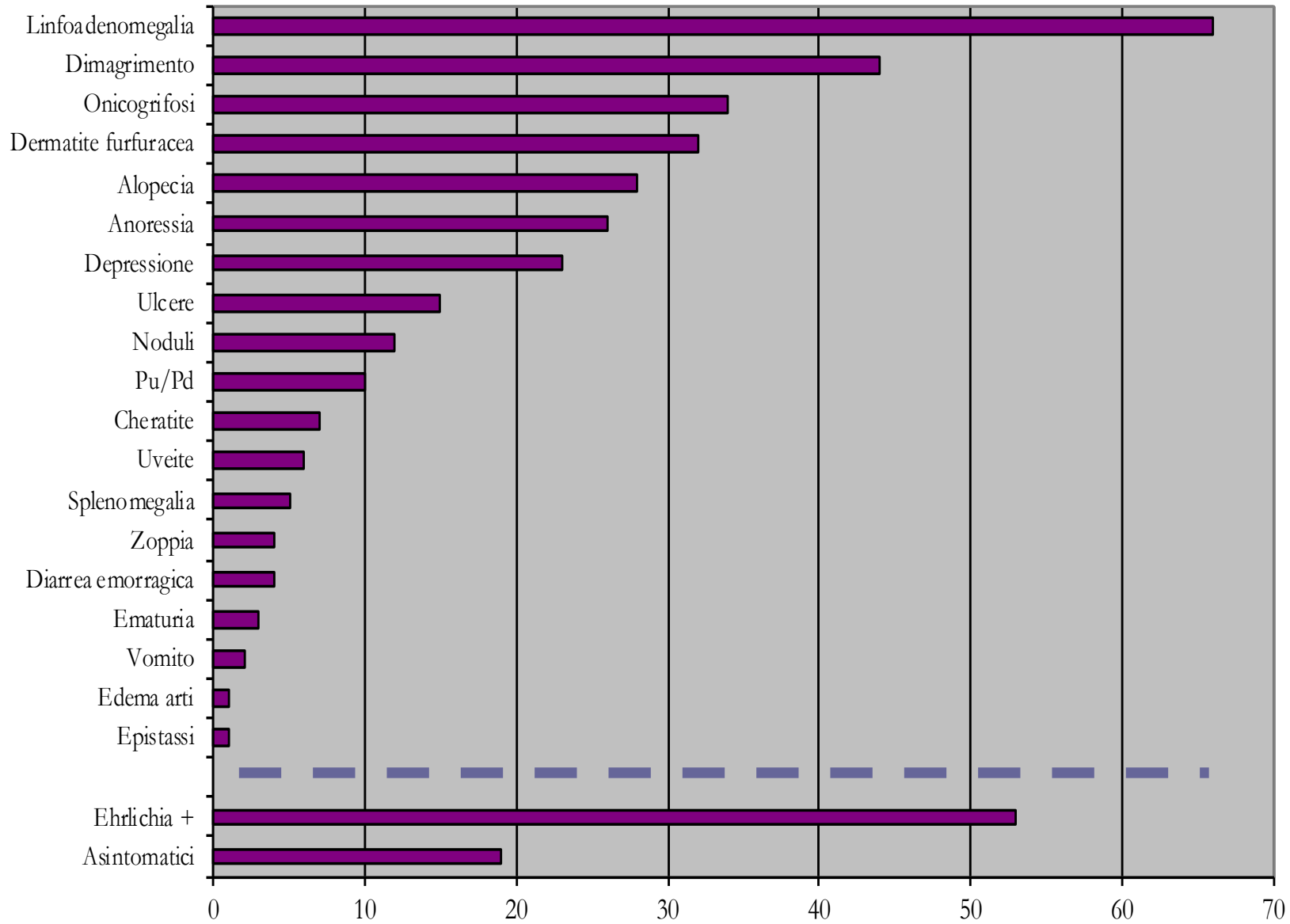
[2]Unit of Vector-Borne Diseases, Department of Infectious Diseases, Istituto Superiore di Sanità, Rome, Italy

[3]ISOQUINEM SL, Sant Feliu de Codines, Spain

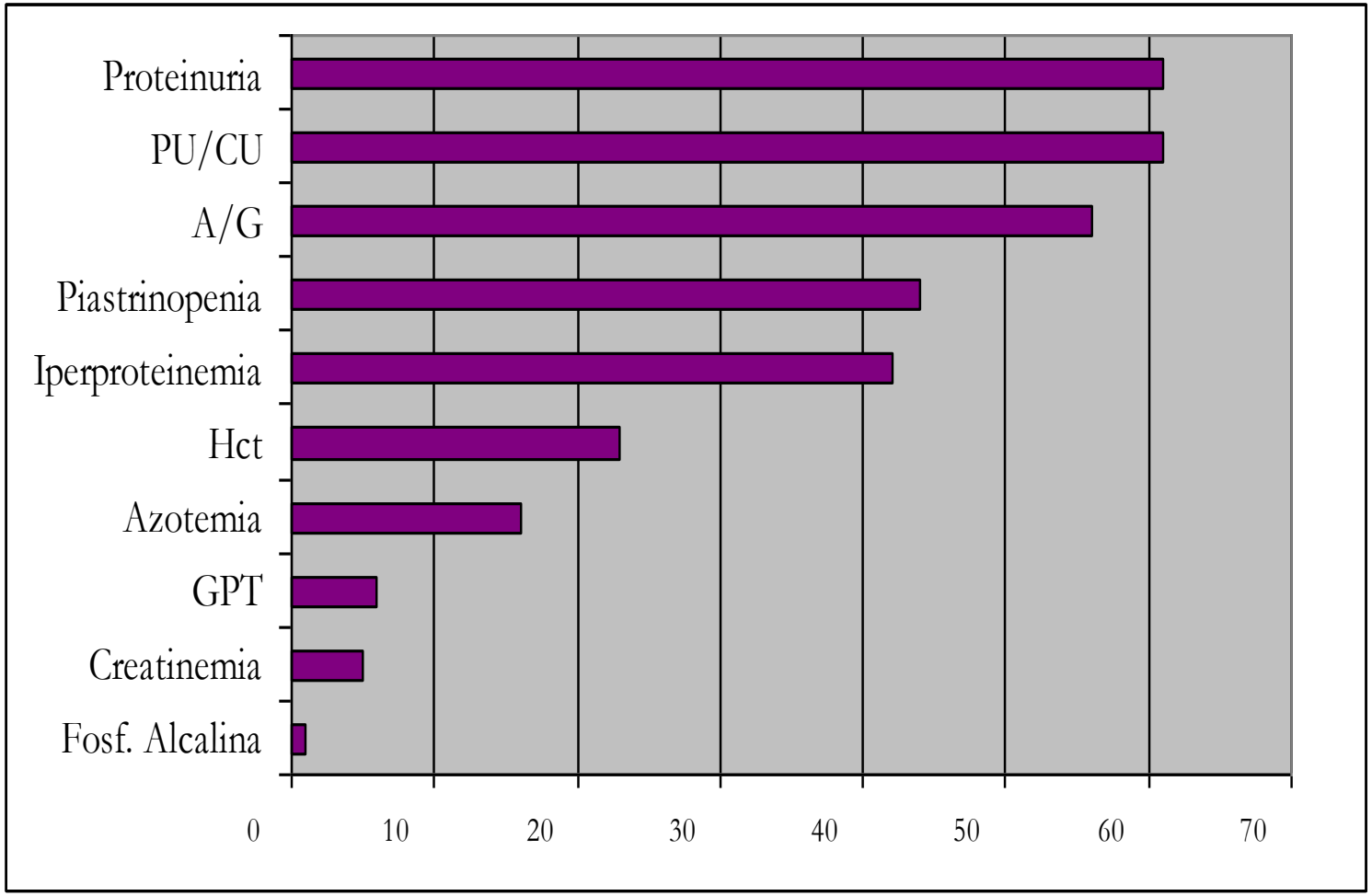
Table 1 Clinical manifestations and laboratory abnormalities found in canine leishmaniosis due to *L. infantum*

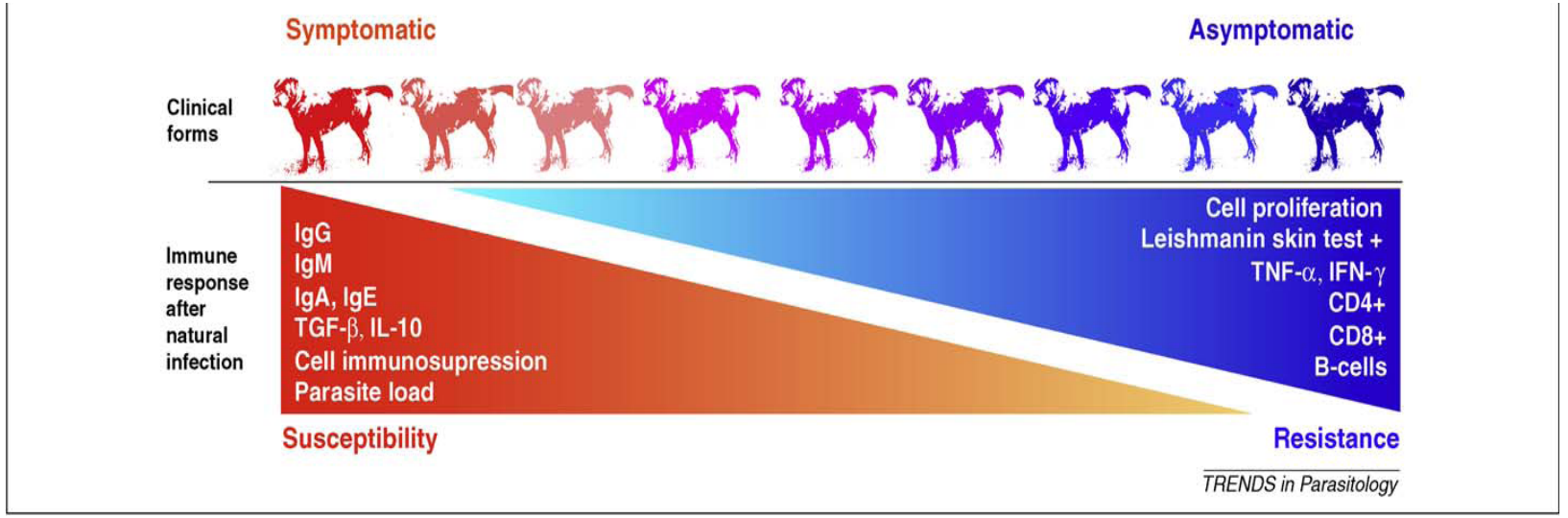
Clinical manifestations	Laboratory abnormalities
General ○ Generalized lymphadenomegaly ○ Loss of body weight ○ Decreased or increased appetite ○ Lethargy ○ Mucous membranes pallor ○ Splenomegaly ○ Polyuria and polydypsia ○ Fever ○ Vomiting ○ Diarrhea (including chronic colitis)	Serum proteins and electrophoretogram ○ Hyperglobulinemia Polyclonal beta and/or gammaglobulinemia ○ Hypoalbuminemia ○ Decreased albumin/globulin ratio
Cutaneous ○ Non-pruritic exfoliative dermatitis with or without alopecia ○ Erosive-ulcerative dermatitis ○ Nodular dermatitis ○ Papular dermatitis ○ Pustular dermatitis ○ Onychogryphosis	CBC/Hemostasis ○ Mild to moderate non-regenerative anemia ○ Leukocytosis or leukopenia ○ Thrombocytopathy ○ Thrombocytopenia ○ Impaired secondary hemostasis and fibrinolysis
Ocular ○ Blepharitis (exfoliative, ulcerative, or nodular) and conjunctivitis (nodular) ○ Keratoconjunctivitis, either common or sicca ○ Anterior uveitis/Endophtalmitis	Biochemical profile/urinalysis ○ Mild to severe proteinuria ○ Renal azotemia ○ Elevated liver enzyme activities
Other ○ Mucocutaneous and mucosal ulcerative or nodular lesions (oral, genital and nasal) ○ Epistaxis ○ Lameness (erosive or non-erosive polyarthritis, osteomyelitis, polymyositis) ○ Atrophic masticatory myositis ○ Vascular disorders (systemic vasculitis, arterial thromboembolism) ○ Neurological disorders	

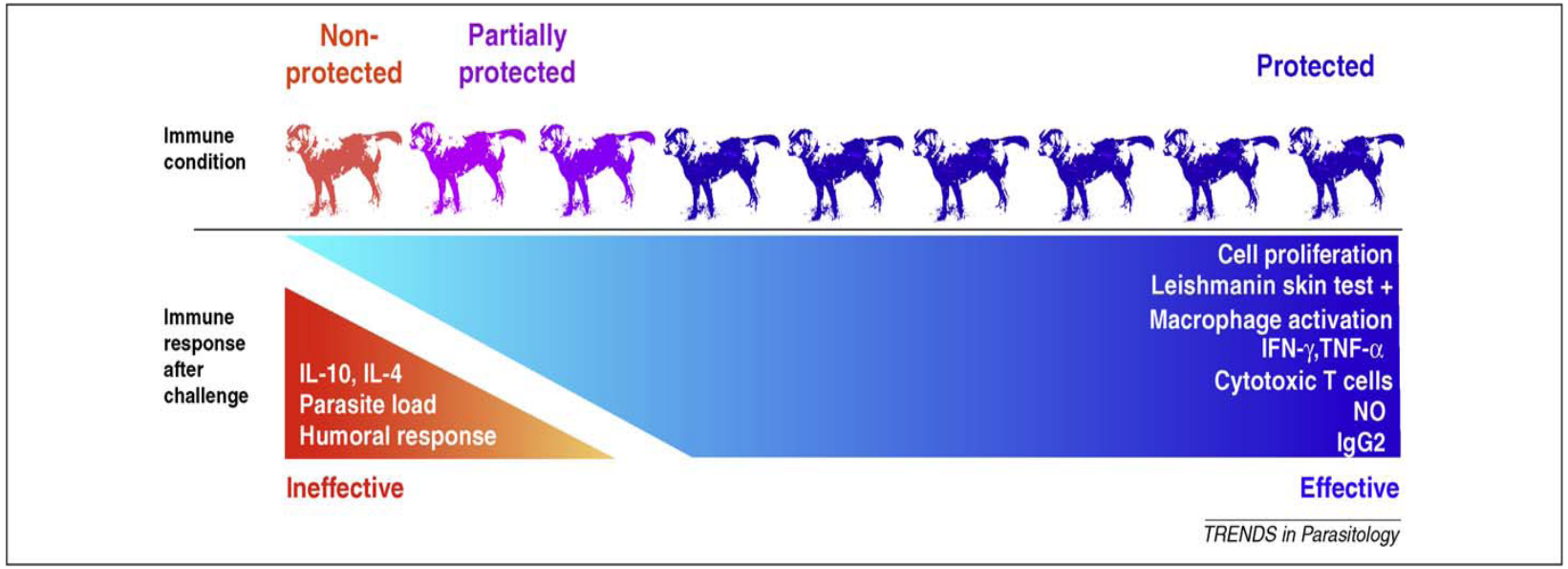
Incidenza (%) dei Segni Clinici (n. 100 casi prima visita)



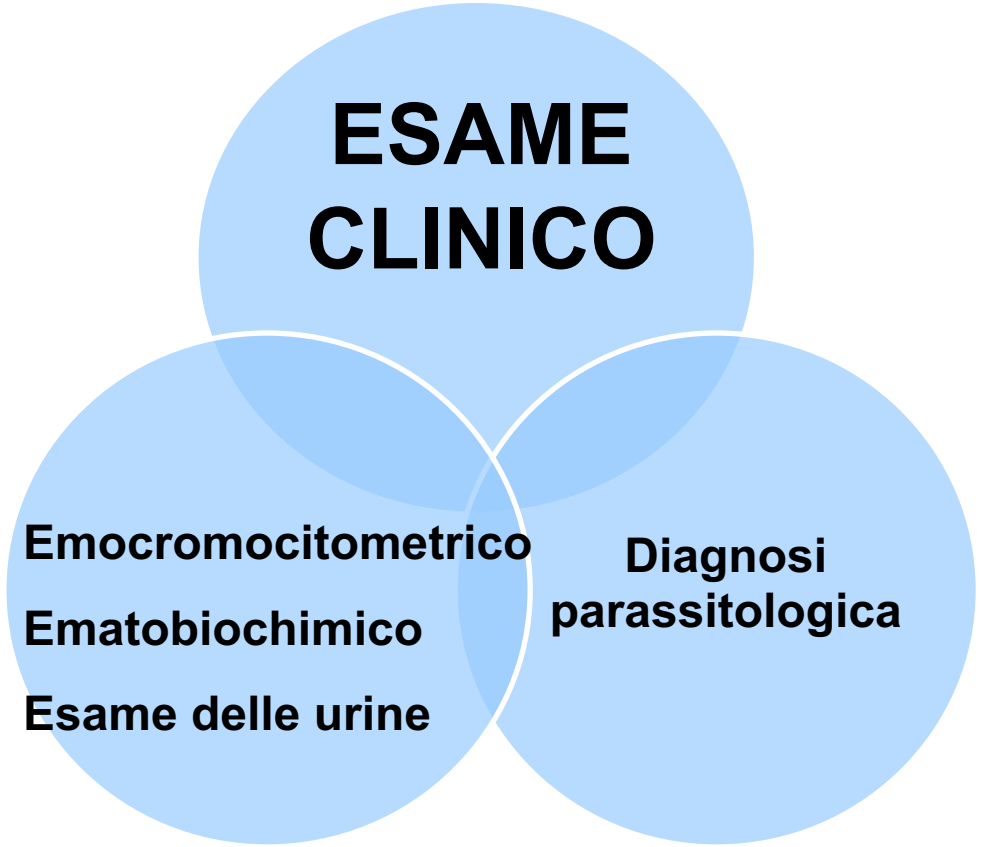
Incidenza (%) delle alterazioni clinico-patologiche (n. 100 casi prima visita)







Reis at al., Trends Parasitolgy 2010



STADIAZIONE

ESAME CLINICO

- SEGNALAMENTO
- ANAMNESI
- ESAME OBIETTIVO GENERALE
- ESAME OBIETTIVO PARTICOLARE
- DIAGNOSI DIFFERENZIALI

- *INDAGINI DI LABORATORIO*
- *DIAGNOSTICA PER IMMAGINI*

Management of canine leishmaniosis in endemic SW European regions: a questionnaire-based multinational survey

Patrick Bourdeau, Manolis N Saridomichelakis, Ana Oliveira, Gaetano Oliva, Tina Kotnik, Rosa Gálvez, Valentina Foglia Manzillo, Alex F Koutinas, Isabel Pereira da Fonseca *and* ***Guadalupe Miró***

Parasites & Vectors 2014

Table 3 Percentages of clinical signs on which veterinarians based their suspicion of CanL

Clinical signs %	France n = 994			Greece n = 201			Italy n = 231		
	Never	Occasional to frequent	Always	Never	Occasional to frequent	Always	Never	Occasional to frequent	Always
Weight loss	4.8	74.8	20.4	0.5	73.7	25.8	0.9	80.4	18.7
Alopecia	12.3	78.3	9.4	2.8	92.7	4.5	2.3	86.7	11
Lymphadenomegaly	9.1	70.6	20.3	0.5	70.8	28.6	4.6	71.2	24.2
Lethargy	13.2	78	8.8	4	88.4	7.5	5.1	87	7.9
Pale mucosa	21.3	73.2	9.4	1.1	87	12	4.2	88.8	7
Exfoliative dermatitis	21.6	35.8	6.8	4.8	91.1	4.1	1.9	87.6	10.5
Onychogryphosis	14.1	77.8	8	5	90	5	6.8	83.1	10
Skin ulcers	22.7	72.9	4.4	5.5	89	5.5	4.7	12.3	83
Pyodermatitis	21	73.3	5.7	12.5	86.9	0.6	0.5	11.7	87.8
Footpad lesions	20.1	76.9	3	19.6	80.4	0	12.7	85.4	1.9
Cutaneous depigmentation	49.8	48.7	1.5	34	66	0	33	64.6	2.4
Cutaneous nodules	48.9	48.2	2.9	46.1	53.9	0	27.6	69	3.4
Renal disease	16.2	79.1	4.7	2.8	97.2	0	4.1	90	5.9
Ocular lesions	25.8	71.1	3	5.5	89.5	5	18.2	0	81.8
Epistaxis	30.1	68.2	1.6	7.5	91.9	0.5	40	6.7	53.3
Arthropathies	42.5	56.3	1.3	16	83.4	0.6	59.2	40.3	0.5
Fever	38.6	58.6	2.9	41.4	58.6	0	35.9	63.2	1
Diarrhoea	58.1	40.9	0.9	33.5	66.5	0	38	60.2	1.9
	Slovenia n = 49			Spain n = 483			Portugal n = 141		
Weight loss	0	81.8	18.2	3.1	70.8	26.1	1.4	66.2	26.6
Alopecia	0	100	0	1.6	85.9	12.5	1.4	80.6	10.1
Lymphadenomegaly	0	100	0	13.0	61.3	25.7	2.9	69.8	18.0
Lethargy	0	81.8	18.2	3	90.4	6.7	5.8	77.0	3.6
Pale mucosa	0	90	10	4.3	87.7	8	6.5	76.3	4.3
Exfoliative dermatitis	9.1	90.9	0	2.8	82.8	14.4	3.6	77.0	6.5
Onychogryphosis	0	100	0	5.7	85.8	8.5	3.6	81.3	5.8
Skin ulcers	0	100	0	5.5	88	6.4	7.2	79.9	2.2
Pyodermatitis	0	90.9	9.1	7.3	86.7	6.1	8.6	78.4	0.7
Footpad lesions	0	100	0	13.2	84.2	2.6	10.8	76.3	1.4
Cutaneous depigmentation	0	100	0	21.9	75.4	2.7	2.9	53.2	3.6
Cutaneous nodules	0	100	0	23.8	73.7	2.5	20.1	48.9	15.8
Renal disease	0	100	0	7	89.1	4	3.6	85.6	1.4
Ocular lesions	0	90	10.0	7.9	87.1	4.9	10.1	77.7	1.4
Epistaxis	11.1	88.9	0	8.2	73	18.8	8.6	79.1	0.0
Arthropathies	0	100	0	13.2	84.9	1.9	21.6	64.7	0.7
Fever	0	90.9	9.1	38.7	60.5	0.7	32.4	54.0	0.0
Diarrhoea	0	90.9	9.1	30.2	69.3	0.5	33.1	51.8	0.0

Table 4 Diagnostic tools used by veterinarians to confirm a suspected case of CanL

Technique %	France n = 994			Greece n = 201			Italy n = 231		
	Never	Occasional to frequent	Always	Never	Occasional to frequent	Always	Never	Occasional to frequent	Always
Cytology									
Lymph nodes	34.6	52.8	12.6	21.4	58.6	20	46.7	48.0	5.3
Bone Marrow	65.5	30.6	3.9	69.6	29.4	1.1	59.9	33.6	6.6
Skin lesions	65	28.9	6.1	56.6	40.4	3	28.8	56.5	14.7
Serology									
IFAT	22.7	28.7	48.6	16	45	39	4.3	48.9	46.8
Rapid tests	42	33.9	24	4.6	37.1	58.3	30.9	38.2	30.9
ELISA	13.5	34.7	51.9	14.3	58.9	26.8	25.2	37.7	37.1
Other techniques									
PCR	55.7	36.6	7.7	52.1	46.4	1.4	20.9	66.9	12.2
Protein electrophoresis	42.3	41	16.8	76.6	20.4	2.1	10.6	39.8	49.7
Histopathology	51.1	45.8	3.1	72.3	27.7	0	64.9	35.1	0
Immunohistochemistry	94.3	4.7	1	94.5	5.5	0	83	13.8	3.2
	Slovenia n = 49			**Spain n = 483**			**Portugal n = 141**		
Cytology									
Lymph nodes	2	4	0	14.3	80.2	5.5	19.4	72.1	8.6
Bone Marrow	2	2	0	18.1	71.4	10.5	36.2	53.2	10.6
Skin lesions	6.1	2	0	34.2	61.8	3.9	82.9	14.6	2.4
Serology									
IFAT	0	4	0	6.3	37.9	55.9	9.4	36.7	25.9
Rapid test	0	2	2	11.5	54.0	34.5	20	43.5	36.5
ELISA	0	2	6.1	42.3	47.3	10.4	43.9	43.9	12.2
Other techniques									
PCR	0	2	2	8.3	86.6	5.1	57.8	37.6	4.7
Protein electrophoresis	0	2	0	nd	Nd	nd	96.5	1.8	1.8
Histopathology	0	4.1	0	35.3	63.9	0.8	91.5	6.8	1.7
Immunohistochemistry	0	2	0	15.0	40.4	44.6	33.8	48.8	17.5

nd: not determined.

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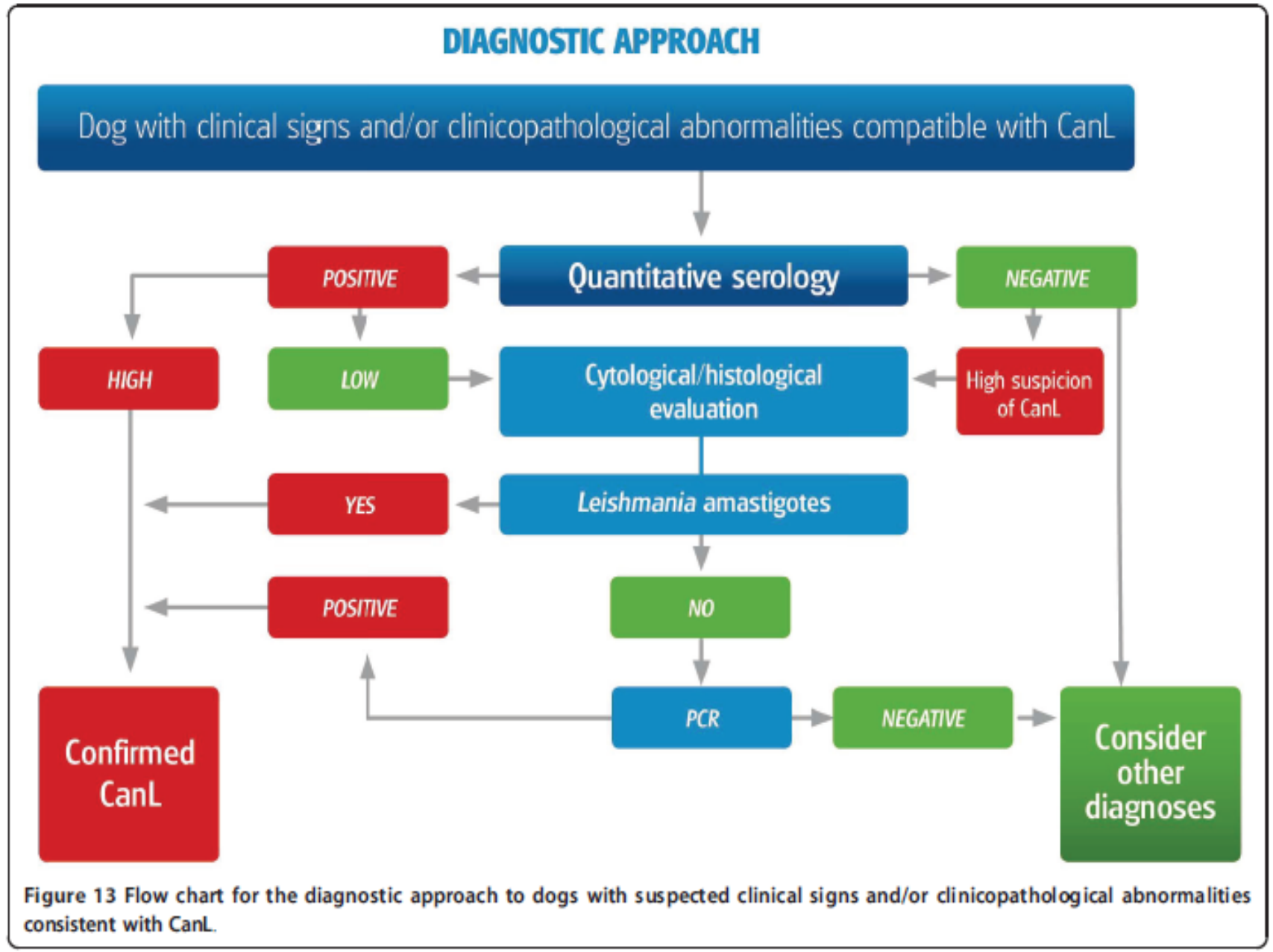

Figure 13 Flow chart for the diagnostic approach to dogs with suspected clinical signs and/or clinicopathological abnormalities consistent with CanL.

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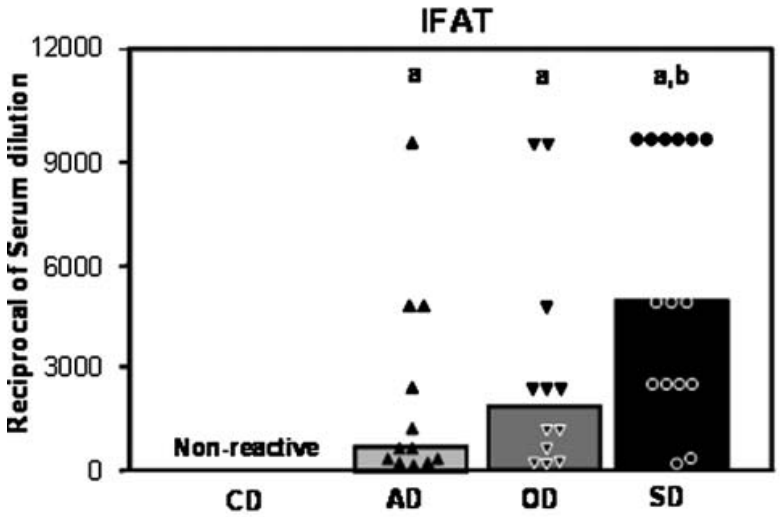
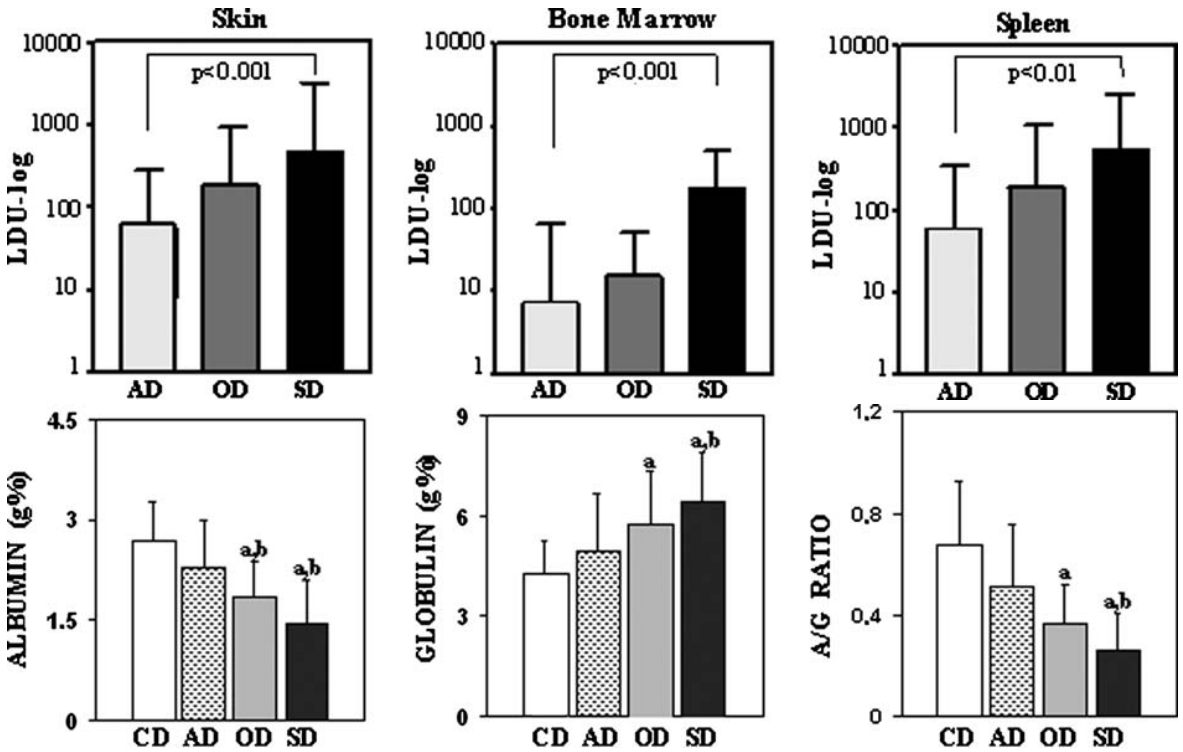
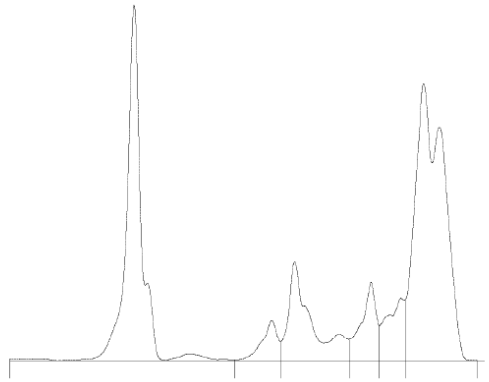
Reis AB et al., Res Vet Sci, 2006







Proteine Totali	**9.13**		(5.70	-	7.70)	g/dl			
Prealbumine									
Albumine	**28.70**	(44.40	-	65.70)	%	Albumine	2.62	(2.40	- 4.90) g/dl
Alfa totali	15.80	(9.30	-	24.00)	%	Alfa totali	1.44		- g/dl
Alfa 1	3.40	(2.00	-	7.30)	%	Alfa 1	0.31	(0.17	- 0.40) g/dl
Alfa 2	12.40	(6.20	-	16.70)	%	Alfa 2	1.13	(0.40	- 1.00) g/dl
Beta Totali	12.50	(9.20	-	31.80)	%	Beta Totali	1.14		- g/dl
Beta 1	6.30	(2.90	-	11.10)	%	Beta 1	0.58	(0.10	- 0.80) g/dl
Beta 2	6.20	(6.30	-	20.70)	%	Beta 2	0.57	(0.40	- 1.60) g/dl
Gamma	**43.00**	(4.50	-	20.10)	%	Gamma	3.93	(0.20	- 1.20) g/dl
Rapporto A/G	**0.40**	(0.80	-	1.90)					

Table 3 Advantages and disadvantages of common diagnostic methods for the detection of *L. infantum* infection in dogs

DIAGNOSTIC TECHNIQUES	ADVANTAGES	DISADVANTAGES
SEROLOGY	• Determination of antibody level which is essential for the diagnosis and establishing a prognosis	• Does not detect the actual presence of the *Leishmania* parasite • Serocrossreactions with trypanosomes
QUALITATIVE	• Rapid in-clinic test	• Provides only positive or negative result • Variable sensitivities and performance with risk of false negatives • A positive result needs to be further evaluated by a quantitative serology
QUANTITATIVE (IFAT, ELISA)	Determines the antibody level • High antibodies levels in the presence of compatible clinical signs and/or clinicopathological abnormalities are conclusive of clinical leishmaniosis	• Performance and accuracy of cut-off will depend on the laboratory • Differences between laboratories and poor standardization of techniques • Low antibody levels will require further work-up
CYTOLOGY/ HISTOPATHOLOGY	Permits direct detection of the parasite itself and the type of pathological findings: - Pathological findings suspicious of infection - Allows exclusion of other differential diagnoses - Rapid and non invasive (cytology)	• Low sensitivity for the detection of *Leishmania* amastigotes in tissues or body fluids • Requires the performance of other diagnostic tests such as immunohistochemistry and/or PCR when parasites are not visualized • Does not reveal the immunological status of the dog • Needs expertise
PCR	• Allows the detection of leishmanial DNA • High sensitivity (kDNA) and specificity • Parasitic load quantification (if Real time-PCR)	• False positive results possible due to DNA contamination • Different standardization and techniques used by different diagnostic laboratories • Does not reveal immunological status • It cannot be performed as the sole diagnostic technique for the confirmation of the disease because a positive result confirms *Leishmania* infection but not disease
PARASITE CULTURE	• Permits the isolation of *Leishmania* parasites • Facilitates the isoenzymatic identification of the parasite	• Time-consuming and laborious diagnostic technique • It can require one month to provide a result • Performed only in research laboratories

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 as examples: 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 instaured 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://www.iris-kidney.com/guidelines/en/staging_ckd.shtml