

Leishmaniasis (cutaneous and visceral)

*Kala-azar, Black Fever,
Dumdum Fever, Oriental Sore,
Tropical Sore, Uta, Chiclero ulcer,
Aleppo boi, Pian bois; Espundia*

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Importance

Leishmaniasis is one of the most important vector-borne diseases of humans. This parasitic disease can be caused by many species of *Leishmania*, most of which are zoonotic. In humans, different species of the parasite are associated with different forms of the disease. Many *Leishmania* spp. cause skin ulcers and nodules. A few of these organisms can also affect the mucous membranes, and may cause disfiguring lesions of the nose. Other species damage the internal organs and cause human visceral leishmaniasis, a life-threatening condition. Among domesticated animals, dogs are the most important species in the epidemiology of this disease. In addition to becoming ill, dogs are reservoir hosts for *L. infantum*, one of the two most important organisms in human visceral leishmaniasis. Skin lesions and, rarely, visceral disease, have also been reported occasionally in other domesticated animals, captive mammals in zoos, and wild animals.

Etiology

Leishmaniasis results from infection by various species of *Leishmania*, a protozoan parasite of the family Trypanosomatidae (order Kinetoplastida). Approximately 30 species have been described, and at least 20 of these organisms are pathogenic for mammals. The genus *Leishmania* contains two subgenera, *Leishmania* and *Viannia*, which are differentiated by where they multiply in the digestive tract of the insect vector. The classification of *Leishmania* is complex and, in some cases, controversial; more than one species name may be used for an organism, and some names may eventually be invalidated.

Human visceral leishmaniasis is primarily caused by *Leishmania donovani* (which includes *L. archibaldi*) and *L. infantum/L. chagasi*. *L. donovani* is anthroponotic; it is mainly transmitted between people, who act as the reservoir hosts. *L. infantum* is zoonotic. At one time, two different names were used for this organism - *L. infantum* in the “Old World” (Eastern Hemisphere) and *L. chagasi* in the “New World” (Western Hemisphere) – and these two organisms were thought to be different species. As a result of genetic studies, they have been reclassified into one species, *L. infantum*. However, some authors argue that *L. chagasi* should be a subspecies of *L. infantum*, and the name *L. chagasi* is still used frequently in South America. Other organisms can occasionally cause visceral leishmaniasis: *L. tropica* and *L. amazonensis*, which usually cause cutaneous leishmaniasis, and a newly described species in Thailand, have been linked to some cases.

Most *Leishmania* species cause cutaneous leishmaniasis in people. In the New World, these organisms include the members of the *L. braziliensis* complex (*L. braziliensis*, *L. panamensis/L. guyanensis*, *L. shawi* and *L. peruviana*), and the *L. mexicana* complex (*L. mexicana*, *L. amazonensis*, *L. venezuelensis*), as well as *L. lainsoni*, *L. naiffi* and *L. lindenbergi*. Old World species that cause cutaneous leishmaniasis include *L. tropica*, *L. major* and *L. aethiopica*, which are all members of the *L. tropica* complex. In addition, some strains of *L. infantum* can cause cutaneous leishmaniasis without affecting the internal organs. With the exception of the anthroponotic species *L. tropica*, all of these organisms are zoonotic. The type of skin lesions, efficacy of treatment, speed of healing and other factors vary with the species. Most Old World and New World species only cause lesions on the skin, but the New World organisms *L. braziliensis* and *L. panamensis/L. guyanensis* may cause either cutaneous or mucocutaneous leishmaniasis.

L. infantum is the most common species reported in domesticated animals, but other species also occur. The distinction between species that cause cutaneous and visceral syndromes is not seen in animals. For example, *L. infantum*, which mainly causes visceral leishmaniasis in people, can cause both visceral and cutaneous disease in dogs, and primarily causes skin lesions in cats and horses. Some *Leishmania* species that have been isolated from animals have not been reported in humans:

Geographic Distribution

With the exception of Antarctica, *Leishmania* spp. have been reported on every continent. These organisms are primarily endemic in tropical and sub-tropical regions,

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and human disease mainly occurs in Africa, parts of Asia, the Middle East, Latin America and the Mediterranean region. In Europe, leishmaniasis appears to be spreading northward from its traditional foci.

The distribution of each species of *Leishmania* affects the type of disease that occurs in each region, as well as its severity. *L. donovani* causes visceral leishmaniasis in South Asia and Africa. *L. infantum* causes this disease in the Mediterranean, the Middle East, Latin America and parts of Asia. Cutaneous leishmaniasis is caused by *L. major* in Africa, the Middle East and parts of Asia, by *L. tropica* in the Middle East, the Mediterranean and parts of Asia, and by *L. aethiopica* in parts of Africa. Many different species may be involved in the Western Hemisphere, where cutaneous leishmaniasis can be found from Mexico through South America.

In North America, limited foci of infection have been reported in Canada and the U.S. Canine leishmaniasis caused by *L. infantum* and occurring mainly in Foxhounds has been reported in a number of U.S. states and parts of Canada. Human cases have not been linked to these animals. In addition, a focus of cutaneous leishmaniasis that has sporadically affected humans or domesticated animals is found in south central Texas, where a species of *Leishmania* (possibly a member of the *L. mexicana* complex) seems to be endemic. Australia appeared to be free of *Leishmania* spp. until 2004, when this organism began to be reported from captive kangaroos, wallabies and other marsupials. Imported cases of leishmaniasis can also be seen in areas where *Leishmania* spp. are not endemic. If appropriate insect vectors are not present, these organisms usually do not become established in the country.

Transmission

Leishmania spp. are usually transmitted indirectly between hosts by sandflies of the genera *Phlebotomus* and *Lutzomyia*, which are biological vectors. Each species of *Leishmania* is adapted to transmission in certain species of sandflies. Only the females feed on blood. Sandfly activity occurs when it is humid, and there is no wind or rain. These insects are usually most active at dawn, dusk and during the night, but they will bite if they are disturbed in their hiding places (animal burrows, holes in trees, caves, houses and other relatively cool, humid locations) during the day. They are attracted to light and may enter buildings at night. Transovarial transmission of *Leishmania* does not seem to occur, and in areas with cold temperatures, the parasite overwinters in mammalian hosts. Other arthropods including ticks (*Dermacentor variabilis* and *Rhipicephalus sanguineus*) and canine fleas may also act as mechanical vectors. Where sandflies transmit *Leishmania* spp., ticks and fleas are probably unimportant in the epidemiology of the disease; however, they might be involved in rare cases of dog-to-dog transmission in other locations.

Mammals can be infected asymptotically for long periods, and they often remain chronically infected even after clinical cure. Subclinically infected animals can transmit *Leishmania* to sandflies. These parasites have also been transmitted via blood transfusions in people and dogs, and by transplacental transmission in dogs, mice and humans. In canine leishmaniasis caused by *L. infantum*, the parasites can sometimes be found in saliva, urine, semen and conjunctival secretions, as well as in blood. Venereal transmission has been proven to occur in dogs, and other routes of spread might be possible. Rare cases of horizontal transmission have been reported between dogs in the same household or kennel. Case histories suggest that some of these animals might have been infected during a fight. In other cases, a dog is known to have licked its companion's lesions or ingested blood during a hemorrhage. Epidemiological investigations in U.S. Foxhounds also suggest that *L. infantum* has been transmitted directly from dog to dog, although sandfly mediated transmission or other arthropod-borne transfer has not been ruled out. In contrast, sandflies are thought to transmit the disease to people from wild mammals in south-central Texas. The risk of direct transmission from infected dogs to humans is unknown.

Epidemiology

Humans and domesticated animals are accidental hosts for many *Leishmania* spp., which are maintained in cycles between wild animals and sandflies. *L. infantum*, *L. peruviana* and possibly other species can be maintained in dogs, increasing the risk of transmission to people. Other domesticated animals might be involved as secondary maintenance hosts. *L. donovani* and *L. tropica* are adapted to humans, but animals can also be infected occasionally.

Disinfection

Leishmania spp. do not remain viable outside a host or *in vitro* culture. They can be inactivated by 1% sodium hypochlorite, 2% glutaraldehyde, or formaldehyde. They are also susceptible to heat of 50–60°C.

Infections in Humans

Incubation Period

People can carry some species of *Leishmania* asymptotically for long periods, without becoming ill. In humans, the reported incubation period for cutaneous leishmaniasis can be as short as 1-2 weeks or as long as several months when it is caused by New World species, and up to three years when Old World species are involved. The incubation period for visceral leishmaniasis is 10 days to several years; most cases seem to become apparent in two to six months.

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Clinical Signs

Two forms of leishmaniasis, cutaneous and visceral, are seen in humans. Some texts also distinguish a mucocutaneous form, while others consider it to be a subset of cutaneous leishmaniasis. The form of the disease and the usual clinical signs vary with the species of *Leishmania*. Some infections remain asymptomatic.

Cutaneous leishmaniasis

Cutaneous leishmaniasis often involves only the skin, and may be characterized by one to dozens of lesions. Depending on the species of *Leishmania*, ulcers, smooth nodules, flat plaques or hyperkeratotic wart-like lesions may be seen. The initial lesions, which occur on skin that was exposed to sandflies, are usually papules. Many lesions remain localized, but in some cases, the parasites may spread via the lymphatics and produce secondary lesions on the skin, or occasionally the mucosa, of other parts of the body. Regional lymphadenopathy sometimes occurs. Cutaneous leishmaniasis is usually painless unless the lesions become secondarily infected, and except in the ear, the ulcers tend to remain confined to the skin and do not affect the subcutaneous tissues. Most skin lesions heal spontaneously; however, the speed of healing varies with the species of *Leishmania*. In some cases, it may take several months to a year or longer. Some forms leave permanent scars. HIV-infected individuals can have unusually severe cases, and the disease is more difficult to cure. Steroid treatment or other forms of immunosuppression can also result in unusually severe disease.

Disseminated leishmaniasis is a rare form of cutaneous disease. It is seen especially with *L. amazonensis* in the Western Hemisphere, although other organisms can also be involved. It also occurs in the Eastern Hemisphere, often in people who have concurrent HIV infections. In diffuse cutaneous leishmaniasis, the nodules do not ulcerate but they spread widely on the skin. They may cause damage to deep tissues, and can persist indefinitely. The diffuse form can be incurable in some cases.

Leishmaniasis recidivans (lupoid leishmaniasis), another rare form, is characterized by the development of new lesions around the edges of a healed skin lesion. It is most often caused by *L. tropica* or *L. braziliensis*, and it does not heal without treatment.

Mucocutaneous leishmaniasis (espundia) usually occurs in Latin America, where it is caused by *L. braziliensis braziliensis* and, less often, by *L. panamensis/ L. guyanensis*. Mucocutaneous leishmaniasis tends to occur 1 to 5 years after cutaneous leishmaniasis caused by these organisms has healed, but it can also be seen while skin lesions are still present. The initial signs are erythema and ulcerations at the nares, followed by destructive inflammation that can spread to involve the nasal septum, and in some cases, the pharynx or larynx. Frequent nosebleeds can be an early sign. The inflammation may perforate the nasal septum, cause severe disfigurement of the face, or

block the pharynx or larynx. In some cases, the genitalia may also be involved. Mucocutaneous leishmaniasis does not heal spontaneously.

Visceral leishmaniasis

Visceral leishmaniasis is usually an insidious, chronic disease among the inhabitants of endemic areas; however, the onset may be acute in travelers from *Leishmania*-free areas. In some cases (especially in Africa), a primary granuloma appears on the skin before the systemic signs. The most common symptoms of visceral leishmaniasis are a prolonged undulant fever, weight loss, decreased appetite, signs of anemia, and abdominal distension with splenomegaly and hepatomegaly. Thrombocytopenia may cause bleeding tendencies, including petechiae or hemorrhages on the mucous membranes, and leukopenia can result in increased susceptibility to other infections. Other symptoms may include coughing, chronic diarrhea, darkening of the skin, lymphadenopathy, and in many cases, signs of chronic kidney disease. Mild cases with only a few symptoms may resolve spontaneously. Unless they are treated, most other cases are eventually fatal, often from secondary infections and other complications. Fulminant disease or atypical cases can also occur, especially in patients co-infected with HIV. People with successfully treated infections continue to carry the parasite, and the disease may recur if they become immunosuppressed. Similarly, asymptotically infected individuals may later develop clinical signs.

Post-kala azar dermal leishmaniasis (PKDL) occurs after recovery in some cases of visceral leishmaniasis caused by *L. donovani*. This syndrome is characterized by a maculopapular, macular or-nodular rash around the mouth, which spreads. In Africa, PKDL is common, usually occurs within 6 months of visceral leishmaniasis, and typically disappears within a year without treatment. In South Asia, this syndrome is relatively rare, occurs several years after visceral leishmaniasis has been cured, and required prolonged treatment. In India, PKDL is seen in 1-3% of successfully treated cases of visceral leishmaniasis.

Communicability

Leishmaniasis is usually vector-borne, but person-to-person transmission including vertical (congenital) transmission, venereal transmission, and transmission by blood transfusion has been reported. Newborns can be infected whether or not the mother was symptomatic. Humans infected with some species of *Leishmania* can infect sandflies.

Diagnostic Tests

Cutaneous leishmaniasis can be diagnosed by direct observation of the parasites in skin scrapings, impression smears or skin biopsies stained with Giemsa, Leishman's, Wright's or other stains. Amastigotes are easiest to find in recent or active lesions. Polymerase chain reaction assays

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(PCR) are often used for diagnosis in areas where they are available. *Leishmania* spp. can also be cultured. However, each species will grow only in certain media, and some species can be difficult to isolate. Novy-MacNeil-Nicole (NMN) medium, brain–heart infusion (BHI) medium, Evan’s modified Tobie’s medium (EMTM), Grace’s medium and Schneider’s *Drosophila* medium might be used initially. Animal inoculation into hamsters may also be valuable, especially with contaminated material. Diagnosing leishmaniasis by *in vitro* culture requires 5 to 30 days, while animal inoculation can take weeks or months. The species, subspecies and/or strain can be identified by PCR, DNA hybridization, kinetoplast DNA restriction endonuclease analysis, isoenzyme analysis, or immunological techniques that use monoclonal antibodies. A delayed hypersensitivity test, the leishmanin skin test (Montenegro skin test), is useful in the diagnosis of cutaneous and mucocutaneous leishmaniasis, but it is usually negative in the diffuse cutaneous form. Antibodies are often slow to develop and of low titer.

Visceral leishmaniasis can be diagnosed using some of the same techniques, including direct observation of the parasites. Amastigotes may be found in peripheral blood, or more often, in aspirates or biopsy smears from the spleen, bone marrow or lymph nodes. PCR, culture or animal (hamster) inoculation may be particularly useful early, when parasite numbers are low. Serology can also be helpful in this form of leishmaniasis. Common serological tests used in humans include the immunofluorescent antibody test (IFA), direct agglutination, enzyme-linked immunosorbent assay (ELISA), fast agglutination-screening test (FAST), and a rapid immunochromatographic assay (K39 dipstick or strip-test). Other assays including gel diffusion, complement fixation, indirect hemagglutination and counter-current electrophoresis have also been used. Cross-reactions can occur in some serological tests with leprosy, Chagas disease, malaria and schistosomiasis. The leishmanin skin test/ Montenegro skin test is usually negative in cases of visceral leishmaniasis, but reactions can be seen once the disease is cured.

Treatment

Visceral or cutaneous leishmaniasis can usually be cured in immunocompetent individuals. Pentavalent antimonials can be used where the parasites are sensitive to these drugs, but resistance is a major problem in some areas. Other drugs such as allupurinol, amphotericin B or liposomal amphotericin B, and miltefosine may also be used. Most of the drugs used to treat leishmaniasis must be given parenterally. Visceral leishmaniasis in AIDS patients is often resistant to treatment, and many patients relapse.

Cutaneous leishmaniasis may be treated to speed healing, decrease scarring and decrease the risk of mucosal disease or relapse. Intralesional, topical or systemic

drugs may be used, depending on the species of *Leishmania* and the risk of more serious complications. Cryotherapy, thermotherapy, or curettage have also been employed in some cases. Some cutaneous leishmaniasis lesions that are improving may simply be observed, if they are caused by relatively benign organisms. Mucosal leishmaniasis is a serious condition and it is treated with systemic drugs.

Prevention

Preventative measures against sandflies include using insect repellents such as DEET, covering exposed skin, and staying on higher floors of buildings in the evening or at night, as these insects are poor fliers. Fans can also be helpful, and insecticidal sprays can be used to kill the insects inside houses. Insecticide-treated bed nets decrease bites from these insects at night. Untreated bed nets are not generally useful: sandflies are very tiny and can pass through the mesh of most nets, while bed nets with a very narrow mesh may be too hot in warmer climates. Insecticide-treated bed sheets, window curtains and slow-release paint have also been used. Insecticide spraying programs have been conducted in some countries.

Treatment of human patients may be helpful in areas where anthroponotic transmission is important. Decreasing the incidence of *L. infantum* in dogs can help protect people from this organism. Some studies have shown that insecticide-impregnated dog collars protected both dogs and children in areas where they were used. Infected dogs have been culled in some countries; however, there are doubts about the efficacy of these programs, and in some countries, such programs would also not be accepted. Many species of *Leishmania*, particularly species that cause cutaneous leishmaniasis, have wild animals as their reservoir hosts. The only practical way to decrease the incidence of these diseases is personal protection with insect repellents and other measures.

Morbidity and Mortality

Leishmaniasis is a seasonal disease in temperate regions. Infections are acquired in the warmer months when sandflies are active, and the number of cases fluctuates with changes in their populations. Approximately 1–1.5 million cases of cutaneous leishmaniasis and 500,000 cases of visceral leishmaniasis are estimated to occur worldwide each year. However, this is probably an underestimate, as many cases are not diagnosed.

The anthroponotic form of visceral leishmaniasis, caused by *L. donovani*, can affect all ages. Healthy people are not particularly susceptible to *L. infantum*, which causes the zoonotic form of this disease. Asymptomatic infections with this organism are common, and illness tends to occur mainly in young children, or in people who are malnourished or immunosuppressed. The case fatality rate for untreated disease is 75–95%. The parasites probably persist after clinical cure, and symptoms can reappear

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if the individual becomes immunosuppressed. Even with good treatment, approximately half of HIV-infected patients relapse between 1 month and 3 years later.

Cutaneous leishmaniasis is rarely fatal. This form of leishmaniasis often heals spontaneously, although some lesions may persist for long periods or leave scars. The mucocutaneous form caused by *L. braziliensis* or *L. panamensis*/*L. guyanensis* rarely heals spontaneously and is disfiguring. Mucocutaneous lesions in the nasopharynx can be fatal.

Infections in Animals

Species Affected

Among domesticated animals, dogs are the most commonly affected species. Most cases of canine leishmaniasis are caused by *L. infantum*, but other organisms can also be found. Clinical cases are also seen occasionally in cats, horses, donkeys and mules infected with various species of *Leishmania*. Leishmaniasis is not a significant disease in livestock other than equids, but rare, isolated cases of cutaneous leishmaniasis have been seen in sheep, goats and cattle in Africa, and a *Leishmania*-infected pig was documented in South America. Antibodies to *Leishmania* spp. have also been reported in donkeys, cows, and goats in Africa, and pigs in Brazil. Experimentally infected sheep or pigs did not become ill.

Clinical cases have been reported occasionally in wild animals or captive wild species including non-human primates, bush dogs (*Speothos venaticus*), hoary zorros (*Lycalopex vetulus*), gray wolves (*Canis lupus*) and maned wolves (*Chrysocyon brachyurus*). Some experimentally infected crab-eating foxes (*Cerdocyon thous*) and red foxes (*Vulpes vulpes*) also became ill. In Australia, a *Leishmania* spp. has been reported to cause cutaneous lesions in captive kangaroos, wallaroos and wallabies (*Macropus* spp.).

Each species of *Leishmania* has one or more primary reservoir hosts, although it may also infect and cause disease in other species. Canids seem to be the reservoir hosts for *L. infantum*, and dogs are the most important species in maintaining this parasite in domestic cycles. It also occurs in various wild canids including wolves, foxes, jackals, hoary zorros and bush dogs. Infections with *L. infantum* have been reported in a wide variety of domesticated and wild animals including cats, equids, wild agouti (*Dasyprocta agouti*), white-eared opossums (*Didelphis albiventris*), Egyptian mongooses (*Herpestes ichneumon*), genets (*Geneta geneta*), Iberian lynxes (*Lynx pardinus*), rodents, a seal and at least one species of bat (*Carollia perspicillata*). Some of these organisms, including cats, might act as secondary reservoirs in some areas.

Known reservoir hosts for the Old World species that cause cutaneous leishmaniasis include gerbils, girds and other rodents for *L. major*, and members of the Hyracoidea (hyraxes) for *L. aethiops*. The New World species

that cause cutaneous leishmaniasis are often maintained among animals that live in forests. The primary reservoir host(s) for *L. braziliensis* are not known; however, a variety of species including carnivores, rodents and perissodactyls, as well as dogs, cats and equids, are reported to be infected with this species. It is possible that different reservoir hosts are important in different areas. Important reservoir hosts for other New World species include sloths for *L. guyanensis*/*L. panamensis*, armadillos for *L. naiffi*, and rodents for *L. mexicana*, *L. amazonensis* and *L. lainsoni*. Marsupials including members of the genera *Didelphis*, *Philander*, *Marmosa*, *Caluromys* and *Metachirus*, and the crab-eating fox can also be infected with *L. amazonensis*, although rodents are thought to be the primary reservoirs. Dogs are the only known reservoir hosts for *L. peruviana*, which causes human cutaneous leishmaniasis in the Peruvian Andes. Arboreal mammals are suspected to be the reservoir hosts for *L. shawi*, which has been reported in monkeys (the black bearded saki, *Chiropotes satanas*), sloths (*Choloepus didactylus* and *Bradypus tridactylus*) and coatis (*Nasua nasua*). The reservoir hosts for *L. venezuelensis*, which has been reported in humans and cats, are unknown. Humans are the reservoir hosts for two Old World species: *L. tropica*, which causes cutaneous leishmaniasis, and *L. donovani*, which causes visceral leishmaniasis.

Incubation Period

Animals are often infected asymptotically with *Leishmania* spp. The reported incubation period for *L. infantum* in dogs varies from three months to seven years. In some dogs, severe clinical signs occur soon after animal becomes infected. Other dogs remain asymptotically infected, in some cases for a lifetime. These animals can become ill at any time, particularly when they become immunosuppressed.

Clinical Signs

Dogs

Both visceral and cutaneous manifestations may be found simultaneously in dogs; unlike humans, separate cutaneous and visceral syndromes are not seen. The clinical signs are variable and can mimic other infections. Asymptomatic infections can also occur.

In symptomatic cases, common visceral signs include lethargy, weight loss, a decreased appetite, anemia, splenomegaly and local or generalized lymphadenopathy. Fever can be intermittent, and is absent in many cases. Bleeding disorders including epistaxis, hematuria and melena can also be seen. In some cases, profuse epistaxis is the only presenting sign. Chronic renal disease is common in dogs infected with *L. infantum*; it may be the only syndrome, and it is often the cause of death. Some animals may also have ocular, skin or mucosal lesions, sneezing, chronic diarrhea, vomiting, chronic relapsing colitis, chronic hepatitis, osteolytic and osteoproliferative

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bone lesions, meningitis, autoimmune disorders, and cardiovascular signs from pericarditis, thromboembolism, vasculitis and serum hyperviscosity. Erosive or nonerosive polyarthritis may be seen, and chronic polymyositis can cause progressive muscle atrophy. In symptomatic cases, the disease is usually slowly progressive.

Skin lesions are common in dogs with visceral disease, but they can also occur separately. The most common cutaneous syndrome is a non-pruritic exfoliative dermatitis, found especially around the eyes and on the face, ears or feet. There may be areas of alopecia, especially around the eyes, and silvery white scales in the areas of alopecia. In some cases, the lesions may be generalized. Cutaneous disease characterized by nodules, ulcers or scabs can also occur in dogs. Atypical skin lesions including pustular rashes, panniculitis, depigmentation, erythema multiforme, digital and nasal hyperkeratosis, and cases that resemble alopecia areata or pemphigus foliaceus have also been reported. Secondary bacterial infections are common. In some dogs with cutaneous lesions, the nails may be abnormally long and brittle. Marked wasting of the temporal muscles may also be seen.

Ocular lesions may be seen independently from systemic signs, and can occur before or after treatment. The most common ocular signs are blepharitis, conjunctivitis, keratitis and anterior uveitis. Some animals have multiple granulomas at the eyelid margins, nictitating membrane margins, conjunctival limbus, cornea, or anterior chamber. Sequelae may include glaucoma, keratoconjunctivitis sicca, corneal pigmentation, iris atrophy, cataracts, retinal detachment, panophthalmitis or phthisis bulbi.

Cats

Clinical cases are uncommon in cats. Most reported cases have been characterized by cutaneous signs without visceral lesions. Localized nodules, papules and chronic crusted or ulcerated lesions are most often found on the nose, ears (pinnae), eyelids or lips, but they can also occur on other sites such as the paws. The nasal mucosa may be involved, and the regional lymph nodes may be enlarged. Generalized dermatitis, alopecia and scales can also be seen. Both fatal cases and spontaneous cures have been reported. In one otherwise healthy cat infected with *L. mexicana*, skin lesions recurred two years after surgical treatment, and were refractory to therapy.

Visceral lesions and signs are rare. Systemic cases in cats have involved the liver, spleen, lymph nodes and kidney. Fever, jaundice, vomiting, lymphadenopathy, oral and ocular lesions, anemia and leukopenia have been reported. Severe pancytopenia was the main syndrome in one infected cat presented for depression and loss of appetite. Some sick cats were co-infected with immunosuppressive viruses such as feline immunodeficiency virus or feline leukemia virus, but others were not.

Equidae

Horses, mules and donkeys may develop skin lesions, particularly on the head, ears, neck, legs and scrotum. The most common lesions are solitary or multiple papules or nodules, which are often ulcerated. Disseminated skin disease has been reported, but visceral leishmaniasis has not been documented in equids. Some lesions regress spontaneously.

Other domesticated animals

Skin lesions were the only clinical signs reported in a sheep, goat and calf in Africa. The goat also had enlarged lymph nodes. Experimentally infected sheep had no clinical signs except an elevated temperature. Experimentally infected pigs remained asymptomatic.

Captive wild species and wild animals

Infections seem to be inapparent in many infected wild animals. In rodents, the *L. mexicana* complex may cause swellings with hair loss or ulcers, particularly at the base of the tail but also on the ears or toes. The few reported cases in captive or wild canids have resembled canine leishmaniasis. In a captive bush dog infected with *L. infantum*, the clinical signs included progressive weight loss, vomiting, diarrhea, anemia and signs of kidney disease including polyuria and polydipsia. This animal later developed ascites and cervical edema, and eventually died. A hoary zorro infected with the same organism developed an enlarged cervical lymph node, followed by ulcerated skin lesions, anemia, weakness, prostration and weight loss. Multiple chronic ulcerative skin lesions were seen in a captive maned wolf. Fatal *L. infantum* infection was also reported in a wild gray wolf in Croatia. The animal was found dead, with generalized alopecia, decreased elasticity of the skin, skin ulcers, white scaling, and disseminated crusted erosions. Generalized lymphadenopathy, hepatosplenomegaly, cardiac dilation, hydropericardium and hydrothorax, as well as pulmonary edema, consolidation and disseminated focal pulmonary hemorrhages were found at necropsy.

Captive Australian marsupials developed skin lesions consisting of focal to coalescing areas of thickened skin, or raised crusted or ulcerative pale nodules. Some nodules were found around the eyes or on the cloaca.

Communicability

Transplacental transmission has been documented in dogs and rodents, and venereal transmission has been seen in experimentally infected dogs. *Leishmania* spp. can also be acquired in blood transfusions. Case histories suggest that, in rare cases, these parasites might have been transmitted between dogs during fights, or acquired during other forms of close contact, possibly when a dog licked another dog's wounds or ingested blood during hemorrhages. In general, horizontal transmission between dogs seems to be rare. The risk of transmission to humans is unknown.

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Dogs and cats can transmit *Leishmania* spp. to sandflies; however, experimentally infected pigs could not. Some animals may act as bridges that bring parasites found in sylvatic cycles closer to humans.

Post-Mortem Lesions [Click to view images](#)

The gross lesions are highly variable and may be minimal. In canids, the lesions may include cachexia, signs of anemia, generalized lymphadenopathy, hepatosplenomegaly, areas of alopecia with desquamation on the head and trunk, and cutaneous ulcers or nodules. Ulcers and petechiae are occasionally seen on the mucous membranes, and in some cases, hemorrhages may be evident in internal organs. Small, light colored nodular foci (granulomas) may be found in a variety of organs, including the kidney, liver, and pancreas. In experimentally infected dogs, fetuses had no lesions despite the presence of parasites in their tissues.

In a cat with severe pancytopenia caused by leishmaniasis, the only gross lesions were poor condition, mild hepatomegaly and pulmonary edema.

Diagnostic Tests

In animals, leishmaniasis may be diagnosed by direct observation of the parasites using Giemsa, Wright's, Leishman's or other stains. *Leishmania* amastigotes are round to oval parasites, with a round basophilic nucleus and a small rod-like kinetoplast. They are usually found in macrophages or freed from ruptured cells. In dogs, amastigotes can sometimes be found in lymph node, spleen, or bone marrow aspirates, or in skin scrapings from lesions. In sick animals, they may also be found in other affected tissues, including ocular granulomas. However, parasites are sometimes undetectable even in clinical cases, and they are often absent in asymptotically infected animals. Histopathology with immunohistochemistry can increase the likelihood of detecting the organism when few parasites are present.

PCR is particularly sensitive, and can be used to detect *Leishmania* spp. in blood, skin biopsies, lymph nodes, bone marrow and conjunctival swabs. *Leishmania* species can also be cultured in a variety of media. However, there is no single universal culture medium for this organism; each species will grow only in certain media and some can be difficult to isolate. Media that can be used for *Leishmania* spp. include Novy-MacNeil-Nicole (NMN) medium, brain-heart infusion (BHI) medium, Evan's modified Tobie's medium (EMTM), Grace's medium or Schneider's *Drosophila* medium. Animal inoculation into hamsters may also be valuable, especially with contaminated material. Diagnosing leishmaniasis by *in vitro* culture requires 5 to 30 days, while animal inoculation can take weeks or months. The species, subspecies, and/or strain is identified by specialized techniques including isoenzyme analysis, PCR, DNA hybridization,

kinetoplast DNA restriction endonuclease analysis, or immunological methods that use monoclonal antibodies.

The most commonly used serological tests are the indirect fluorescent antibody test and ELISAs. A rapid immunochromatographic assay (rK39 dipstick or strip-test) is also available. Other serological tests including direct agglutination, counterimmunoelectrophoresis, complement fixation, indirect hemagglutination, latex agglutination, immunodiffusion or immunoblotting may also be available. Most, but not all, symptomatically infected dogs are seropositive. However, only a percentage of asymptotically infected dogs have detectable antibodies, and these animals may or may not become ill. Antibodies are not always found in animals that only have localized skin lesions; in cats, titers may not be detected until the lesions are resolving. Serological studies also suggest that *Leishmania* titers may be lower in cats than dogs. Cross-reactions can occur with other parasites, particularly *Trypanosoma cruzi*; these reactions are more common in tests that use crude antigen preparations. The delayed hypersensitivity test, which is used in humans, is not useful for dogs.

Treatment

Treatment can produce clinical improvement, although it may not eliminate the parasite. Pentavalent antimonials are often used for treatment where they are available. In the U.S., these drugs are provided through the Centers for Disease Control and Prevention (CDC). Other drugs used in humans, such as allopurinol, amphotericin B, or second line drugs may also be employed, either alone or in combination. Allopurinol has been used as a maintenance drug to prevent relapses. The prognosis is poorer in dogs that are severely ill and animals with kidney disease. In areas where leishmaniasis is not endemic, euthanasia may be considered to decrease the risk of transmission to humans, particularly if a competent sandfly vector is present.

Prevention

Insecticide-impregnated collars or topical insecticides are used in dogs to decrease bites from sandflies. Keeping susceptible animals, including dogs, cats and horses, indoors between dusk and dawn can be helpful during the warmer months when sandflies are active. Kennels and homes may be sprayed with insecticides, and insecticide-treated door and kennel nets and curtains may be helpful in keeping sandflies out. These insects are tiny and can get through untreated mesh unless it is extremely fine. However, they are poor fliers and are deterred by wind; fans can be helpful. Habitat modifications around the home can also be considered.

Because congenital infections can occur, it may not be advisable to breed from infected dogs. A vaccine has recently been licensed for dogs in Brazil.

Leishmaniasis (cutaneous and visceral)

Morbidity and Mortality

Leishmaniasis is a seasonal disease in temperate regions. Infections are acquired in the warmer months when sand flies are active, and the number of cases fluctuates with changes in the number of vectors. When the densities of both dogs and sandflies are high, *L. infantum* can be transmitted widely and rapidly among dogs. In endemic areas, up to 63-80% of the canine population can be infected with this organism. However, far fewer dogs will develop clinical signs. Although some dogs become severely ill soon after they are infected, up to 90% or more of *L. infantum*-infected dogs may be asymptomatic. Some of these dogs will develop clinical signs after months to years, often when they become immunosuppressed. Others may never become ill. Asymptomatic *L. infantum* infections also seem to be common in other canids. Only 6 of 75 experimentally infected crab-eating foxes, and 2 of 30 infected red foxes developed clinical signs. Similarly to dogs, the prevalence of this organism may be high in wild canids.

Sporadic cases of leishmaniasis, usually of the cutaneous form, occur in cats, horses, donkeys and rarely other species. One experimental study suggested that cats have some natural resistance to *Leishmania*. Because clinical cases are uncommonly reported in this species, *Leishmania* infections were also assumed to be rare. However, recent studies suggest that significant numbers of cats might be subclinically infected in some areas. Serological surveys in Europe have found antibodies to this organism in 0.6-60% of cats. In one study from Spain, 60% of the cats tested were seropositive and *L. infantum* DNA was found in 26%, with some animals infected for months. In another Spanish study, 4% of the cats were seropositive and one cat (0.43%) was positive by PCR. In the Middle East, a study found a seroprevalence of approximately 7% among cats in Israel, and parasites were isolated from 4 of 40 cats (10%) in Iran. Amastigotes were also found in spleen smears from 16 of 78 cats (20%) in Jordan. In Brazil, a study in 1938 and one in 1996 found very few infected cats, but a 2008 study that used PCR reported that 2 of 8 asymptomatic cats were infected.

Internet Resources

- Centers for Disease Control and Prevention (CDC)
<http://www.cdc.gov/ncidod/dpd/parasites/leishmania/default.htm>
- Medical Microbiology
<http://www.gsbs.utmb.edu/microbook>
- Public Health Agency of Canada. Material Safety Data Sheets
<http://www.phac-aspc.gc.ca/msds-ftss/index.html>
- The Merck Manual
<http://www.merck.com/pubs/mmanual/>

- The Merck Veterinary Manual
<http://www.merckvetmanual.com/mvm/index.jsp>
- World Health Organization
<http://www.who.int/leishmaniasis/en/>
- World Organization for Animal Health (OIE)
<http://www.oie.int>
- OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals
http://www.oie.int/eng/normes/mmanual/a_summry.htm
- OIE Terrestrial Animal Health Code
http://www.oie.int/eng/normes/mcode/en_sommaire.htm

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*Link defunct as of 2007