Chapter 13
Dirofilaria Infections in Humans and Other Zoonotic Filarioses

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Abstract *Dirofilaria repens* and *Dirofilaria immitis,* the main filariae of domestic and wild carnivores, are responsible for most cases of human infections by zoonotic filariae. Other species of animal filariae that have been reported in human patients include species from the genus *Dirofilaria* and nematodes from genera *Onchocerca*, *Brugia*, and *Molinema*. The higher frequency of human infection by *Dirofilaria* spp. compared to infections by other zoonotic filariae may be due to various factors. For example, awareness and attention of physicians for zoonotic filarial infection is higher in developed countries, where the dog represents an important reservoir for *Dirofilaria* worms. Climate change, together with the movement of infected dogs to previously unsuitable areas, is likely responsible for the increase in areas endemic for *D. immitis* and *D. repens*, with the consequence of an increase risk of infection for humans in temperate countries. Infection by *D. repens* is more frequent in Europe, where the documented infections by *D. immitis* appear rare, but the situation is different in other countries, e.g., in the USA, where human infections by *D. immitis* are frequently recorded. Infections by *Dirofilaria* worms are generally paucisymptomatic, but cases are also reported characterized by a severe clinical picture. The control of *Dirofilaria* infections in humans is essentially based on the control of the infection in dogs, and particular attention should be devoted to the transit of unprotected dogs (i.e., dogs that do not receive prophylactic treatment) in endemic areas, increasing the risk of acquiring filarial infections and of importing the infection in non-endemic areas.

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13.1 The Main Agents of Zoonotic Filarioses: An Introduction

The main agents of zoonotic filarial infections are also the main agents of filariases in domestic and wild carnivores: *Dirofilaria immitis* Leidy 1856, the causative agent of canine and feline heartworm disease, and *D. repens* Railliet and Henry 1911, the main causative agent of subcutaneous filarial infections (McCall et al. 2008). While heartworm infection is distributed worldwide, *D. repens* has until now been found in Europe, Asia, and Africa. Both parasites are mosquito-transmitted nematodes belonging to the family Onchocercidae (Anderson 2000). Adult worms are thin and females are up to about 15–17 cm in *D. repens* and 25–30 cm in *D. immitis*. Circulating embryos (microfilariae) are found in the bloodstream of infected dogs (cats are generally amicrofilaremic), which act as reservoir (McCall et al. 2008). In the USA, other than domestic dogs, coyotes are an important reservoir of heartworm infection (Lee et al. 2000).

Microfilariae are taken up by blood-sucking female mosquitoes mostly of the genera *Culex* and *Aedes* (McCall et al. 2008) and develop to the infective larval stage (L_3) which is transmitted to the final host through the subsequent blood meal of the infected mosquito. Several mosquito species can act as competent vectors. In Europe, a very efficient vector of *Dirofilaria* spp. is *Culex pipiens*; other species that might contribute to the transmission of these nematodes are *Aedes* (*Stegomyia*) *albopictus* and *Aedes caspius* (Genchi et al. 2011a). The species that take their blood meal on both humans and animals, and during both the day and the night (e.g., *C. pipiens* and *Ae. albopictus*), are those that are more likely to play a role in the transmission of the infection to human hosts. This might explain the high levels of seroprevalence for IgG antibodies against antigen parasites (up to about 30 %) in endemic areas of Spain and Italy, where these mosquito genera are widely diffused (Simón et al. 2005).

The final location of *D. immitis* adult worms in animal hosts is the pulmonary arteries and the right heart ventricle, though in very severe infections adult worms can be found in the right atrium and in the caudal and cranial venae cavae (McCall et al. 2008). Circulating microfilariae are 290–330 μm in length. Ectopic localizations such as eye, brain, and testes are occasionally reported. According to Webber and Hawking (1955), the prepatent period lasts about 180 days. Heartworm infection is a severe/very severe life-threatening condition in both dogs and cats, although it is completely preventable by treating animals with antiparasitic macrocyclic lactones, such as ivermectin, milbemycin oxime, selamectin, and moxidectin throughout the mosquito transmission season (McCall et al. 2008). The infection prevalence in endemic or high endemic areas ranges from 5 to $>$ 40 % in untreated dogs.

D. repens life cycle is similar to that of *D. immitis*, but adult worms are located mainly in subcutaneous tissues, although the parasite can be found in the abdominal cavity and along connective muscular fasciae (Genchi et al. 2011a). According to Webber and Hawking (1955), Cancrini et al. (1989), and Genchi et al. (2013), the prepatent period is around 200 days. Circulating microfilariae are 300–370 μm in length.

The infection often goes unnoticed. However, it has been reported that dogs with *D. repens* infection can present cutaneous disorders of varying severity, such as pruritus, dermal swelling, subcutaneous nodules containing the parasites, and ocular conjunctivitis (Genchi et al. 2011a). Severe infections with allergic reactions likely due to sensitization toward the microfilariae have also been reported. The infection prevalence in dogs in highly endemic areas ranges from around 30 % in Italy to over 35 % in Hungary (Genchi et al. 2011a).

In dogs, the diagnosis of dirofilarial infection is based on clinical findings and confirmed by testing for both microfilariae and circulating antigens (from adult female) in the bloodstream in the case of *D. immitis* infection and for circulating microfilariae in the case of suspected *D. repens* infection (McCall et al. 2008). Circulating microfilariae of the two species can be differentiated morphologically by microscopical observation after application of a modified Knott test (Knott 1939); histochemical staining or molecular methods can aid the identification (for more information, see Genchi et al. (2011b) and ESCCAP Guidelines No. 5).

13.2 *Dirofilaria* Infections in Humans: Epidemiology and Clinical Manifestations

Both *D. immitis* and *D. repens* are zoonotic and are able to cause benign to severe/very severe conditions in humans (Theis 2005; Genchi et al. 2011a). However, in Europe, human *Dirofilaria* infections are caused mainly by *D. repens* (Genchi et al. 2011a; Simón et al. 2012). For a recently described case of infection caused by *D. immitis* in Italy, see Avellis et al. (2011).

The number of human cases from the most endemic areas of canine *Dirofilaria* infections available in international data banks has been summarized by Simon et al. (2012). Even though caution is needed when comparing studies and clinical cases published by different authors along a range of over 50 years (also considering the different awareness of medical doctors in different countries and along the years), it is clear the number of cases in Europe (>1,400) is dramatically higher compared to the rest of the world, including the USA, where 110 have been recorded (Theis 2005; Lee et al. 2010), and Japan, with 390 cases (Akao 2011). Most cases in Europe have been attributed to *D. repens*. A rough estimation of the number of *D. immitis* human infections per year shows about 1.8 cases in the USA throughout 60 years and 7.1 cases in Japan throughout 39 years; in Europe, the average is about 39 cases throughout 37 years, attributed to *D. repens* infection. It must be noted that most cases in Europe have been diagnosed quite recently (roughly from 2000) and include the cases of individuals traveling or spending holidays in endemic areas of southern Europe, such as Italy, Spain, and Greece (for a review, see Genchi et al. 2011a). Therefore, the number of cases in people living in areas previously not considered at risk has dramatically increased (Genchi et al. 2010; Simón et al. 2012; Masny et al. 2013).

The increased number of human infections in Europe is most likely a consequence of (1) the changing climate, with increasing temperatures, which allows the survival and the expanding seasonal activity of mosquitoes and (2) the movement and relocation of microfilaremic dogs from the well-known endemic areas of southern Europe, such as Italy, toward the northern and eastern countries. The number of published human cases in Italy has increased from 4.5 per year from 1986 to 1998 to 15.6 per year in the last decade (1999–2009) (Pampiglione et al. 1995, 2009; Pampiglione and Rivasi 2000). Autochthonous human cases have been reported from Austria, France, Greece, Croatia, Hungary, Slovak Republic, Poland, Romania, Ukraine, Russia, Turkey, and in other countries such as Africa and Middle and Far East (reviewed by Genchi et al. 2011a; Simón et al. 2012; Kartashev et al. 2011; Masny et al. 2013) (Table 13.1). Furthermore, the infection has been diagnosed in North American individuals traveling or spending their holidays in endemic European areas.

In most cases, the parasite is not able to develop to the adult, sexually mature stage, and infection is characterized by the presence of preadult stages located in subcutaneous tissues of the different body areas, near the point of mosquito vector bite, although at least three cases of microfilaremic zoonotic infections have been reported in Europe and one in Iran. Interestingly, in all the American individuals, who acquired the infection within the previous 8 months–8 years, adult female worms were found. In two cases, worms were still viable (see Genchi et al. 2011a). Women are more commonly affected than men, although there is no statistical difference (Pampiglione and Rivasi 2000). To note that, of more than 1,400 reported cases, the parasite was localized in the ocular region (e.g., orbital region, eyelid, subconjunctival, and intravitreal) in about 23 % of cases (Table 13.1), probably as a consequence of the perception of a "foreign body" by the human body and possibly also for the easy observation by the oculist, compared to the deeper localizations of the worm.

Impaired vision and floater-like mobile shadows seem to be the most frequent symptoms, but the infection is seldom accompanied by loss of vision or serious ocular complications. Intravitreal ocular infection is quite rare, but at least three cases have been reported in Europe (Angunawela et al. 2003; Gorezis et al. 2006; Gungel et al. 2009).

Besides subcutaneous and ocular localization, *Dirofilaria* spp. have been shown to infect viscera (the lungs and mesentery) as well as the female breast and male genitalia (e.g., scrotum, verga, spermatic cord, epididymis). At least 27 cases of pulmonary localization have been reported from 1981 to 2010. The lesions are usually identified by X-ray as a coin lesion. To note visceral and lung localization usually lead to suspect a malignant tumor, thus requiring biopsy or more invasive surgery for differential diagnosis through histology and morphologic identification of the parasite. In some cases, infections have been described as mimicking either cervical intradural Langerhans cell histiocytic tumor (Perret-Court et al. 2009) or scrotal tumors (Fleck et al. 2009); intraperitoneal localizations are also recorded, causing severe consequences (Abbas et al. 2006).

Table 13.1 Human *Dirofilaria repens* infection in Europe and other countries of the Old World

Country	No. of cases	Ocular	Pulmonary	Other unusual and seriousness localization
Austria	>16			Intradural tumor like abdominal cavity, spermatic cord, spermatic duct, scrotum, epididymis associated with meningoencephalitis (surgery in Germany)
France	91	22	2	
Greece	38	7	3	
Hungary	39	19		
Italy	341	68	22	
Spain	16		8	
Russia[a]	624[1]	54		
Ukraine[b]	51	18	2	
Turkey	22	12	3	
Other countries[c]	192	134	2	
Total	1,430	334	42	

[a]Sergiev et al. (2009) reported worms from 140 individuals identified as *D. repens*; such a figure has not been added to Russian cases because of incomplete description

[b]Masny et al. (2013) estimated about 900 cases; such a figure has not been added to Ukraine cases because of incomplete description

[c]Albania, Bulgaria, Croatia, former Yugoslavia, Georgia, Kazakhstan, Poland, Romania, Serbia, Montenegro, and Slovenia

Human dirofilariasis is currently considered an emerging zoonosis in Italy (Genchi et al. 2011a), France (Raccurt 1999), Hungary (Szénási et al. 2008), in central and easter Europe (Masny et al. 2013), and Russia (Kartashev et al. 2011). Importantly, many infections, mainly the benign forms, likely go unnoticed due to a lack of awareness among the medical profession and to diagnostic uncertainty. In fact, until the recent introduction of molecular methods based on PCR and sequencing, diagnosis was usually carried out after surgery and examination of histological sections of the infected tissue, except for some subconjunctival cases where it was possible to see and remove the parasite. Serology, using crude, secretory/excretory *Dirofilaria* antigens, and recombinant antigens or surface proteins of *Wolbachia*, the bacterial endosymbiont of filarial worms, is still not fully reliable because of insufficient specificity, i.e., these antigens do not allow to distinguish infections by *D. immitis* or *D. repens* (or other *Dirofilaria* spp.). However, detection of anti-*Dirofilaria* antibodies can anyway be useful, even with the current antigens, in at least two situations: (1) both pulmonary and subcutaneous *Dirofilaria* nodules can lead to the suspicion of a malignant tumor; detection of anti-*Dirofilaria* antibodies can help to discard the malignant origin of the nodule (Simón et al. 2003), being the specific diagnosis of the *Dirofilaria* species involved an irrelevant matter; and (2) in epidemiological surveys, serology of *Dirofilaria* antibodies can be an adequate way to evaluate the risk of infection in human populations living in endemic areas. For example, the recent seroepidemiological survey of human dirofilariasis carried out in Spain that revealed that 11 % of the sera were positive was performed using the crude antigen of adult *D. immitis* (Morchón et al. 2010).

13.3 Is the Spread of *Dirofilaria* Infection an Actual Trend?

In North America, where *D. immitis* is endemic, canine heartworm infection has gradually expanded its geographical range since 1950 from hyperendemic foci (e.g., Mississippi River coastal area) to more northern areas. At that time, the cause was attributed to two main factors: (1) movement of dogs for hunting, breeding, and shows and (2) improved awareness of the infection by veterinarians. Nowadays, heartworm is endemic in all 50 states of the USA (Lee et al. 2000), and the infection risk has increased, at least at the regional level, due to the exportation of heavily infected dogs (prevalence 34–51 %) from the New Orleans area and other areas near Louisiana to northern states and Canada in the aftermath of Hurricane Katrina in August 2005 (Levy et al. 2007).

In Europe, until the second half of the last century, both filarial infections (*D. immitis* and *D. repens*) were diagnosed mainly in southern regions, and the highest endemic area was the Po River Valley in Italy. At that time, no autochthonous cases were found in northern Europe, even though several cases of heartworm infection were diagnosed in dogs which had visited endemic areas. After the introduction of the Pet Travel Scheme in 2000, which allows a more easy movement of animals throughout the European Union, the risk of *Dirofilaria* is spreading.

Besides movement of infected dogs, climate plays a critical role in the transmission and spread of *Dirofilaria* infections. The latest report by the Intergovernmental Panel on Climate Change (IPCC 2007) estimates current global warming to be almost 0.8 °C above preindustrial levels and foresees a further rise of 1.1–6.4 °C by 2100 (IPCC 2007). Global warming is defined as an average increase in the temperature of the atmosphere near the Earth's surface and in the troposphere, which can contribute to changes in global climate patterns. There is now strong scientific consensus that (1) global warming is occurring, (2) it is largely attributable to human emission of greenhouse gases, (3) the effects are now observable, (4) further warming will occur, and (5) that climate change has a potentially serious impact on public and animal health (Bernardi 2008). By altering the global environment, climate change has the significant potential to intensify certain diseases, particularly those transmitted by vectors (Khasnis and Nettleman 2005). Global climate change can affect disease vector behavior, which in turn may alter the current patterns of vector-borne diseases transmitted by the bite of hematophagous arthropods (Rogers and Randolph 2006). Important examples are canine leishmaniosis and dirofilariasis in Italy: both these arthropod-borne infections have changed distribution patterns; *Leishmania infantum* was endemic in southern areas of the country until the late 1990s, but it is now increasingly diagnosed in northern areas. Dirofilariasis, which was endemic in canine populations in northern Italy, is now spreading all over the country (Otranto et al. 2009; Traversa et al. 2010).

Mosquitoes, intermediate hosts and vectors of *Dirofilaria* spp., are cold-blooded animals, meaning that their internal temperature is affected by the temperature of

their environment. Thus, for many terrestrial arthropod species, a northward range expansion can be expected in response to projected climate change as recently observed in Germany (Sassnau and Genchi 2013). An example is the mosquitoes accidentally introduced in Europe from Far East and America, such as the case of Asian tiger mosquito *Ae. albopictus*, which was imported into Italy in 1990 and then spread throughout Europe as far as the Netherlands (Scholte et al. 2008). Furthermore, vector-borne pathogens are sensitive to climate, and there is some evidence that anthropogenic climate change can play a role in increasing their incidence and intensity (Purse et al. 2005).

Transmission of dirofilariasis is dependent on the presence of (1) sufficient numbers of microfilaremic dogs (microfilaremia is usually absent in cats and their role as reservoirs is not relevant), (2) susceptible mosquitoes, and (3) a suitable climate to permit extrinsic incubation of *Dirofilaria* in the mosquito intermediate host (Genchi et al. 2011b). Temperature, precipitation, and relative humidity are the main factors that determine the abundance of mosquitoes and the prevalence of mosquito-borne diseases such as filarial infection, and there is a strong temperature dependence for the development of the parasites within the mosquito vectors. Even though a holistic approach of vector-borne diseases should consider, besides temperature, other factors such as human activity and the ecology and behavior of both hosts and the vectors, models based on temperature have shown to be able to predict the spread of *Dirofilaria* infection in Europe (Genchi et al. 2005, 2011b; Mortarino et al. 2008). Climate-based forecast systems usually employ the concept of growing degree days, i.e., 1 degree day occurs when the mean temperature for the day is 1 °C above the threshold temperature. For *D. immitis* infections, climate-based models that determine the effect of temperature on the extrinsic incubation of larval stages are based on the study of Fortin and Slocombe (1981). The rationale of this model is that climate dictates the seasonal occurrence of *Dirofilaria* transmission and there is a threshold of about 14 °C below which development will not proceed. The authors demonstrated that at 30 °C, the development of *D. immitis* microfilariae to infective L3 larvae was completed in 8–9 days in the mosquitoes. This increased to 10–14 days at 26 °C, 17 days at 22 °C, and 29 days at 18 °C. The seasonal transmission model assumes a requirement of 130 *D. immitis* Development Units (DiDUs) for larvae to reach infectivity and a maximum life expectancy of 30 days for a vector mosquito (Slocombe et al. 1989; Lok and Knight 1998). Based on these assumptions, climate-based models have been used in order to predict the occurrence and seasonality of *Dirofilaria* in Europe (Genchi et al. 2009, 2011a), in the UK (Medlock et al. 2006), and Argentina (Vezzani and Carbajo 2006).

For *D. repens*, the development times of microfilariae to the infective stage at the different temperatures are quite similar: 8–13 days at 28–30 °C, 10–11 days at 26 °C, and 16–20 days at 22 °C. In *Ae. albopictus*, the development from the microfilarial stage to infective larvae takes 14–18 days at 26 °C for *D. immitis* and 16–18 days for *D. repens* (reviewed by Genchi et al. 2011a). In a recent study (Genchi et al. 2009), a threshold value of 130 cumulative Development Units (DUs) was accepted for both *Dirofilaria* species only if it was reached in 30 consecutive days and the data was interpolated utilizing the linear kriging function of a Geographical Information

System (GIS) to calculate the number of *Dirofilaria* generations. The input of the model was based on the average temperature of the last 15 years, for a total 5475 temperature measures per station and above 19,000,000 values processed. The outputs of this model were predictive maps which assessed the duration of the *Dirofilaria* transmission risk period and monthly maps showing the stations that reached the 130 *Dirofilaria* DUs (DDUs). Most stations located in southern, central, and eastern Europe have reached the 130 DDUs at least once in the years studied. Note that, previously, this model had correctly predicted the spread of *Dirofilaria* infections into several eastern European countries. Indeed, studies from Hungary, the Czech Republic, Slovakia, and northern Serbia confirmed that areas formerly free of *Dirofilaria* infection are now endemic (Genchi et al. 2011b). Further empirical data has confirmed such a trend, and recently autochthonous *D. repens* infections in dogs have been reported from northern Germany, Austria, and the Netherlands (reviewed by Genchi et al. 2011a, 2013).

Interestingly, most of these studies report the presence of *D. repens* both in animals and in humans and, when *D. immitis* is also present in dogs, *D. repens* shows higher prevalences. It is thus of interest to try to understand why *D. repens* is spreading more rapidly than *D. immitis*. A possible explanation could be that most *D. repens* infections in dogs are asymptomatic, while heartworm infections usually cause severe clinical disease. It is thus likely that dogs which have traveled to endemic areas of southern Europe become infected and when they return to northern areas, having no apparent symptoms, act as donors of microfilariae to local mosquito populations. On the contrary, dogs with heartworm infection are usually referred to veterinary clinics and cured. If such a hypothesis is confirmed, considering that an increasing number of dogs travel for holidays or relocation and that pet travel is now facilitated by the new schemes in many European countries, subcutaneous dirofilarial infection could continue its spread. Furthermore, many in clinic, rapid kits for the serological diagnosis of *D. immitis* are available on the veterinary market while it does not exist for *D. repens*.

13.4 Prospects for the Control of *Dirofilaria* Infections in Humans

During the recent years Europe has experienced the introduction of vector-borne diseases from tropical regions such as the recent outbreak of chikungunya virus epidemics in Italy (Rezza et al. 2007) and West Nile virus (Sambri et al. 2013) or, as it is the case of *Dirofilaria,* the spread of the infection from southern Mediterranean regions toward northern and eastern areas. Although it has been argued that climate change is the key factor responsible for the more northerly distribution of vectors and their possibility to transmit pathogens, other drivers, notably travel and trade and insecticide resistance, are also likely to have played a role in these processes (Knols and Takken 2007). Transport networks continue to expand so that pathogens and their vectors and animal reservoirs can now move further and faster than ever

before (Tatem et al. 2006). Thus, in addition to climate changes and global warming, it is also important to consider the effects of global movement as an important factor inducing the spread of vector-borne diseases, such as *Dirofilaria* infection, whose epidemiology has now the following characteristics:

- The spread of the infection has increased in endemic areas.
- Areas formerly free from the infection are now endemic.
- In dogs untreated with preventive drugs, both the abundance and the incidence of *Dirofilaria* infections have increased (Genchi et al. 2007).
- *Ae. albopictus* is now considered an important, competent vector of *Dirofilaria* infections. This mosquito species could spread from southern to northern European countries in the near future (Medlock et al. 2006; Takumi et al. 2009), changing the epidemiological patterns of dirofilariasis in both humans and animals.
- Human infections have dramatically increased; the infection is more and more frequently diagnosed and severe/very severe conditions have been reported.

From a practical point of view, to prevent the further spread and endemicity of *Dirofilaria* infections and to control the risk of human infections, epidemiological surveys should now be carried out in different European countries to assess the actual prevalence values, such as that recently done in Germany (Pantchev et al. 2009). Furthermore, all traveling dogs should be examined for circulating microfilariae, treated with preventative drugs (Genchi et al. 2010, 2013) or microfilaricidal drugs (Fok et al. 2010) when visiting at-risk areas, and reexamined for circulating microfilariae 6–7 months after their stay abroad. European guidelines for the control and prevention of *Dirofilaria* infections in pets are available at http://www.esccap.org.

13.5 Other Species of Filarial Nematodes Infecting Humans

The most comprehensive and recent review of zoonotic filarial infections is by Orihel and Eberhard (1998). Table 13.2 summarizes published case reports of other filarial nematodes that have been reported in humans (Orihel and Eberhard 1998). These other zoonotic filariae are all parasites of livestock and/or wild animals in various parts of the world. Even though unequivocal identification of the worms has not always been possible, the geographical location of affected individuals and the histological features, when available, almost always allowed genus, if not species, identification.

The genus *Dirofilaria* contains other species besides *D. immitis* and *D. repens* that have been reported as infecting humans, including *D. ursi*, which parasitizes bears, and *D. subdermata*, a parasite of porcupines in the northern USA and Canada (Beaver et al. 1987; Gutierrez 1990; Orihel and Isbey 1990). Most infections regard the subcutaneous tissue and the eye.

Table 13.2 Summary of published reports of zoonotic infections with filarial worms (other than *Dirofilaria immitis* and *Dirofilaria repens*)

Parasite	Definitive hosts	Vector	Affected organs	Reference
Dirofilaria			Skin/	Beaver et al. (1987),
D. ursi	Bear	Mosquitoes	subcutaneous	Gutierrez (1990), Orihel
D. subdermata	Porcupine		tissue	and Isbey (1990)
D. striata	Wild felids			
Onchocerca spp.[a]	Cattle, equids, cervids, and others	*Simulium* flies	Skin/ subcutaneous tissue	Ali-Khan (1977), Azarova et al. (1965), Beaver et al. (1974, 1989), Siegenthaler and Gubler (1965), Takaoka et al. (1996)
Brugia spp.[a]	Raccoons, rabbits, monkeys, and others	Mosquitoes	Lymphatics	Baird and Neafie (1988), Menendez and Bouza, (1988), Orihel and Beaver (1989), Elenitoba-Johnson et al. (1996)
Molinema (*Dipetalonema*)		Mosquitoes		Beaver et al. (1980)
D. arbuta	Porcupine			
D. sprenti	Beaver			
Loaina (*Pelicitus*)				Botero et al. (1984)
L. uniformis	Rabbits	Mosquitoes	Eye	
L. scapiceps	Rabbits			
L. roemeri	Kangaroos			

[a]Unidentified at the species level

Worms of the genus *Onchocerca* can also cause zoonotic infections occasionally. *Onchocerca volvulus* is the most widespread species of the genus and is a parasite of humans. However, many other species of *Onchocerca* are natural parasites of animals including horses and cattle worldwide, and several cases of human infections with these species have been reported. In fact, zoonotic onchocerciasis has been described in the USA, Canada, Switzerland, Russia, and Japan. Infections usually present as firm subcutaneous nodules in different locations on the body or in the eye (Azarova et al. 1965; Siegenthaler and Gubler 1965; Beaver et al. 1974, 1989; Ali-Khan 1977; Takaoka et al. 1996).

Nematodes of the genus *Brugia* include species that are parasites of human (*B. malayi*, *B. timori*), together with several species which infect a wide variety of animals across the globe. For example, there are species of *Brugia* which infect monkeys in Southeast Asia and others that are parasites of raccoons and rabbits in the USA. There have been nearly 30 recognized cases of zoonotic infections by *Brugia* in the USA and several more from different countries around the world, including Colombia, Brazil, Peru, and Ethiopia (Baird and Neafie 1988; Menendez and Bouza 1988; Orihel and Beaver 1989; Elenitoba-Johnson et al. 1996). The localization of

adult worms varies in affected patients, and the lymph nodes of the groin, head/neck, and torso may be involved. Several cases of ocular infection by zoonotic nematodes of the genera *Molinema* (*Dipetalonema*) (*M. arbuta* and *M. sprenti;* Beaver et al. 1980) and *Loaina* (*Pelicitus*) (*L. uniformis*, *L. scapiceps*, *L. roemeri;* Botero et al. 1984) have also been reported in the literature. The apparent tropisms of these parasites in human infections likely mimic their biological behavior in the natural host (beaver, raccoon, kangaroo, etc.).

Finally, there have been several reports of "zoonotic microfilariae" of unknown origin and without definitive identification of the parasite (Orihel and Eberhard 1998). While the prevention of zoonotic infections with *D. immitis* and *D. repens* is feasible and requires adequate preventive treatment of the definitive host, the other filarial species which are parasites of livestock and/or wild animals that may infect humans are nearly impossible.

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