## **Trypanosomatid Pathogens**

Subjects: Microbiology

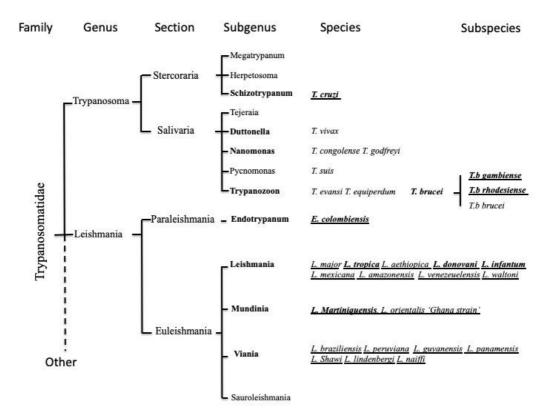
Contributor: Denis Sereno, Mohammad Akhoundi, Kourosh Sayehmri, Asad Mirzaei, Philippe Holzmuller, Veerle Lejon, Etienne Waleckx

Unicellular eukaryotes of the Trypanosomatidae family include human and animal pathogens that belong to the *Trypanosoma* and *Leishmania* genera. Diagnosis of the diseases they caused requires the sampling of body fluids (blood, lymph, peritoneal fluid, cerebrospinal fluid, etc.) or organ biopsies (bone marrow, spleen, etc.), which are mostly obtained through invasive methods. Body fluids or appendages can be alternatives to these invasive biopsies but their appropriateness remains poorly studied. To further address this question, we perform a systematic review on clues evidencing the presence of parasites, genetic material, antibodies, and antigens in body secretions, appendages, or the organs or proximal tissues that produce these materials.

Keywords: Trypanosoma; Trypanosomiasis; Leishmaniasis; Chagas disease; Canine Leishmaniasis; Human African Trypanosomiasis; Sleeping sickness; Animal trypanosomiasis; Dourine; Nagana; Canine visceral leishmaniasis; Feline leishmaniasis; Diagnosis; Noninvasive biopsy; Urine; Feces

## 1. Introduction

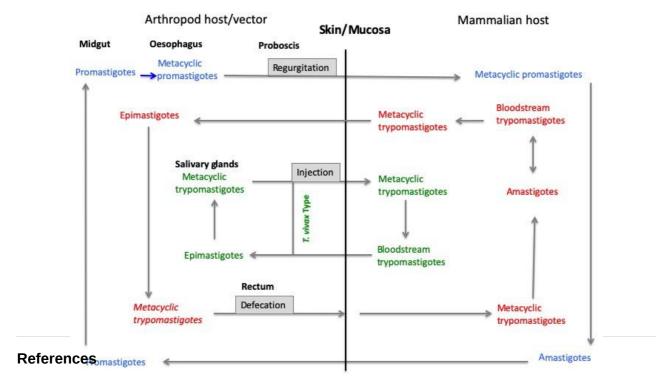
Unicellular eukaryotes of the Trypanosomatidae family include human and animal pathogens that belong to the *Trypanosoma* and *Leishmania* genera (including *Endotrypanum*) (Figure 1). *Leishmania* and possibly *Trypanosoma* are probably descended from the parasites of blood-sucking insects that survived accidental transmission to a vertebrate host during feeding  $^{[1]}$ .



**Figure 1. Classification of human and animal pathogenic trypanosomatids.** Human pathogenic species are underlined, and pathogens causing systemic infection are in bold.

They possess a complex life cycle that includes arthropod vectors belonging to the Hemiptera and Diptera orders (Figure 2). Two *Trypanosoma* subspecies of *T. brucei* (i.e., *Trypanosoma brucei gambiense*, *T. brucei rhodesiense*) and *T. cruzi*, along with 21 species of *Leishmania*, are pathogenic for humans. They cause human African trypanosomiasis (HAT or

sleeping sickness), Chagas disease (CD), and cutaneous (CL), muco-cutaneous (MCL) or visceral (VL) leishmaniases  $^{[2]}$  (http://leishmania.ird.fr/). Occasional infections in humans with *T. evansi*, *T lewisi*, *T. brucei brucei* or *T. congolense* have been described, but little is known about the public health importance of these diseases  $^{[6]}$ .



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- Figure 2: Developmental life cycle of Leishmania (blue), *T. cruzi* (red), and *Trypanosoma sp* (green) 2. NTD Modelling Consortium Discussion Group on Gambiense Human African Trypanosomiasis; Insights from In auditivative their implaematival mandelliague, the problems of all sold their considerations of the second of the
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Gilberto Silva Nunes Bezerra; Walter Lins Barbosa; Elis Dionisio Da Silva; Nilma Cintra Leal; Zulma Maria De Refinements in PCR technologies included the development of nested PCR and of multiplexed PCR methodologies that Medeiros, Urine as a promising sample for Leishmania DNA extraction in the diagnosis of visceral leishmaniasis - a have increased sensitivity and discriminative capacity of the stest 19ther refinement in the detection of the amplified review. The Brazilian Journal of infectious Diseases 2019, 23, 111-120, 16-10-1016, 17-10product includes PCR-ELISA (Enzyme-Linked Immunosorbent Assay). PCR-RFLP (Restriction fragment Lenght 34 Tribhuvan M. Mohapatra: Dharmendra P. Singh: Rahul K. Goval: Rahul K. Singh: S. Sundar: In Search of an Ideal Test Polymorphism) allows detecting variation between DNA fragments patterns, generated by restriction enzyme digestion for Diagnosis and Prognosis of Kala-azar. *Journal of Health, Population and Nutrition* **2010**, 28, 281-285, 10.3329/jhpn. caused by alternative nucleotides at the restriction sites that can be used for *Leishmania* and trypanosome species discrimination. PCR-HRM (High Resolution Melting) detects dsDNA alternatives by ascertaining changes in the Skudiesteracenweasityich Tardnanvaadaalainiynaaqquikiadyavatdisabcidiian; Badelssicivaatiiae; Alapadondvanalsuna) to singlivertrande Sabrias est; bhay. 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LAMP can be more sensitive than conventional PCR for the detection of steisemaniand: Typanosonabasacies: 1501/6 Adder 22: 1700 die 22: 1700 is basedenadeardelsyecutyaethyaansassiivitytebtoh) opertionaanisedfalloving genadermal injurior fotiokilach bleis/vooria proTnasti@0163; indo,tilde-si/2n forearm. It does not require biological sampling. Indirect immunofluorescence (IFAT) relies on 3be Nicolas veitrida vered on esturorescent glass slide that is used to test the presence of anti-parasites anti-hodies in the patient; salejan dibie lands colonius, van disa ke bog the perchiagase is na in bagas i dispase calcroing si khansa ke shananiasis and harumal to make the personal residents with Cuttratous the dology cistaffeous edifferous ediffe viswalian in the original specific than viswalian specific than the original specific than the origina ELISA (see below). The direct agglutination test (DAT), further modified for detection of the agglutination activity on a card 39. Laia Solano-Gallego; Alheli Rodriguez-Cortés; Michele Trotta; Claudia Zampieron; Luis Razia; Tommaso Furlanello; (CATT) allows the visualization of the precipitin activity. It uses whole micro-organisms as a mean of looking for serum Marco Caldin; Xavier Roura; J. Alberola; Detection of Leishmania infantum DNA by fret-based real-time PCR in urine antibodies. CATT is a commonly serological test for HAT and is still in use for ArT secodiagnosis [21/27]. The agglutination from dogs with natural clinical leishmaniosis. Vererinary Parasirology 2007, 147, 315-319, 10:1016/j.vetpar.2007.04.01 methodology can also be performed with antibody coated latex beads to trap antigen. KAtex, a commercialized latex agglutination test, is developed for the diagnosis of visceral leishmaniasis and use a specific Leishmania antibody coated 40. Laura Manna: Stefano Reale: Esther Picillo: Fabrizio Vitale: Angelo Elio Gravino: Urine sampling for real-time on latex particles. Enzyme linked immunoabsorbent assays (ELISA) can be performed to detect and quantify polymerase chain reaction based diagnosis of canine leishmaniasis.. *Journal of Veterinary Diagnostic Investigation* antibodies or antigens in samples. Alternatively, sandwich ELISA can be used to detect circulating parasite's antigens, that 2008, 20, 64-67, 10.1177/104063870802000112. informs on the ongoing infectious process. Immunochromatography (ICT) or lateral flow test is based on a series of 42a Girkido Belds Grisholfas Charlea Fachlytaitia alashdri fillina saovillandan shanfile anailyte Ispaeacysilen han an Zetiad ackorand then sphritters 1985 militrates 16 176 fils 1016/s0040 4039 4039 5155 15 15 19 1016 soaked, the 42uid arigratesobnithe erganot etement incomigenanden anderdater tackere is persentrivation junition with actoe enparticles in the an ally treaming rates Biockheemit har dan ab Biophysic ad fixthere at east, Communitation tis 0.6922, 282, immobilized to stop the flow. 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- gen: genera. sp: species. DTU: discrete typing unit. NA: not available. DAT: direct agglutination test. CATT: card 78. Hall, J.E.; Seed, J.R. Quantification of aromatic amino acid catabolites in urine of mice acutely infected with agglutination test for trybanosomiasis. MLEE: multilocus enzymatic electrophoresis. MALDI-TOF: matrix-assisted laser Trypanosoma brucei gambiense. Comp. Biochem. Physiol 1981, 69B, 791-796. desorption ionization-time of flight. ICT: immunochromatographic test. ELISA: enzyme-linked immunosorbent assay. 7PCRUOCS FORMINE PORTION PORTION PARTICION PORTION PORT
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## 8<mark>2.3ulie:Systematile Gareview</mark>ut offer:Non-invasiveuetSamplingle:Strategiesga;forepithe Diagnosis;and:Detections offsTrypanosomatid PathogensaandaInfections

biological fluids of Trypanosoma brucei gambiense-infected subjects. Journal of Proteomics 2019, 196, 150-161, 10.10

The exploition of theory propriate biopsy for diagnoses relates to the physiopathology of the diseases, reflecting the disease pathogens within its host. Therefore, the diagnosis of these 83. Simaren, J.; Ogunnalke, M. Urinary biochemical changes, histopathologic effect of kidney damage observed in rats diseases requires the sampling of body fluids (blood, lymph, peritoneal fluid, cerebrospinal fluid, etc.) or organ biopsies infected with Trypanosoma B. brucei. Tropical Medicine and Parasitology 1989, 11, 35-46.

(bone marrow, spleen, etc.), which are mostly obtained through invasive methods. Alternative biological samples, such as Brown of Subjections (milk, safiva, urine, selfiel, has secretion, flacing fruid, early str., ssonganyi, E. Magnus; Absence of body seterions (milk, safiva, urine, selfiel, has secretion, flacing fruid, early str., swonganyi, E. Magnus; Absence of the Litat 13 (CATT antigen) gene in Trypanosoma brucei, dampiense stocks from Cameroon, Acta Tropica 1992, 51 (nail, hair, bristles, etc.) finat are constantly produced, might be an interesting alternative to invasive biopsies. No-invasive biological sampling that do not require trained professional and are easy and safe to collect would render the diagnosis 85 older or well-be an interesting alternative invasive the library for such Trypangsama are adultified also paper. A schematic overview is given in the Figure anti-phila and paper.

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- 3.1 Trypanesoma cruzi urinary antigen.. *Journal of Clinical Microbiology* **1989**, *27*, 145-151, <u>10.1128/jcm.27.1.145-151.198</u>
- 94' iResis an east to be lifet, secretion that is produced daily. Therefore a large amount of information; has been gathered on the presence of trypandamental pages to swithing this lifet.

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 antigens or DAT. The detection of the antibody response against Leishmania infection, due to L. major, L. tropica or L. 103. Jan Votýpka; Barbora Paťco; David Modrý; Donald Mbohli; Nikki Tagg; Klára J. Petrželková; An unexpected diversity of infantum, was also investigated using Western blot [36][39]. IgA or IgG are detected in the urine of dogs suffering from, trypanosomatids in fecal samples of great apes. International Journal for Parasitology: Parasites and Wildlife 2018, 7, leishmaniasis [60] where antibodies directed against L. infantum are present [61][62][63]. Because of the persistence of artibodies the content of the persistence of the persistenc
              antibodies after cure, these tests cannot be used to diagnose VL in people with a past history of VL. A search for
  104 Denis Sereno: F. Dorkeld: Mohammad Akboundi; Pascale Perijg; Pathoges Species Identification from Metagenomes.
             of infected individuals [67]. In L. infantum-infected patients, Iron superoxide dismutase, L. infantum tryparedoxin, and L.
             Tools. 2018, 10.20944/preprints201807.0124.v1. infantum nuclear transport factor 2 (LI-ntiz) were identified by mass spectrometry analysis [65,66]. When used in a
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 107 uAlexandre Fernandes Salinas Mayo Africae Trypanosomiases. Sheila M.E. Mendonga De Souza: Unit Dran and Dodies or
            Ferreira: Ana Carolina P Vicente: Ana M Jansen; Pre-Columbian Chagas disease in Brazil: Trypanosoma cruzi I in the antigens in the urine of human individuals affected by sleeping sickness was collected during the systematic review. The archaeological remains of a human in Peruacu Valley, Minas Gerais, Brazil. Memórias do Instituto Oswaldo Cruz 2008, sole evidence on the presence of genetic material in urine comes from an experimental infection of vervet monkeys by 103, 514-516, 10.1590/s0074-02762008000500021.

In this model, Trypanosoma DNA could be amplified from urine, with LAMP as early as 17 days postinfection [78].
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              experimentally 2nfacted 16/50156e6bishy agreement amino acid catabolism by African trypanosomes was associated
            with the large decrease in free serum levels of aromatic amino acids and with alterations in host tyrosine and 11. Michael Lewis; Amanda Fortes Francisco; Martin C. Taylor; Hollie Burrell-Saward; Alex P. McLatchie; Michael A. Miles; phenylalanine metabolism. These events correlate with the pathology of sleeping sickness and the depletion reported in John M. Kelly; Bioluminescence imaging of chronic Trypanosoma cruziinfections reveals tissue-specific parasite certain amino acids (tryptophan), which would lead to the depletion of essential metabolites such as serotonin and the dynamics and heart disease in the absence of locally persistent infection. Cellular Microbiology 2014, 16, 1285-1300, 1 toyicity of each products such as phenylayuruste reviewed in 1861. Changes in the urinary proteome of natients suffering
              toxicity of end proguets such as phenylpyruvate reviewed in [86]. Changes in the urinary proteome of patients suffering
              from sleeping sickness were observed, notably, in proteins related to several infectious processes. These changes can be
 112. Laura-Isabel McCall: Anupriva Tripathi: Fernando Vargas: Rob Knight: Pieter C. Dorrestein: Jair L. Siqueira-Neto: the fationale for developing moninvasive tools aimed at tracking the disease stage [87]. In animal models, P. brucei Experimental Chagas disease-induced perturbations of the fecal microbiome and metabolome. PLOS Neglected parasites are observed in the kidney glomeruli of infected rats, and T. lewisi in the kidney capillaries [88,89]. T. musculi, a Tropical Diseases 2018, 12, e0006344, 10.1371/journal.pntd.0006344.

parasite specific to mice, resides in the blood and lacks intracellular stages. After immune clearance of the flagellates from
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             Charges Disease Evidence on the capacity of cruzi to survive in urine came along with those on Leishmania [24], and \tau. cruzi amastigotes have been occasionally detected in the kidney [91]. Parasite DNA was detected in the urine of
115. Maria E. E. Brito: Ericka Lima Almeida: Angela Cristina Rapela Medeiros: Roberto Pereira Werkhauser: Joanna Lucia experimentally infected pigs (Sus scrota) or fince [92-94]. The crossing of T. Cruzi to urine in experimentally infected mice De Almeida Alexandre: Bruna Santos Lima Figueiredo Sá: Eduardo Henrique Gomes Rodriques: Sinval Pinto Brandão-is apparently independent of renal injuries [94]. The presence of DNA in urine is associated with the presence of parasite Filho: Leishmania (Viannia) braziliensis isolated from the saliva of patients in a cutaneous leishmaniasis-endemic area DNA in blood and heart and with a high level of parasite DNA in blood, but not with the presence of parasites in kidney or of northeastern Brazil. Memórias do Instituto Oswaldo Cruz 2018, 113, 10.1590/0074-02760170250.
kidney injury [94]. The detection of antigens within the urine of patients suffering from acute or chronic CD [95-97] has
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- 123. 2. Pricela Lombardo; Maria-Grazia Pennisi; Tiziana Lupo; Antonella Migliazzo; Alessandra Caprì; Laia Solano-Gallego; Detection of Leishmania infantum DNA by real-time PCR in canine oral and conjunctival swabs and comparison with Huntar ariatomanial techniques set entropy of an existence para and and conjunctival swabs and comparison with Huntar ariatomanial techniques set entropy of an existence para and and conjunctival swabs and comparison with Huntar ariatomanial techniques set entropy of an existence para and existence para and
- 125. Ben-Abid, M.; Galaï, Y.; Habboul, Z.; Ben-Abdelaziz, R.; Ben-Sghaier, I.; Aoun, K.; Bouratbine, A. Diagnosis of Humediterranea Two and sension and the control of the
- Chargast Briseast 1900 a Thom is a factor of the presence of 1274 in D. White the substantial particles in the substant of the presence of the
- mouse model of infection. In these experiments, parasite DNA was detected in the small intestine and rectum of the 128. P.D. Marsden; J.W.C. Hagstrom; Experimental Trypanosoma cruzi infection in beagle puppies. The effect of variations animals [119,120]. In infected mice, the gut is the primary site of parasite persistence in the BALB/c model of chronic in the dose and source of infection. Chagas dispasse of the infection.

  Chagas dispasse of the Royarsociated of Wildpicar Medicinie and Hygierlet 1968; 62, 816-824, 120, 1016/00335 9203 (68) 900105 massupialis), one of the multiple wild reservoirs of T. cruzi, the developmental cycle that usually occurs in the intestine of
- the triatomine vector can take place in the anal odoriferous glands [123]. In human feces, to our knowledge, no 129, R.T. Pinho; R.C. Pedrosa; P. Costa-Martins; L.R.R Castello-Branco; Saliva ELISA: a method for the diagnosis of information is currently published.

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  Nitz; Ludmilla M.S. Aguiar; Rodrigo Gurgel-Gonçalves; High frequency of trypanosomatids in gallery forest bats of a Hullandrian and the same and th
- amplified in *L. martiniquensis*-HIV positive and negative patients [41,126-129] but also in kala-azar patients infected by *L.* 133. Dongmei Yuan; Hanxiao Qin; Jianguo Zhang; Lin Liao; Qiwei Chen; Da-Li Chen; Jian-Ping Chen; Phylogenetic analysis donovani [73,130] and in dogs suffering from CVL [131,132]. In 1994, a report discussed the presence of agglutinating of HSPYO and cyt b gene sequences for Chinese Leishmania isolates and ultrastructural characteristics of Chinese anti-Leishmania activity in the saliva of kala 2018; Patients [132]. The corpositive of anti-Leishmania antibodies present in the saliva to be used to diagnose CVL and VL was investigated more recently. For CVL, the detection of IgG2 and IgA 134. P. Reinecke: H. Gabbert: W. Strunk; C. Losche: Ocular scleromalacia caused by leishmaniasis: a rare cause of scleral antibodies targeting specific recombinant K39 protein (rK39) in saliva demonstrated the usefulness of this test to diagnose perforation. *British Journal of Ophthalmology* 2001, 85, 238-238, 10.1136/bjo.85.2.238c.

  CVL and to differentiate between seropositive and seronegative dogs [134]. In humans, a preliminary experiment involving
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- gallery forest bats [141].
  141. Reza Razeghinejad, Ahmad Monabati; Mohammad Rahim Kadivar; Abdolvahab Alborzi; Conjunctival leishmaniasis in a
  3.4. Conjunctival Swab/Lacrimal Fluid/Occular
- 142. Perrin-Terrin, A.; Auriol, S.; Mahieu, L.; Debard, A.; Eden, A.; Cassagne, M.; Pagot-Mathis, V.; Malecaze, F.; Soler, V. A swell-in-anishall-pirsa-left-order-in-territorial was the companied of the companies of the compani
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- bearing amastigote forms of *Leishmania*, in the ciliary body, sclerocorneal limbus, iris, and lacrimal duct but also in 146. Richter; Schaarschmidt, K.; Krudewig. Ocular signs, diagnosis and long-term treatment with allopurinol in a cat with smooth and striated muscles [158-161]. *Leishmania* were observed in squamous carcinoma cells from conjunctival swab leishmaniasis. Schweizer Archiv fur Tierheilkunde 2014, 156, 289-294, doi:10.1024/0036-7281/a000593. samples in an HIV+ patient [162]. *Leishmania* DNA can be detected and quantified by qPCR in the lacrimal glands of
- 143ymb@araincAlogsq1639; Niethe&Elanesh lavermoresh of the any nouse [16441894] and fracking suitabline in the any nouse [16441894] and fracking suitabline distribution of the any nouse in the any nouse in the control of the any nouse in the control of the cont
- 141.714.47.22 des García Alonso; A. Blanco; D. Reina; F.J. Serrano; C. Alonso; C.G. Nieto; Immunopathology of the uveitis in canine leishmaniasis. *Parasite Immunology* **1996**, *18*, 617-623, <u>10.1046/j.1365-3024.1996.d01-39.x</u>. Human African Trypanosomiasis & Animal Trypanosomiases. In humans, eye pathologies associated with trypanosome
- 149. Virginia Rodelão, Richini Prepaira: Pâmela Merlo Marson; Enio Yoshinot Hayasaka: Cassiano Victoria: Rodrigo Silva: Infections remain unusual [173], and an investigation for the presence of parasites, DNA or antibodies within conjunctival Langoni; Molecular detection of Leishmania spp. in road-killed wild mammals in the Central Western area of the State swabs has not been performed. In dogs infected by p. pucer, the eyes are one of the most severely affected organs, and of São Paulo, Brazil. Journal of Venomous Animals and Toxins including Tropical Diseases 2014, 20, 27-27, 10.1186/1 infection by T. evansi can provoke blindness [174,175]. Experimental infections of cats with T. brucei [176] and of cats and 678-9199-20-27. goats with T. evansi highlight their disseminative capacity in the eye, with their presence being detected in the aqueous
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- cruzi infection later known as Romana's sign [179]. The invasion of the human host by T. cruzi occurs in various ways but 151. V.1. Barbosa; M.A.G. Silva; M.G. Sousa; A.P. Gering; H.D. Santos; J.L. Laus; Detecção de formas amastigotas em mainty via parasitologico de esfregaçio obtivol a partil de stiable confuntiva de case dem resignation de confuntiva de case de com resemble viscenario de case de com resemble de case de case de com resemble de case de
- infects the most proximal tissues lined with cuboidal and columnar epithelial cells [181,182]. Surprisingly, reports on eye 152. Brett P. Bielory; Hamed B. Lari; Neena Mirani; Rajendra Kapila; Valerie A. Fitzhugh; Roger E. Turbin; Conjunctival pathology in CD patients are very scarce. Recently, the first case of *Trypanosoma cruzi*—associated retinitis was Squamous Cell Carcinoma Harboring Leishmania Amastigotes in a Human Immunodeficiency Virus—Positive Patient. diagnosed [183]. The presence of *T. cruzi* amastigotes in the conjunctiva, corneal stroma, the adjacent ocular muscle and *Archives of Ophthalmology* **2011**, *129*, 1230, 10.1001/archophthalmol.2011.252. the interstitial macrophages of *Thrichomys apereoides* (Rodentia, Echimyidae) experimentally infected with *T. cruzi* is
- 1530 Carreline Varanjo; Dolors Fondevila; Laura Altet; Olga Francino; J. Ríos; Xavier Roura; Teresa Peña; Evaluation of the presence of Leishmania spp. by real-time PCR in the lacrimal glands of dogs with leishmaniosis. *The Veterinary*

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  inflammation [185]. Chagas disease is associated with male hormonal changes and a loss in sperm quality due to
- 155a Kantes to Edguni etten Paresi rait Julia Scistiate de Marsi; the Imavatarke Buzreti; Discontiaga poil Mai Holana changes ir ninketa to overpredakteid; Brodring Martins, Segresa Vera Hatticio Discote and Bulitis. Tricia Marijan Ferreita es Sursa plustrina in the specificant can be considered to daring in the privile by grand as well as daring to de the reproductive organise of the privile of the privile
- 156. Sidney De Almeida Ferreira; Leonardo Trindade Ituassu; Maria Norma De Melo; Antero Silva Ribeiro De Andrade;

  Huevanuandnanimal deighmaniassaub eishmaniasis dengeleishmaniasstoliaga bisaga bisa
- and humans [186-189]. In humans, lesions in the male genitalia associated with the presence of parasites are well 157. Rodrigo Souza Leite; Sidney De Almeida Ferreira; Leonardo Trindade Ituassu; Maria Norma De Melo; Antero Silva documented [190-192], with the presence of parasites [193,194]. In dogs. genital lesions associated with visceral Ribeiro De Andrade; PCR diagnosis of visceral leishmaniasis in asymptomatic dogs using conjunctival swab samples. leishmaniasis and the shedding of *Leishmania* in the semen of naturally or experimentally infected dogs is described and

can/vetadinter/inflamilitivo/1095, 2960, It70) & Otte200c.e19nt0106/invettian2019.02020 parasite burden has been 158 tricked warda is associated with inflormation essaticular reageneration catrophy unrichtsence of sparmategenesis, and negrais Marin; Juliaherstinagseninghubohistorang matagraphwilahaysak khatuzatik colnishonawab dosa tandetasi of asyreriamatia dobs iwecas ositivsidos lasiremanio da labatostia. Voasa da en 120120 en 1225 <u>koars 6615004 sorroro</u>i and asymptomatic leishmaniasis, respectively, in the epididymal duct. The detection of Leishmania parasites in semen has been evidenced through parasite culture [29], microscopic observation or immunohistology [195,197], and 159. Julia Cristina Benassi; Graziella U. Benvenga; Helena L. Ferreira; Vanessa F. Pereira; Lara B. Keid; Rodrigo Soares; polymerase thain reaction [195,196,198], ACVI, experimental infection of 8 female dons pinnoints that yulvar swab is at least as sensitive as oral swab for the detection and quantification of Leishmania kDNA and this methodology is proposed quantificative real-time PCR. Experimental Parasirology 2017; 177, 53:34, 40:1016/1.2xpparai.comp.04.004.

to confirm Leishmania infection in seropositive dogs [199]. The presence of L. infantum amastigotes in the genital tract of 160. Mehmet Karakus: Suha Kenan Arserim: Özge Erişöz Kasap; Metin Pekağırbaş; Duygu Aküzüm; Bülent Alten; Seray naturally infected bitches is documented [200]. Töz; Yusuf Özbel; Vector and reservoir surveillance study in a canine and human leishmaniasis endemic area in most Huwastean read of Tubbros Gravaburen Andrea Tropica 2019 nibses 177-182 n 2019 166 nada tropica 2018 d 1.020 ess. sterility or 161194111Wannon the Anisa dealine of the contract of the contr clinicial macrifestations lares deservibed. Easalmand in extend of the control of equipendums in strong industrinces are wealth term smithed indicates and beautiful and continued and indicates and the continued and the c in attention of parasites in semen [207,208]. For Trypanosoma vivax, in addition to tsetse flies, transmission routes include transplacental and sexual routes, and parasites were detected in the 162. Ln Nsiangani, D Kalmbo Wa Kalmbo, Mi Kazumba, Anterior uveitis as the first sign of human African trypanosomiasis: semen of infected animals [203,209], In naturally acquired of sementally included animal trypanosomiasis caused by brucei or T. congolense, a decrease in semen production associated with an alteration in spermatogenesis is recorded 163. W. I. Morrison, M. Murray, P. D. Sayer, J. M. Preston. The pathogenesis of experimentally induced Trypanosoma brucei [210-214]. Histological lesions characterized by testicular degeneration, epididymitis and epididymal epithelial hyperplasia infection in the dog. I. Tissue and organ damage... The American Journal of Pathology 1981, 102, 168-181, were detected in the same animals and suggested the participation of the parasite in the pathogenic mechanism of 164 Monigrahi, Ribim Aleherrikane Kiliy Jerapostodi, Berharia Ricimaliani S., 1209121K., 2097, Sn Trypoen from any anno diffection cie. 

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- patients suffering from leishmaniasis.
  174. Malihe Nourollahpour Shiadeh; Maryam Niyyati; Shirzad Fallahi; Ali Rostami; Human parasitic protozoan infection to Human harafilistican yayamatis of history panets of
- 17時,「中央の一個では、「中央の一のでは、「中央の一のでは、「中央の一のでは、「中央の一のでは、「中央の一のでは、「中央の一のでは、「中央の一のでは、「中央の一のでは、「中央の一のでは、「中央の一のでは、「中央の一のでは、「中央の一のでは、「中央の一のでは、「中の一のでは、「中の一のでは、「中の一のでは、「中の一のでは、「中の一のでは、「中の一のでは、「中の一のでは、「中の一のでは、「中の一のでは、「中の一のでは、「中
- by Henry and Guilhon in 1944 [231]. During the 1910-1930 period, a set of experimental procedures was employed to 176. Veera Karkamo, Anu Kaistinen, Anu Nareaho, Kati Dillard, Katri Vainio-Siukola, Gabriele Vidgren, Niina Tuoresmaki, Marjukka Anttila; The first report of autochthonous non-vector-borne transmission of canine leishmaniosis in the Nordic countries.. Acta Veterinaria Scandinavica 2014, 56, 84, 10.1186/s13028-014-0084-9.

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- 13000 to open drather this from a registant water a \$600 to 1300 to 13
- bleeding [241] Nevertheless, the capacity of *T. cruzi* to invade the mammary gland of infected females has been 181. Francisco Martinez-Garcia; Javier Regadera; Rodolfo Mayer; Susan Sanchez; Manuel Nistai; Protozoan Infections in undertaken and These histological investigations of mayer from the Male Genital Tract. Journal of Urology **1996**, 340-349, 10:1016/s0022-5347(01)65846-4. mammary gland alveoli, excretory ducts, the connective tissue envelope of the ducts, inter- and intralobular connective
- 182 Soraia De Araújo Diniz: M.S. Melo: A. M. Borges: R. Bueno: B. P. Reis: W. I. Tafuri: E. F. Nascimento: Renato De Lima fissue, flistiocytes, adipose tissue, the sebaceous glands of the nipple, striated muscle fibers beneath the nipple, and Santos Gential Lesions Associated with Visceral Leishmaniasis and Shedding of Leishmania sp. in the Semen of inside the duct lumen [242]. Such proximity of *T. cruzi* parasites with colostrum or milk argues for the inactivation of *T.* Naturally Infected Dogs. *Veterinary Pathology* **2005**, 42, 650-658, 10.1354/vp.42-5-650.
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- Fabiano Borges Figueiredo: Francisco Das Chagas De Carvalho Rodrigues; Valéria Da Costa Oliveira; Raquel De secretion [132]. Parasité DNA has also been detected in the clinically unaffected nasal mucosa of patients infected by *L.* Vasconcellos Carvalhaes De Oliveira; Rodrigo Caldas Menezes; Occurrence of Leishmania infantum and associated braziliensis [245]. Among the clinical presentation of human leishmaniasis, mucocutaneous alterations are described. histological alterations in the genital tract and mammary glands of naturally infected dogs. *Parasitology Research* **2016**, They are mainly present in South America and are caused by a restricted number of *Leishmania* species [4]. Nevertheless, this uncommon presentation is also reported to be caused by some Old World species [246], suggesting
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  - Hulmadie/frieca/le/terrippárinassozforasess/kia/2014 | 66/pzis/bs/c3/doj.alses/55/0/1/167/84/alf62/66a/thered during the study.
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- 3.9. Hair/Bristles
  191. Keisuke Suganuma; Sandagdorj Narantsatsral; Banzragch Battur; Shino Yamasaki; Davaajav Otgonsuren; Simon

  Appeter Musinguzi; Batdorj Davaasuren; Badgar Battsetseg; Noboru Inque; Isolation, cultivation and molecular characterization of a new Trypanosoma equiperdum strain in Mongolia. Parasites & Vectors 2016, 9, 481, 10,1186/s13 proliferation. Therefore, only a few studies were performed using these materials for the investigation of trypanosomatic of 171-016-1755-3.
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- compounds specific to the infection [252,253]. Therefore, with this methodology, it is not the infectious agent that is 193. Ahmed, Y.; Hagos, A.; Merga, B.; Van Soom, A.; Duchateau, L.; Goddeeris, B.M.; Govaere, J. Trypanosoma detected, nor the immunologic response but the set of volatile controlled by the left 2018, 87, 66-75. known as a target tissue for Leishmania, an investigation of Leishmania DNA was undertaken on CVL in a mouse
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