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Review

Onchocercosis: A newly recognized disease in dogs

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Abstract

In the past 15 years, onchocercosis has been reported with increasing frequency in dogs in Europe and the United States, and 64 cases have been described so far. According to some authors, the *Onchocerca* sp. responsible for canine cases spills over from domestic or wild ungulates into dogs. However, canine *Onchocerca* does not match any of the descriptions for species of *Onchocerca* reported from domesticated and wild animals in Europe or North America. The nucleotide sequences of canine *Onchocerca* are also unique within the genus. Moreover, patent *Onchocerca* infections can be seen only in accidental hosts closely related to the natural hosts. In canine onchocercosis cases, high microfilarial load could be observed indicating that canids might be the definitive hosts of the parasite. Therefore, others suggested that *Onchocerca lupi* Rodonaja, 1967 originally described from a wolf (*Canis lupus*) can be responsible for these infections, which is a typical example for host switch and site shift, the dominant modes of speciation of the genus *Onchocerca*. The morphology, molecular characteristics, phylogeny, life cycle, host specificity, geographical distribution of *Onchocerca* sp. infecting dogs, as well as the clinical signs, pathology, laboratory diagnosis, therapy and possible zoonotic significance of canine onchocercosis are reviewed. Research into human onchocercosis has been hampered by the lack of analogous models. As infections in dogs may provide a practical experimental system, further studies should be encouraged to try to establish experimental *Onchocerca* infections in dogs.

Keywords: *Onchocerca lupi*; Dog; Wolf; Canids; Eye disease; Dermatitis; Zoonoses; Animal model

Contents

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1. Introduction

Onchocerca lupi as a distinct species was originally described in the periocular tissues of a Caucasian wolf (*Canis lupus*) in Gruziya (Rodonaja, 1967). In the past 15 years, onchocercosis has been reported with increasing frequency in dogs. Eight cases have been reported from south-western United States (Arizona, California, Utah) (Orihel et al., 1991; Gardiner et al., 1993; Eberhard et al., 2000; Gionfriddo et al., 2005; Zarfoss et al., 2005), and altogether 56 cases have been diagnosed in southern and central Europe (Germany, Greece, Hungary, Portugal, Switzerland) (Széll et al., 2001a,b; Egyed et al., 2002a; Komnenou et al., 2002, 2003; Hermosilla et al., 2005; Schäffer et al., 2006; Sréter-Lancz et al., 2007). According to some authors, canine onchocercosis is an aberrant infection by *Onchocerca lienalis* of cattle in an accidental host with ectopic location (Orihel et al., 1991; Gardiner et al., 1993; Eberhard et al., 2000; Zarfoss et al., 2005). Others suggested that a previously unrecognized species of *Onchocerca* is responsible for canine onchocercosis, which spills over from wild ungulates into canines with regularity (Komnenou et al., 2002). However, canine *Onchocerca* sp. only matches the description for species of *O. lupi* reported from domesticated and wild animals in Europe or North America (Egyed et al., 2001), and the nucleotide sequences of canine *Onchocerca* are also unique within the genus (Egyed et al., 2001, 2002b; Sréter-Lancz et al., 2007). Moreover, the host range of all *Onchocerca* spp. is very narrow (Rommel et al., 2000), and patent *Onchocerca* infection can be seen only in accidental hosts closely related to the natural host (e.g., in chimpanzees infected with *Onchocerca volvulus* of man) (Eberhard et al., 1995; Orihel and Eberhard, 1998). However, in canine onchocercosis cases, mature males, gravid females and high microfilarial load could be observed (Orihel et al., 1991; Gardiner et al., 1993; Eberhard et al., 2000; Széll et al., 2001a,b; Egyed et al., 2001; Komnenou et al., 2002, 2003; Gionfriddo et al., 2005; Hermosilla et al., 2005; Zarfoss et al., 2005; Schäffer et al., 2006) indicating that dogs or closely related canids, for example, wolves, might be the definitive hosts of this parasite. Therefore, other authors came to the conclusion that most likely *O. lupi* originally described from a wolf is responsible for canine onchocercosis (Széll et al., 2001b; Egyed et al., 2001, 2002b; Hermosilla et al., 2005; Schäffer et al., 2006; Sréter-Lancz et al., 2007; Krueger et al., 2007; Uni et al., 2007). The origin of the genus *Onchocerca* was referred to the Miocene radiation of the cervids and bovids, which form the majority of hosts (Bain, 2002). In the genus *Onchocerca*, it is clear that co-speciation between hosts and parasites is not the dominant mode of speciation. The results showed evidence of sympatric speciation both through host switch and site shift (Bain et al., 1977, 1993; Bain and Nasher, 1981; Bain, 2002; Chabaud and Bain, 1994; Morales-Hojas et al., 2006; Krueger et al., 2007). The case of *O. volvulus* of man, *Onchocerca dewittei* of wild boar, *Onchocerca ramachandrini* of warthog and *Onchocerca fasciata* of camel can be considered as typical examples for host switch. *Onchocerca gutturosa* and *O. lienalis* infecting cattle are the best examples for site shift. *O. lupi* of dogs can be another example for both modes of speciation. Herein we summarise the current knowledge on canine onchocercosis.

2. Morphology

Male worms are white, fragile and slender, measuring 43–50 mm in length by 0.1–0.2 mm in diameter (Table 1). The anterior end is rounded; the cuticle is 4–5 μm thick and bears faint transverse striations (Rodonaja, 1967; Egyed et al., 2001). The caudal papillae are large and fleshy. The left spicule is slightly curved, tubular and tapered and 160–203 μm long, and the right spicule is 75–94 μm long, curved, tubular, broad and heavily cuticularised at its proximal end but narrowing distally to a knobbed end (Demiaszkiewicz et al., 1991; Egyed et al., 2001; Komnenou et al., 2002).

As it is difficult if not impossible to remove complete female worms from the nodules, the total length of females is unknown but the longest fragments were 100–165 mm (Rodonaja, 1967; Komnenou et al., 2002). Several enzyme treatments were tested for the release of complete female worms, but none of them was successful (Egyed et al., 2001). Females are white, fragile, long and slender, measuring 0.2–0.4 mm in maximum diameter (Table 1). The anterior end is rounded; the vulva is located 638–1000 μm from the anterior end (Demiaszkiewicz et al., 1991; Komnenou et al., 2002). The tail is rounded with transverse striations of the cuticle

Table 1
Major morphometric differences between *Onchocerca lienalis* and canine *Onchocerca* sp.[a]

		O. lienalis	Canine *Onchocerca* sp.
Males	Average length (mm)	22 (19–25)	47 (43–50)
	Average width (μm)	60 (50–80)	155 (110–200)
	Length of oesophagus (μm)	702 (590–800)	565 (480–650)
	Nerve ring from anterior end (μm)	140 (110–170)	350 (320–380)
	Length of spicules (μm)		
	Right	70 (60–80)	85 (75–94)
	Left	210 (190–230)	182 (160–203)
	Spicule ratio (left/right spicule)	3:1 (2.4–3.8:1)	2.1:1 (1.8–2.7:1)
Females	Average length (mm)	560 (330–850)	ND
	Average width (μm)	180 (150–220)	310 (200–420)
	Length of oesophagus (μm)	900 (740–1250)	917 (638–1200)
	Nerve ring from anterior end (μm)	140 (120–180)	282 (175–390)
	Vulva from the anterior end (μm)	360 (280–460)	820 (638–1000)
Microfilariae	Length of microfilariae (μm)	236 (213–250)	108 (98–118)
	Width of microfilariae (μm)	6 (5–7)	6 (5–7)
	Body ratio (length/width)	39:1 (30–50:1)	18:1 (14–24:1)
	Number of nuclei		
	In head (first row)	1	2–3
	In tail	5	3

Abbreviation: ND, not determined.
[a] Based on data provided by Rodonaja (1967), Eberhard (1979), Demiaszkiewicz and Matsaberidze (1991), Orihel et al. (1991), Gardiner et al. (1993), Eberhard et al. (2000), Széll et al. (2001a,b), Egyed et al. (2001), Komnenou et al. (2002), Gionfriddo et al. (2005), Hermosilla et al. (2005), Zarfoss et al. (2005), Schäffer et al. (2006), and Uni et al. (2007).

(Demiaszkiewicz et al., 1991). The cuticle is composed of two distinct layers over all body extremities (Fig. 1); the outer layer bears ring-like ridges, which are interrupted and sometimes bent or branched over lateral chords (Demiaszkiewicz et al., 1991; Egyed et al., 2001). Anteriorly, the ridges are small, close together, becoming taller and farther apart in the posterior direction. In the posterior part of the body, the ridges diminish in size, and no striae are evident near the ends of the body (Demiaszkiewicz et al., 1991). In the midbody, the ridges are rounded in shape, 3–5 μm high and spaced 7–12 μm apart (Orihel et al., 1991; Eberhard et al., 2000; Egyed et al., 2001; Hermosilla et al., 2005; Komnenou et al., 2002). The distance between two cuticular ridges is 32–62 μm (Demiaszkiewicz et al., 1991; Orihel et al., 1991; Eberhard et al., 2000; Egyed et al., 2001; Komnenou et al., 2002). The cuticular layer below the ridges contains striae, on average one stria under every ridge and one between neighbouring ridges (Fig. 1 and Table 2). In the midbody, the striations are elongated, rounded, 4–7 μm thick and 20–34 μm in length (Eberhard et al., 2000; Egyed et al., 2001; Komnenou et al., 2002).

The intrauterine and skin microfilariae are straight, unsheathed, 98–118 μm long by 5–7 μm wide (Fig. 2) (Table 1). Fixed and stained microfilariae are slightly smaller (Fig. 2) (Széll et al., 2001b). The anterior end is bluntly rounded, and contains two to three nuclei per row. The tail tapers gradually to a point, and in tail, the nuclear column is reduced to a single row of three (Table 1).

The morphology of adults and microfilariae of canine *Onchocerca* sp. differs considerably from that of all other European or North American *Onchocerca* spp. including *O. lienalis* (Tables 1 and 2). The females and males of canine *Onchocerca* are twice as large as that of *O. lienalis*, while its microfilariae are less than half of the size of *O. lienalis* microfilariae (Table 1). Microfilariae are the smallest within the genus known so far (Bain and Chabaud, 1986). Morphology-based cluster analysis revealed that the canine *Onchocerca* is separated from other *Onchocerca* spp. early in its evolution (Egyed et al., 2001).

3. Molecular characterization and phylogeny

As it was demonstrated, sequences of canine *Onchocerca* sp. are unique within the genus (Egyed et al., 2001, 2002b; Sréter-Lancz et al., 2007). Phylogenetic analyses demonstrated that the genus *Onchocerca* is a sister group of genus *Dirofilaria* (Bandi et al., 1998, 2001; Bazzocchi et al., 2000; Casiraghi et al., 2001). Based on mitochondrial cytochrome oxidase subunit I gene (COI) and NADH dehydrogen-

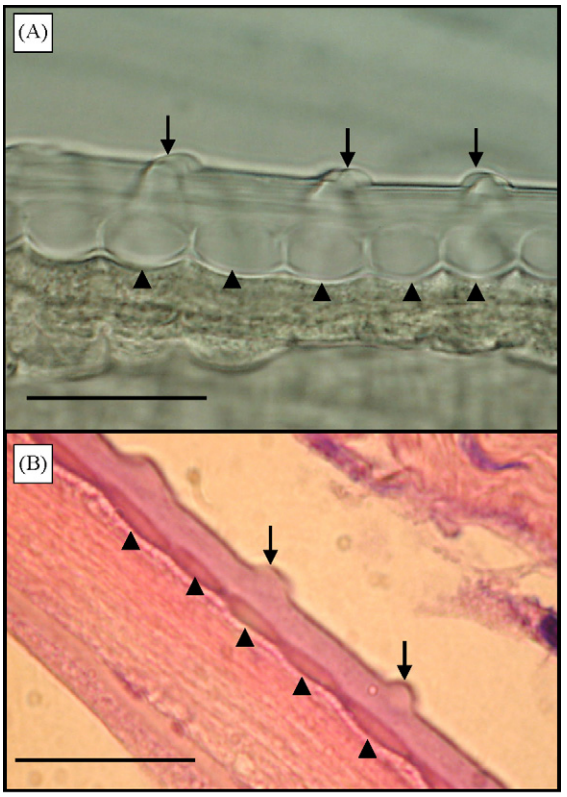

Fig. 1. Characteristic cuticular ridges (arrows) and striae (arrowheads) in the female of canine *Onchocerca* sp. (Széll et al., 2001a,b). (A) Worm isolated from the subconjunctiva and cleared in lactophenol, scale bar = 50 μm; (B) histologic section of a subconjunctival nodule, H&E stain, scale bar = 50 μm.

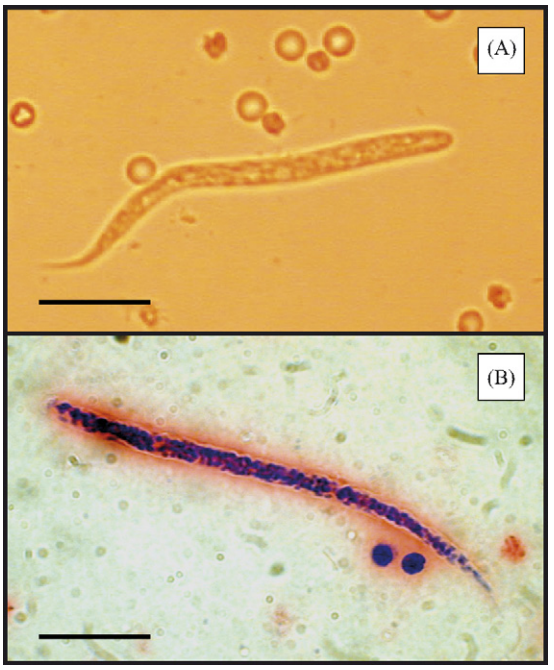

Fig. 2. Microfilariae of canine *Onchocerca* sp. (Széll et al., 2001b). (A) Unfixed and unstained microfilariae, scale bar = 25 μm; (B) stained with haematoxylin, scale bar = 25 μm.

ase subunit 5 (ND5) gene sequences, the phylogenetic position of *O. lupi* is basal (Sréter-Lancz et al., 2007) (Fig. 3), confirming the results of the morphology-based cluster analysis (i.e., canine *Onchocerca* is an atypical *Onchocerca* sp. showing both primitive and evolved

Table 2
Host range of *Onchocerca* spp. infecting wild and domesticated animals in Europe and North America and the comparison of the maximum width and cuticular morphology of their females[a]

Species	Host	Maximum width (μm)	Ridges	Shape of striae	Striae per ridge	BD per DBR
O. cervicalis	Horse	360–570	Prominent	Teeth-like	3–4	4:1
O. reticulata	Horse	275–400	Prominent	Triangular	1	20:1
O. gutturosa	Cattle	200–330	Prominent	Teeth-like	4	3–4:1
O. lienalis	Cattle	150–260	Small	Elongated	2	5–6:1
O. stilesi	Cattle	140–220	Prominent	Elongated	2–3	3–4:1
O. garmsi	Red deer	343–405	Small	Elongated	3	7–8:1
O. jakutensis	Red deer	387–455	Small	Elongated	3–4	8:1
O. tarsicola	Red deer, reindeer	170–330	Small	Elongated	4	5:1
O. flexuosa	Red deer, fallow deer	240–400	One prominent, two small	Wave-like	4 (per prominent)	NA
O. alcis	Elk	200–300	Prominent	Teeth-like	4	6:1
Canine *Onchocerca* sp.	Dog, wolf	200–420	Prominent	Elongated	2	7–10:1
Subconjunctival *Onchocerca* sp.	Man	230–260[b]	Prominent	Elongated	2	10:1

Abbreviations: BD:DBR, ratio of body diameter to the distance between ridges; NA, not applicable.

[a] Based on data provided by Azarova (1965), Rodonaja (1967), Bain and Schulz-Key (1974, 1976), Bain (1975, 1981), Schulz-Key and Bain (1976), Eberhard (1979), Bain and Rehbinder (1986), Demiaszkiewicz (1989), Orihel et al. (1991), Demiaszkiewicz (1993), Gardiner et al. (1993), Eberhard et al. (2000), Egyed et al. (2001), Pampiglione et al. (2001), Komnenou et al. (2002), Gionfriddo et al. (2005), Zarfoss et al. (2005), Schäffer et al. (2006), and Uni et al. (2007).

[b] For the two immature and unfertilized females recovered.

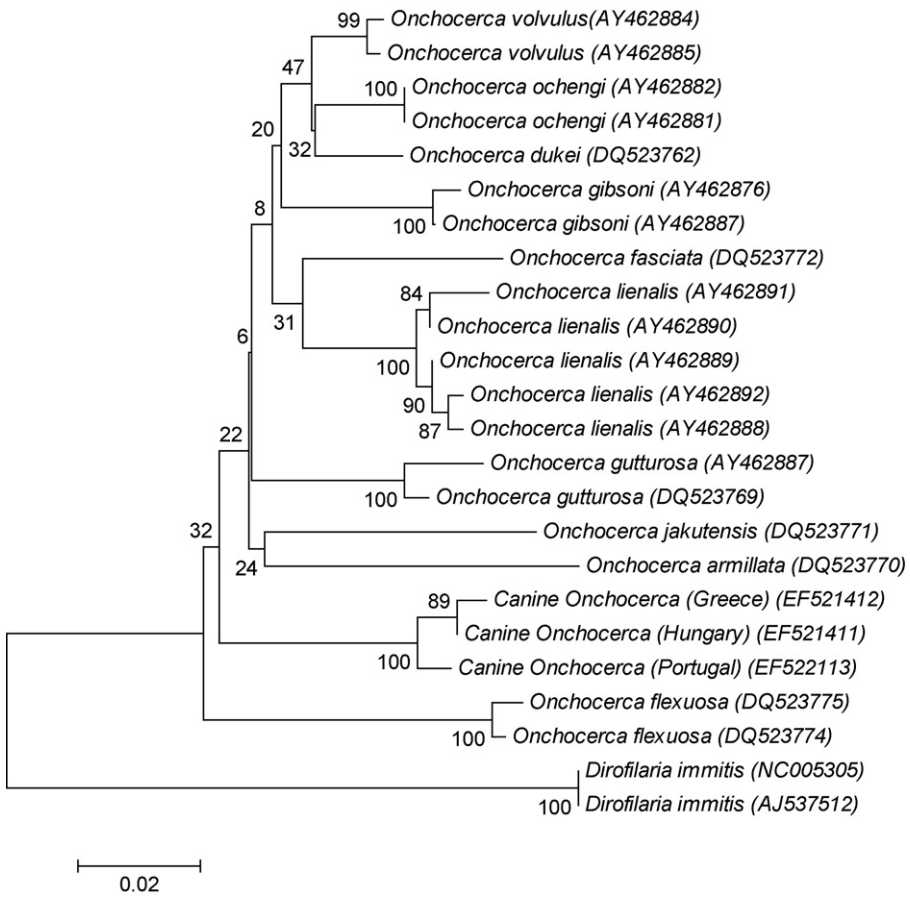

Fig. 3. Phylogenetic relationships of canine *Onchocerca* sp. and some other *Onchocerca* spp. inferred from neighbour-joining analysis of the mitochondrial NADH dehydrogenase subunit 5 gene sequences (Sréter-Lancz et al., 2007). Numbers above and below nodes represent bootstrap values (%). The scale bar indicates evolutionary distances as the number of substitutions per nucleotide. The GenBank accession numbers for each sequence are shown adjacent to each strain.

characters). The evolutionary divergence between COI and ND5 sequences of Greek, Hungarian and Portuguese strains of canine *Onchocerca* sp. were similar in magnitude to that seen within *Thelazia callipaeda* or *O. lienalis*. The evolutionary divergence between the sequences of canine *Onchocerca* sp. and other *Onchocerca* spp. including *O. lienalis* were similar or higher in magnitude to that seen between other *Onchocerca* spp. (Sréter-Lancz et al., 2007). The phylogenetic trees generated for the COI and ND5 sequences were congruent with each other (Sréter-Lancz et al., 2007).

Infection with the endosymbiotic bacteria *Wolbachia* is widespread in filarial nematodes including the majority of *Onchocerca* spp. (Taylor et al., 2005). These bacteria play a significant role in the pathogenesis of onchocercosis (Taylor, 2003). The phylogeny of filariae appears to be congruent with that of their wolbachiae due to the long co-evolutionary history and co-speciation (Bandi et al., 1998, 2001; Casiraghi et al., 2001), and the phylogenetic analyses using different *Wolbachia* genes resulted in similar trees (Bandi et al., 1998, 2001; Bazzocchi et al., 2000; Casiraghi et al., 2001), indicating that organismal phylogenies as opposed to gene phylogenies can be reconstructed. The surface protein gene (*wsp*) and cell-cycle gene (*ftsZ*) of the *Wolbachia* endosymbionts of canine *Onchocerca* sp. were also sequenced (Egyed et al., 2002b). The phylogenetic trees obtained for *wsp* and *ftsZ* sequences were congruent with each other and with trees obtained for mitochondrial genes of the worms.

4. Life cycle, host specificity and geographical distribution

The life cycle and host range of canine *Onchocerca* sp. are not fully known, but may be similar to those of other *Onchocerca* species. The life cycle of all

Onchocerca spp. is indirect, blackflies (*Simulium* spp.) and/or biting midges (*Culicoides* spp.) serve as intermediate hosts (Rommel et al., 2000). The prepatent period and patency of all other *Onchocerca* spp. are long, lasting for several months and several years, respectively (Rommel et al., 2000). Until now, the infection has been described in 64 dogs in south-western United States (Arizona, California, Utah), southern and central Europe (Germany, Greece, Hungary, Portugal, Switzerland) and a Caucasian wolf in Gruziya. As the disease was first described in dogs in 1991, and the majority of data accumulated in the past 8 years, veterinary ophthalmology and dermatology textbooks do not deal with canine onchocercosis from differential diagnostic point of view, and veterinary parasitology textbooks did not contain any information on this parasitosis. As practicing veterinarians diagnose only those diseases they know, the incidence of canine onchocercosis might be underestimated. Considering the narrow host range of all other *Onchocerca* spp. (Rommel et al., 2000) (Table 2), the parasite most probably infects only canids and may persist in wild canid populations, for example, wolves, red foxes, jackals and coyotes. A small-scale study was carried out on the possible infection of red foxes with the parasite without success (Sréter et al., 2003). However, none of the foxes came from the region where the canine cases were detected. Out of 64 cases reported in Europe and North America, 50 cases were identified in three restricted regions, in Vác region of Hungary, Thessaloniki region of Greece and Algarve region of Portugal, probably indicating the clumped distribution of vectors in Europe.

5. Symptoms and pathology

As the life cycle of all *Onchocerca* spp. is indirect (i.e., both an intermediate and a final host is involved), and the development of these parasites in the final host is slow (Rommel et al., 2000), the disease has been recognized only in adult dogs. The mean age of affected dogs was 5.3 years (range: 1–15), and 78% of dogs belonged to the age class of 1–7 years (Orihel et al., 1991; Gardiner et al., 1993; Eberhard et al., 2000; Széll et al., 2001a,b; Egyed et al., 2001; Komnenou et al., 2002, 2003; Hermosilla et al., 2005; Zarfoss et al., 2005; Schäffer et al., 2006; Omonte, personal communication). The majority of dogs (70%) were males. The sex differentiation in parasite infections is a well-known phenomenon, although its background is not fully known (Klein, 2004). Although 32% of dogs were German shepherds, it is probably not be a breed predisposition, as this is the most popular breed worldwide, and these dogs are generally kept outdoors (i.e., more exposed to vector attack).

In the majority of cases, *Onchocerca* infection generally remains undetected in horses and cattle, as the adult worms are located in subcutaneous tissues and ligaments and are not responsible for clinical signs or aesthetic problems (Rommel et al., 2000). The localization of canine *Onchocerca* sp. might be similar in some cases, although there is only one report from Greece describing the parasite in such a location. In this case, the disease was recognized as subcutaneous *Onchocerca* nodule protruding into the tracheal lumen caused coughing, dyspnoea, suffocation and death in a dog (Papaioannou et al., 2004).

In the majority of cases, canine onchocercosis was reported as an acute or chronic ocular disease. In acute cases, conjunctivitis, exophthalmos, periorbital swelling, photophobia, discomfort, lacrimation and discharge have been observed without granuloma or cyst formation around the worms (Eberhard et al., 2000; Széll et al., 2001b; Egyed et al., 2002a,b; Omonte, personal communication). In these cases, fragments of free parts of gauze plug thread-like female worms could be removed by forceps from the surface of the conjunctiva (Eberhard et al., 2000; Egyed et al., 2002a,b; Omonte, personal communication). The

Table 3
Ophthalmic manifestations in 61 dogs with chronic ocular onchocercosis[a]

Ophthalmic manifestations	Number of affected animals
Unilateral involvement	32
Bilateral involvement	29
Exophthalmos	59
Conjunctival congestion	57
Discharge	57
Periorbital swelling	56
Granuloma formation	53
Protrusion of nictitating membrane	51
Lacrimation	49
Discomfort	48
Corneal oedema (localized or generalized)	44
Photophobia	40
Anterior or posterior uveitis	34
Blepharitis	11
Corneal ulcer	9
Cyst-like formation	8

[a] Based on data provided by Orihel et al. (1991), Gardiner et al. (1993), Eberhard et al. (2000), Széll et al. (2001a,b), Egyed et al. (2002a), Komnenou et al. (2002, 2003), Gionfriddo et al. (2005), Hermosilla et al. (2005), Zarfoss et al. (2005), Schäffer et al. (2006), and Omonte (personal communication).

diagnosis can be based on the characteristic cuticular structure of the female worms and the size and morphology of microfilariae removed from the uterus of worm fragments or isolated from the skin of dogs. In chronic cases, the clinical signs are variable as summarised in Table 3. The worms are incorporated in pea- to bean-sized subconjunctival granulamatous nodules or cysts in various parts of periocular tissues (Fig. 4) including the retrobulbar space, orbital fascia, third palpebra, eyelid (Orihel et al., 1991; Gardiner et al., 1993; Eberhard et al., 2000; Széll et al., 2001a,b; Egyed et al., 2002a; Komnenou et al., 2002; Hermosilla et al., 2005; Zarfoss et al., 2005; Schäffer et al., 2006). The surface of the nodules is generally irregular, with nodular thickenings due to the strongly coiled adult worms. Surgical excision of the masses reveals in many cases that the masses deeply infiltrate the periocular connective tissues and can be up to 2 cm in length in some dogs (Széll et al., 2001b; Egyed et al., 2002a). Thin, white, gauze plug thread-like fragments of worms are often visible at the base of masses and can be removed from the surrounding tissues (Fig. 4D). Several sections of coiled gravid male and female nematodes can be detected on histopathological examination of the masses (Fig. 5). The parasites are surrounded by collagenous connective tissue or granulamatous tissue, characterised by the presence of eosinophil granulocytes, plasma cells, histiocytes, fibroblasts and newly formed blood vessels (Orihel et al., 1991; Gardiner et al., 1993; Széll et al., 2001a,b; Komnenou et al., 2002; Hermosilla et al., 2005; Zarfoss et al., 2005; Schäffer et al., 2006). Fresh haemorrhages and tissue destruction due to microfilarial migration and large number of microfilariae can also be observed (Fig. 5B) (Széll et al., 2001a; Komnenou et al., 2002; Gionfriddo et al., 2005; Schäffer et al., 2006). Species identification

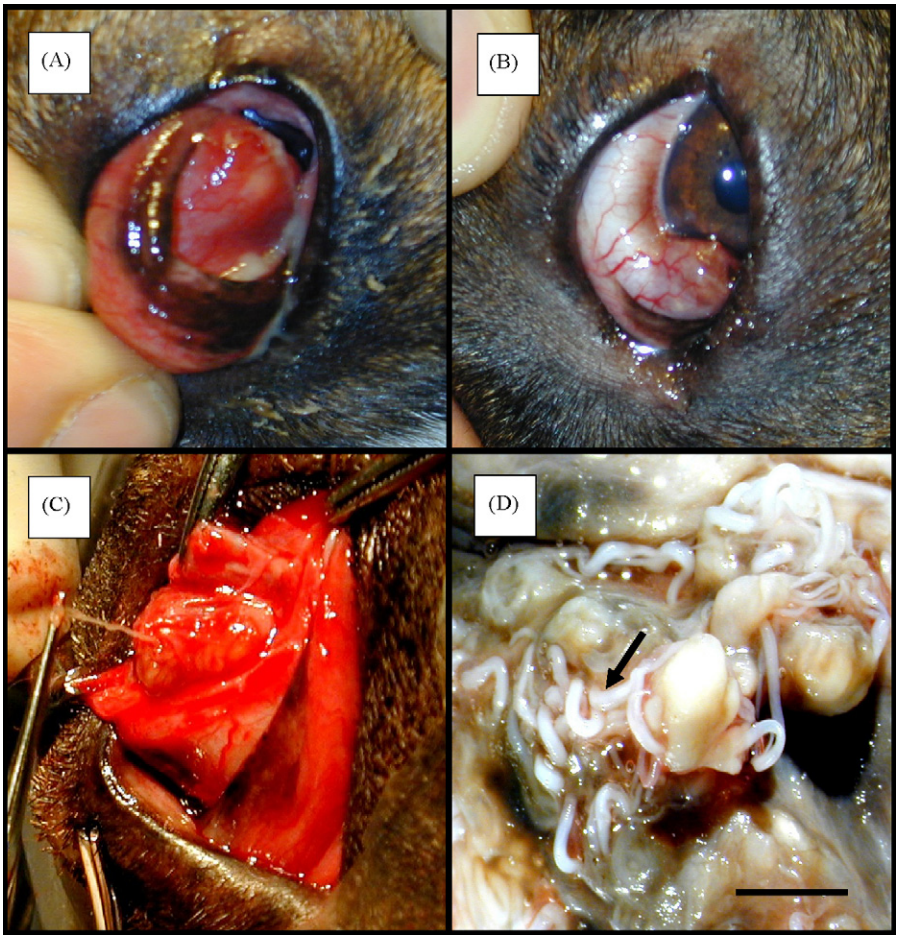

Fig. 4. Clinical signs of canine ocular onchocercosis (Széll et al., 2001b). (A) Worm nodule on the internal surface of third palpebra (arrow); (B) nodule in the retrobulbar space (arrow); (C) mass recovered from the eye. Notice the worm removed from the mass (arrow); (D) ventral view of the mass. Notice coiled *Onchocerca* specimens, scale bar = 5 mm.

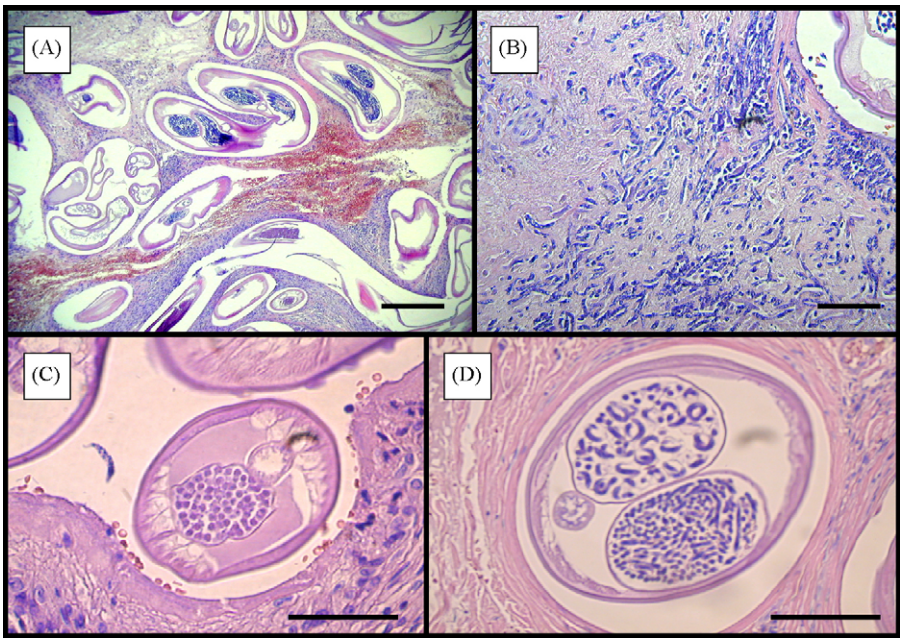

Fig. 5. Histopathology of canine ocular onchocercosis. H&E stain (Széll et al., 2001a). (A) Panoramic view of the lesions and several sections of coiled gravid male and female worms, scale bar = 300 μm; (B) microfilariae in the surrounding tissues, scale bar = 150 μm; (C) cross-section of a male, illustrating the rounded testis filled with spermatocytes, scale bar = 50 μm; (D) cross-section of a female, the paired uteri filled with microfilariae, scale bar = 50 μm.

of the worms can be based on the size of the parasites, the characteristic cuticular structure of the females and the size and morphology of microfilariae removed from the uteri of females, observed in tissue sections or isolated from the tissues removed during surgical intervention. The eye lesions have been erroneously regarded retrobulbar abscesses (Gardiner et al., 1993; Schäffer et al., 2006), tumours (Eberhard et al., 2000; Széll et al., 2001a) and prolapse of nictitate gland (Széll et al., 2001b). Nevertheless, this parasitosis might have diagnosed as other helminthic disease with ectopic location (Table 4) or other ocular diseases (Gelatt, 2007) in the past.

The microfilarial concentration in the skin of infected dogs can be high (50–3600 g^{-1}) in all regions of the body (Széll et al., 2001a,b; Egyed et al., 2002a). *Onchocerca* spp. are the only filarial worms in which microfilariae are pathogenic. The large number of microfilariae in the skin causes severe acute and chronic eosinophilic dermatitis in infected people, horses and cattle irrespective of the *Onchocerca* sp. involved (Bwangamoi, 1969; Herd and Donham, 1983; Pollitt et al., 1986; Voung et al., 1994; Beitut et al., 2005; John and Petri, 2006). Acute skin disease can be characterised by severe pruritus and pustular dermatitis. In chronic cases, hyperkeratosis, atrophy, hypo- or hyperkeratosis are the most important

Table 4
Ocular helminthic infections reported from dogs[a]

Parasite (stage)	Ocular location of worms	Involvement	Clinical signs
Thelazia spp. (mature adults)	Conjunctiva	Bilateral	Conjunctivitis, photophobia
Canine *Onchocerca* sp. (mature adults)	Subconjunctiva, retrobulbar space	Unilateral or bilateral	See Table 3
Ancylostoma sp. (immature adults)	Posterior chamber	Unilateral	Endophthalmitis, glaucoma
Dirofilaria immitis (immature adults)	Anterior chamber	Unilateral	Uveitis, corneal oedema, glaucoma
Angiostrongylus vasorum (larvae)	Anterior chamber	Unilateral or bilateral	Panuveitis, retinopathy
Toxocara canis (larvae)	Choroid, retina	Unilateral or bilateral	Exophthalmos, chorioretinitis
Trichinella sp. (larvae)	Eyelid	Unilateral or bilateral	None

[a] Reviewed by Sréter et al. (2002a,b) and Zarfoss et al. (2005).

clinical signs. Similar symptoms were observed in some *Onchocerca*-infected dogs (Széll et al., 2001b), thus it cannot be excluded that this parasite might be responsible for dermatitis of unknown origin in dogs. The skin lesions should be differentiated from scabies, demodicosis, eczema, senile atrophy and some other skin diseases (Scott et al., 2000).

6. Laboratory diagnosis

6.1. Identification of adults

Because the worm fragments are white and slender, they can be mistaken for gauze plug threads during surgical intervention. The differentiation of canine *Onchocerca* sp. and other tissue nematode occurring in or near the eye can be based primarily on the characteristic cuticular morphology of the female worms (Fig. 1). Generally, the cuticle of onchocercae is composed of one layer at the extremities and of two distinct layers at the midbody, with the single layer at the extremities and the inner layer at the midbody exhibiting striae and the outer layer at the midbody bearing ridges (Fig. 1). The pattern of two striae/cuticular ridge, the shape and height of ridges, the ratio of body diameter to the distance between the ridges of cuticle of canine *Onchocerca* sp. differ from those of other nematodes infecting dogs and those of other *Onchocerca* spp. occurring in Europe and North America (Table 2).

6.2. Identification of microfilariae

Microfilariae of *Onchocerca* spp. occur in the skin, never the bloodstream. The mean concentration of *Onchocerca* microfilariae found in the skin of the head and abdominal region of dogs (475 g^{-1}; range 50–3600 g^{-1}) (Széll et al., 2001a,b; Egyed et al., 2002a) is comparable with the concentration observed in *O. volvulus* infections of man (John and Petri, 2006). Therefore, the superficial skin biopsy (''skin snip technique'', John and Petri, 2006) should be used in the diagnosis of canine onchocercosis. A small skin snip (0.1 g) collected from the head or umbilical region should be stored in a small tube (e.g., Eppendorf tube) containing 250–500 μl physiological saline solution at room temperature for 2–4 h. After the host tissues have been removed and the remaining fluid has been centrifuged at 350 g for 3 min, the sediment can be examined directly on microscopic slide or can be fixed and stained with haematoxylin. The microfilariae of canine *Onchocerca* sp. (Fig. 2) can be differentiated from the larvae of other nematodes infecting dogs and accidentally contaminating biopsy materials on the basis of their morphometric characteristics (Table 5). The truncheon-like, slowly moving microfilariae of canine *Onchocerca* sp. is less than 120 μm in length, whereas the microfilariae of all other filarioid parasites or larvae of nematodes occurring in the skin of dogs or contaminating skin biopsy materials are longer than 150 μm.

6.3. Serology, immunohistochemistry, molecular diagnostics

In contrast with dirofilariae (Genchi et al., 2007b), currently no serological tests for the detection of canine *Onchocerca* are available on the market. It was recently demonstrated that the identification of *Wolbachia*

Table 5
Morphometric data, presence of sheath and shape of the tail end of microfilariae of canine *Onchocerca* sp. in the skin of dogs and other nematode larvae, which may occur or contaminate canine skin biopsy materials in Europe and North America[a]

Taxon	Length (μm) (range)	Width (μm) (range)	Length per width	Other diagnostic features
Canine *Onchocerca* sp.	108 (98–118)	6.0 (5–7)	18:1	No sheath; tail straight
Dirofilaria repens	325 (283–386)	7.0 (6–8)	46:1	No sheath; tail umbrella handle-like
D. immitis	310 (290–330)	7.0 (6–8)	44:1	No sheath; tail straight
Acanthocheilonema (*Dipetalonema*) *reconditum*	248 (213–283)	4.5 (4–5)	55:1	No sheath; tail hooked and curved
Acanthocheilonema (*Dipetalonema*) *dracunculoides*	224 (190–258)	5.2 (4–6.5)	46:1	Sheath; tail straight
Cercopithifilaria (*Dipetalonema*) *grassii*	614 (567–660)	13.7 (12–15.5)	45:1	Sheath; tail slightly curved
Strongyloides stercoralis	410 (228–600)	17.0 (8–26)	24:1	No sheath; tail straight
Rhabditis strongyloides	550 (400–700)	21.0 (17–27)	26:1	No sheath; tail straight
Ancylostoma and *Uncinaria* spp.	600 (500–700)	23.0 (22–24)	26:1	No sheath; tail straight

[a] Based on data provided by Soulsby (1965), Mehlhorn et al. (1993), Széll et al. (2001a,b), Egyed et al. (2001), Bowman (2002), Komnenou et al. (2002), Tarello (2004), Gionfriddo et al. (2005), Hermosilla et al. (2005), Zarfoss et al. (2005), Schäffer et al. (2006), and Genchi et al. (2007b).

endosymbionts of *Dirofilaria* spp. by both direct and indirect methods (immunohistochemistry, PCR, ELISA), seems an excellent complementary data and constitute an effective tool for epidemiological studies on dirofilarioses (Simón et al., 2007). As canine *Onchocerca* sp. and other filarioid nematodes infecting dogs also contain wolbachiae (Egyed et al., 2002a; Sréter-Lancz et al., 2007), both direct and indirect methods may detect the endosymbionts of these parasites. Therefore, *Wolbachia*-positive dogs should be tested for *Onchocerca* and *Cercopithifilaria* infection by skin snip technique and for *Acanthocheilonema* spp. by Knott test (Genchi et al., 2007b). Nevertheless, *Wolbachia* detection methods can also be useful in epidemiological surveys on canine onchocercosis and other filarioid nematode infections of dogs (Table 5). PCR-sequencing methods amplifying the mitochondrial ND5 and COI genes of canine *Onchocerca* sp. can also be used for identification of the worms as the sequences of these genes are available in the GenBank. As the PCR-based amplification of DNA is generally difficult from formalin-fixed materials, a part of any nodules or worms should be fixed in 70% ethanol.

7. Therapy and control

The only known treatment for ocular onchocercosis is the surgical removal of the nodules containing the worms. Complete excision is not always possible, as masses occasionally have deep extension and involve the sclera (Széll et al., 2001b; Komnenou et al., 2002). Based on the diagnosis of retrobulbar abscess, the eye was enucleated in several cases (Gardiner et al., 1993; Eberhard et al., 2000; Zarfoss et al., 2005; Schäffer et al., 2006), which is not necessary in canine onchocercosis cases. Post-operatively, macrofilaricid drugs (melarsomine), systemic and topical antibiotics (e.g., amoxicillin–clavulanate orally and topical neomycin–polymixin–dexamethasone ointment) and anti-inflammatory drugs (e.g., prednisolone, carprophen) should be added for 14 days (Komnenou et al., 2002; Gionfriddo et al., 2005). However, the developmental stages present in periocular tissues and other parts of the body may survive and cause relapse (Orihel et al., 1991; Hermosilla et al., 2005). It was recently demonstrated that *Wolbachia* bacteria, living in the majority of *Onchocerca* spp., are required for the homeostasis of their hosts (Taylor et al., 2005), and these endosymbiotic bacteria are also present in canine *Onchocerca* sp. (Egyed et al., 2002a,b; Schäffer et al., 2006). Some antibiotics kill these bacteria and have been shown to be active against adult worms and microfilariae both in vitro and in vivo (Townson et al., 2000, 2006; Trees et al., 2000; Taylor et al., 2002). As intermittent treatment with oxytetracycline (Trees et al., 2000; Bandi et al., 2001) was tested in two *Onchocerca*-infected dogs without any significant improvement (Omonte, personal communication), it cannot be excluded that wolbachiae of canine *Onchocerca* are not obligatory endosymbiont of their nematode host. Skin microfilariae are responsible for acute and chronic onchocercal dermatitis and microfilariae are long lived, infected dogs should be treated with microfilaricid drugs. As only ivermectin is the microfilaricid drug with proven efficacy against *Onchocerca* spp. (WHO, 2003), ivermectin is, at present, the drugs of choice for skin manifestations and elimination of microfilariae. Oedematous reaction and itching within one to several days after treatment can be expected, which can be reduced by anti-inflammatory drugs (Herd and Donham, 1983; Pollitt et al., 1986; Komnenou et al., 2002; Gionfriddo et al., 2005). Substantial improvement might be observed only after several days or weeks. Control methods are not available, nevertheless insect repellents may reduce the attacks of the vectors.

8. Probable zoonotic significance

Altogether 12 zoonotic *Onchocerca* cases have been reported in man from Europe, North America and Japan (Azarova et al., 1965; Von Siegenthaler and Gubler, 1965; Beaver et al., 1974; Ali-Khan, 1977; Beaver et al., 1989; Hashimoto et al., 1990; Takaoka et al., 1996, 2001, 2004; Burr et al., 1998; Pampiglione et al., 2001; Wright et al., 2002; Salló et al., 2005). In the majority of cases, the single, immature worm was identified as *O. gutturosa*, *Onchocerca cervicalis* and *O. dewittei*—parasites normally infect cattle, horse and wild boar, respectively. The taxonomic status of *Onchocerca* involved in two subconjunctival zoonotic infections in Europe has not been unambiguously determined (Azarova et al., 1965; Pampiglione et al., 2001). Zoonotic filariae typically tend to settle into a tissue habitat in man that is similar or identical to the one they exploit in their natural hosts (Orihel and Eberhard, 1998). Of the 10 *Onchocerca* spp. known to occur in Europe (Table 2), only one, the canine *Onchocerca* sp. is found in the periocular tissues of its definitive host. The most likely candidate for the zoonotic *Onchocerca* so far observed in the eyes of humans is therefore the canine *Onchocerca* sp., especially as the clinical signs and histopathology seen in both human cases were almost identical to those seen in *Onchocerca* infections in dogs (Sréter et al., 2002b). However, the location of

the parasite and the clinical signs and pathology it induces is insufficient in themselves to confirm the species involved in the aberrant infections. In tissue sections, the identification of *Onchocerca* spp. is based primarily on the cuticular morphology of female worms. Because of these features (Table 2), the zoonotic *Onchocerca* responsible for subconjunctival infections in man appears to be the canine *Onchocerca* sp. (Sréter et al., 2002b). Interestingly, these cases (Azarova et al., 1965; Pampiglione et al., 2001) were described near to the regions where the canine *Onchocerca* sp. was reported from dogs and a wolf (Rodonaja, 1967; Komnenou et al., 2002, 2003). The number of human cases caused by these parasites is similar to the number of human cases caused by *O. gutturosa* or *O. cervicalis* indicating that the infection pressure of the three parasites for man might be similar.

9. Conclusion

On account of the clinical and possible zoonotic significance of this parasitosis, canine onchocercosis should be included in veterinary parasitology, ophthalmology and dermatology textbooks. Further studies are needed on the efficacy of therapeutic methods used against other filarioid infections of dogs (Genchi et al., 2007a). At present, there are more than 17.7 million people infected with *O. volvulus*—approximately 500,000 with visual impairments, 270,000 of whom are blind (WHO, 2003). The death of microfilariae is also very toxic to the skin, producing terrible itching. The annual economic losses were estimated at US$ 30 million (WHO, 2003). Research into human onchocercosis has been hampered by the lack of analogous models, owing to the species restriction of *O. volvulus* and the absence of *Onchocerca* sp. infecting small mammals (Eberhard et al., 1995; Trees et al., 2000). As infections in dogs may provide a practicable onchocercid experimental system, further studies should be encouraged on the vector range of the parasite and to try to establish experimental *Onchocerca* infections in dogs.

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References

Ali-Khan, Z., 1977. Tissue pathology and comparative microanatomy of *Onchocerca* from resident of Ontario and other *Onchocerca* species from Canada and the USA. Ann. Trop. Med. Parasitol. 71, 469–482.

Azarova, N.S., Miretskii, O.I., Sonin, M.D., 1965. First detection of nematode *Onchocerca* Diesing, 1841 in a person in the USSR. Med. Parasitol. 34, 156–158 (in Russian).

Bain, O., 1975. Redescription de cinq espéces d'onchocerques. Ann. Parasitol. Hum. Comp. 50, 763–788.

Bain, O., 1981. La genre *Onchocerca*: hypotheses sur son evolution et clé dichtomique des espéces. Ann. Parasitol. Hum. Comp. 56, 503–526.

Bain, O., 2002. Evolutionary relationships among filarial nematodes. In: Klei, T.R., Rajan, T.V. (Eds.), The Filaria. Kluwer Academic Publishers, Boston, pp. 21–29.

Bain, O., Chabaud, A.G., 1986. Atlas des larves infestantes de Filaries. Tropenmed. Parasitol. 37, 301–340.

Bain, O., Nasher, K., 1981. Redescription of *Onchocerca fasciata* R and H, 1910, a parasite of the dromedary. Ann. Parasitol. Hum. Comp. 56, 401–406.

Bain, O., Rehbinder, C., 1986. Nouvelle onchocerque, *Onchocerca alcis* n. sp. parasite de l'élan, *Alces alces*, en Suéde. Ann. Parasitol. Hum. Comp. 61, 447–455.

Bain, O., Schulz-Key, H., 1974. Les onchocerques du cerf européen: redescription d'*O. flexuosa* Wedl, 1856 et description d'O. tubingensis n. sp. et *O. tarsicola* n. sp. Tropenmed. Parasitol. 25, 437–449.

Bain, O., Schulz-Key, H., 1976. Une quatriémé espéce d'onchocercque, *O. garmsi* n. sp., chez le Cerf européen. Tropenmed. Parasitol. 27, 474–478.

Bain, O., Ramachandran, C.P., Petter, F., Mak, J.W., 1977. Description of *Onchocerca dewittei* n. sp. (Filaroidea), parasite of *Sus scrofa*, in Malaysia. Ann. Parasitol. Hum. Comp. 52, 471–479.

Bain, O., Wahl, G., Renz, A., 1993. *Onchocerca ramachandrini* n. sp. from the warthog in Cameroon. Ann. Parasitol. Hum. Comp. 68, 139–143.

Bandi, C., Anderson, T.J.C., Genchi, C., Blaxter, M.L., 1998. Phylogeny of *Wolbachia* in filarial nematodes. Proc. R. Soc. Lond. B 265, 2407–2413.

Bandi, C., Trees, A.J., Bratting, N.W., 2001. *Wolbachia* in filarial nematodes: evolutionary aspects and implications for the pathogenesis and treatment of filarial diseases. Vet. Parasitol. 98, 215–238.

Bazzocchi, C., Jamongluk, W., O'Neill, S.L., Anderson, T.J.C., Genchi, C., Bandi, C., 2000. *Wsp* gene sequences from the *Wolbachia* of filarial nematodes. Curr. Microbiol. 41, 96–100.

Beaver, P.C., Horner, G.S., Bilos, J.Z., 1974. Zoonotic onchocerciasis in a resident of Illinois and observations on the identification of *Onchocerca* species. Am. J. Trop. Med. Hyg. 23, 595–607.

Beaver, P.C., Yoshimura, H., Takayasu, S., Hashimoto, H., Little, M.D., 1989. Zoonotic *Onchocerca* in a Japanese child. Am. J. Trop. Med. Hyg. 40, 298–300.

Beitut, E., Akca, A., Bain, O., 2005. Teat onchocercosis in cows with reference to prevalence, species involved and pathology. Res. Vet. Sci. 78, 45–51.

Bowman, D.D., 2002. Georgi's Parasitology for Veterinarians. W.B. Saunders Company, Philadelphia, pp. 1–432.

Burr, W.E., Brown, M.F., Eberhard, M.L., 1998. Zoonotic *Onchocerca* (Nematoda: Filaroidea) in the cornea of a Colorado resident. Ophthalmology 105, 1494–1497.

Bwangamoi, O., 1969. Dermatitis in cattle caused by *Onchocerca ochengi* Bwangamoi, 1969, and the effect of the adult filarial on the finished leather. Bull. Epizoot. Dis. Afr. 17, 435–445.

Casiraghi, C., Anderson, T.J.C., Bandi, C., Bazzocchi, C., Genchi, C., 2001. A phylogenetic analysis of filarial nematodes: comparison with the phylogeny of *Wolbachia* endosymbionts. Parasitology 122, 93–103.

Chabaud, A.G., Bain, O., 1994. The evolutionary expansion of the Spirurida. Int. J. Parasitol. 24, 1179–1201.

Demiaszkiewicz, A.W., 1989. First description of male and redescription of female of *Onchocerca garmsi* Bain and Schulz-Key, 1976, a parasite of roe deer. Acta Parasitol. 34, 161–165.

Demiaszkiewicz, A.W., 1993. Redescription of *Onchocerca jakutensis* Gubanov, 1964 (Nematoda, Filarioidea). Acta Parasitol. 38, 124–127.

Demiaszkiewicz, A.W., Matsaberidze, G.V., 1991. New details on the morphology of *Onchocerca lupi*. Wiad. Parazytol. 37, 255–259 (in Polish).

Demiaszkiewicz, A.W., Matsaberidze, G.V., Kvavadze, E.S., 1991. The female of *Onchocerca lupi* Rodonaja 1967 under a scanning electron microscope. Acta Parasitol. 36, 183–186.

Eberhard, M.L., 1979. Studies on the *Onchocerca* (Nematoda: Filaroidea) found in cattle in the United States. I. Systematics of *O. gutturosa* and *O. lienalis* with a description of *O. stilesi* sp. n. J. Parasitol. 65, 379–388.

Eberhard, M.L., Dickerson, J.W., Tsang, V.C., Walker, E.M., Ottesen, E.A., Chandrashekar, R., Weil, G.J., Trips, M., Strobert, E., Constantinidis, I., 1995. *Onchocerca volvulus*: parasitologic and serologic responses in experimentally infected chimpanzees and mangabey monkeys. Exp. Parasitol. 80, 454–462.

Eberhard, M.L., Ortega, Y., Dial, S., Schiller, C.A., Sears, W., Greiner, E., 2000. Ocular *Onchocerca* infections in western United States. Vet. Parasitol. 90, 333–338.

Egyed, Z., Sréter, T., Széll, Z., Beszteri, B., Oravecz, O., Márialigeti, K., Varga, I., 2001. Morphologic and genetic characterization of *Onchocerca lupi* infecting dogs. Vet. Parasitol. 102, 309–319.

Egyed, Z., Sréter, T., Széll, Z., Nyírő, G., Dobos-Kovács, M., Márialigeti, K., Varga, I., 2002a. Electron microscopic and molecular identification of *Wolbachia* endosymbionts from *Onchocerca lupi*: implications for therapy. Vet. Parasitol. 106, 75–82.

Egyed, Z., Sréter, T., Széll, Z., Nyírő, G., Márialigeti, K., Varga, I., 2002b. Molecular phylogenetic analysis of *Onchocerca lupi* and its *Wolbachia* endosymbiont. Vet. Parasitol. 108, 155–163.

Gardiner, C.H., Dick Jr., E.J., Meininger, A.C., Lozano-Alarcon, F., Jackson, F., 1993. Onchocerciasis in two dogs. J. Am. Vet. Med. Assoc. 203, 828–830.

Gelatt, K.N., 2007. Veterinary Ophthalmology, 4th ed. Lippincott Williams and Wilkins, Philadelphia, pp. 1–1696.

Genchi, C., Guerrero, J., McCall, J.W., Venco, L., 2007a. Epidemiology and prevention of *Dirofilaria* infections in dogs and cats. In: Genchi, C., Rinaldi, L., Cringoli, G. (Eds.), *Dirofilaria immitis* and *D. repens* in Dog and Cat and Human Infections. Rolando Editore, Naples, pp. 145–161.

Genchi, C., Venco, L., Genchi, M., 2007b. Guideline for the laboratory diagnosis of canine and feline *Dirofilaria* infections. In: Genchi, C., Rinaldi, L., Cringoli, G. (Eds.), *Dirofilaria immitis* and *D. repens* in Dog and Cat and Human Infections. Rolando Editore, Naples, pp. 138–144.

Gionfriddo, J.R., Mangan, B., Wilkerson, G., Powell, C.C., Friedman, D.S., Ehrhart, E.J., 2005. A challenging case: a dog with ocular masses. Vet. Med. 100, 570–576.

Hashimoto, H., Muramaki, I., Fujiwara, S., Takayasu, S., Takaoka, H., Uga, S., Akao, N., Kondo, K., Yoshimura, H., 1990. A human case of zoonotic onchocerciasis in Japan. J. Dermatol. 17, 52–55.

Herd, R.P., Donham, J.C., 1983. Efficacy of ivermectin against *Onchocerca cervicalis* microfilarial dermatitis in horses. Am. J. Vet. Res. 44, 1102–1105.

Hermosilla, A., Hetzel, U., Bausch, M., Grübl, J., Bauer, C., 2005. First autochthonous case of canine ocular onchocercosis in Germany. Vet. Rec. 154, 450–452.

John, D.T., Petri, W.A., 2006. Markell and Voge's Medical Parasitology. W.B. Saunders Company, Philadelphia, pp. 1–480.

Klein, S.L., 2004. Hormonal and immunological mechanisms mediating sex differences in parasite infection. Parasite Immunol. 26, 247–264.

Komnenou, A., Eberhard, M.L., Kaldrymidou, E., Tsalie, E., Dessiris, A., 2002. Subconjunctival filariasis due to *Onchocerca* sp. in dogs: report of 23 cases in Greece. Vet. Ophthalmol. 5, 119–126.

Komnenou, A., Egyed, Z., Sréter, T., Eberhard, M.L., 2003. Canine subconjunctival onchocercosis in Greece: report of further 20 cases and molecular analysis of the parasite and its *Wolbachia* endosymbiont. Vet. Parasitol. 118, 151–155.

Krueger, A., Fischer, P., Morales-Hojas, R., 2007. Molecular phylogeny of the filarial genus *Onchocerca* with special emphasis on Afrotropical human and bovine parasites. Acta Trop. 101, 1–14.

Mehlhorn, H., Düwel, D., Raether, W., 1993. Diagnose und Therapie der Parasitosen von Haus-, Nutz- und Heimtieren. Gustav Fischer Verlag, Stuttgart, pp. 1–529.

Morales-Hojas, R., Cheke, R.A., Post, R.J., 2006. Molecular systematics of five *Onchocerca* species (Nematoda: Filarioidea) including the human parasite, *O. volvulus*, suggest sympatric speciation. J. Helminthol. 80, 281–290.

Orihel, T.C., Eberhard, M.L., 1998. Zoonotic filariasis. Clin. Microbiol. Rev. 11, 366–381.

Orihel, T.C., Ash, L.R., Holshuh, H.J., Santenelli, S., 1991. Onchocerciasis in a California dog. Am. J. Trop. Med. Hyg. 44, 513–517.

Pampiglione, S., Vakalis, N., Lyssimachou, A., Kouppari, G., Orihel, T.C., 2001. Subconjunctival zoonotic *Onchocerca* in an Albanian man. Am. J. Trop. Med. Parasitol. 95, 827–832.

Papaioannou, N., Psalla, D., Papadopoulos, E., Adamama-Moraitou, K.K., Petanidis, T., Rallis, T., 2004. Obstructive, granulamatous tracheitis caused by *Onchocerca* sp. in a dog. J. Vet. Med. A 51, 354–357.

Pollitt, C.C., Holdsworth, P.A., Kelly, W.R., Meacham, C.S., Sheahan, B., 1986. Treatment of equine onchocerciasis with ivermectin paste. Aust. Vet. J. 63, 152–156.

Rodonaja, T.E., 1967. A new species of Nematode, *Onchocerca lupi* n. sp., from *Canis lupus cubanensis*. Soobshchenyia Akad. Nauk Gruzinskoy SSR 45, 715–719 (in Russian).

Rommel, M., Eckert, J., Kutzer, E., Körting, W., Schnieder, T., 2000. Veterinärmedizinische Parasitologie. Parey Verlag, Berlin, pp. 1–915.

Salló, F., Eberhard, M.L., Fok, E., Baska, F., Hatvani, I., 2005. Zoonotic intravitreal *Onchocerca* in Hungary. Ophthalmology 112, 502–504.

Schäffer, E.H., Marquart, K.H., Brandes, K., Kunder, S., Jennen, L., 2006. Okulare Onchozerkose bei einem Hund. Tierärzt. Praxis 34, 178–184.

Schulz-Key, H., Bain, O., 1976. Une quatriéme espéce d'onchocerque, *Onchocerca garmsi* n. sp., chez le cerf européen. Tropenmed. Parasitol. 27, 474–478.

Scott, D.W., Miller, W.H., Griffin, C.E., 2000. Muller and Kirk's Small Animal Dermatology. W.B. Saunders Company, Philadelphia, pp. 1–1520.

Simón, F., Kramer, L.H., Morchón, R., Genchi, C., 2007. A possible role of *Wolbachia* in the diagnosis of *Dirofilaria* infections. In: Genchi, C., Rinaldi, L., Cringoli, G. (Eds.), *Dirofilaria immitis* and *D. repens* in Dog and Cat and Human Infections. Rolando Editore, Naples, pp. 74–80.

Soulsby, E.J.L., 1965. Textbook of Veterinary Clinical Parasitology. Vol. I: Helminths. Blackwell Scientific Publications, Oxford, pp. 1–1120.

Sréter, T., Széll, Z., Egyed, Z., Varga, I., 2002a. Ocular onchocercosis in dogs: a review. Vet. Rec. 151, 176–180.

Sréter, T., Széll, Z., Egyed, Z., Varga, I., 2002b. Subconjunctival zoonotic onchocercosis in man: aberrant infection with *Onchocerca lupi*? Ann. Trop. Med. Parasitol. 96, 497–502.

Sréter, T., Széll, Z., Marucci, G., Pozio, E., Varga, I., 2003. Extra-intestinal nematode infections of red foxes (*Vulpes vulpes*) in Hungary. Vet. Parasitol. 115, 329–334.

Sréter-Lancz, Z., Széll, Z., Sréter, T., 2007. Molecular genetic comparison of *Onchocerca* sp. infecting dogs in Europe with other spirurid nematodes including *Onchocerca lienalis*. Vet. Parasitol. 148, 365–370.

Széll, Z., Erdélyi, I., Sréter, T., Albert, M., Varga, I., 2001a. Canine ocular onchocercosis in Hungary. Vet. Parasitol. 97, 245–251.

Széll, Z., Sréter, T., Erdélyi, I., Varga, I., 2001b. Ocular onchocercosis in dogs: aberrant infection in an accidental host or lupi onchocercosis? Vet. Parasitol. 101, 115–125.

Takaoka, H., Bain, O., Tajimi, S., Kashima, K., Nakayama, I., Korenaga, M., Aoki, C., Otsuka, Y., 1996. Second case of zoonotic *Onchocerca* infection in a resident of Oita, Japan. Parasite 3, 179–182.

Takaoka, H., Bain, O., Uni, S., Korenaga, M., Tada, K., Ichikawa, H., Otsuka, Y., Eshita, Y., 2001. Human infection with *Onchocerca dewittei japonica*, a parasite from wild boar in Oita, Japan. Parasite 8, 261–263.

Takaoka, H., Bain, O., Uni, S., Korenaga, M., Kozek, W.J., Shirasaka, C., Aoki, C., Otsuka, Y., Fukuda, M., Eshita, Y., Daa, T., 2004. Zoonotic onchocerciasis caused by a parasite from wild boar in Oita, Japan. A comprehensive analysis of morphological characteristics of the worms for its diagnosis. Parasite 11, 285–292.

Tarello, W., 2004. Identification and treatment of *Dipetalonema grassii* microfilariae in a cat from central Italy. Vet. Rec. 155, 565–566.

Taylor, M.J., 2003. *Wolbachia* in the inflammatory pathogenesis of human filariasis. Ann. NY Acad. Sci. 990, 444–449.

Taylor, M.J., Bandi, C., Hoerauf, A.M., Lazdins, J., 2002. *Wolbachia* bacteria of filarial nematodes: a target for control? Parasitol. Today 16, 179–180.

Taylor, M.J., Bandi, C., Hoerauf, A., 2005. *Wolbachia* bacterial endosymbionts in filarial nematodes. Adv. Parasitol. 60, 245–284.

Townson, S., Hutton, D., Siemienska, J., Hollick, L., Scanlon, T., Tagboto, S.K., Taylor, M.J., 2000. Antibiotics and *Wolbachia* in filarial nematodes: antifilarial activity of rifampicin, oxytetracycline and cloramphenicol against *Onchocerca gutturosa*, *Onchocerca lienalis* and *Brugia pahangi*. Ann. Trop. Med. Parasitol. 94, 801–816.

Townson, S., Tagboto, S., NcGarry, H.F., Egerton, G.L., Taylor, M.J., 2006. *Onchocerca* parasites and *Wolbachia* endosymbionts: evaluation of a spectrum of antibiotic types for activity against *Onchocerca gutturosa* in vitro. Filaria J. 5, 4.

Trees, A.J., Graham, S.P., Renz, A., Bianco, A.E., Tanya, V., 2000. *Onchocerca ochengi* infections in cattle as a model for human onchocerciasis: recent developments. Parasitology 120, S133–S142.

Uni, S., Bain, O., Agatsuma, T., Harada, M., Torh, H., Fukuda, M., Takaoka, H., 2007. Onchocerca eberhardi n. sp (Nematoda: Filarioidea) from sika deer in Japan; relationships between species parasitic in cervids and bovids in the holarctic region. Parasite 14, 199–211.

Von Siegenthaler, R., Gubler, R., 1965. Paraarticuläres Nematodengranulom (einheimische *Onchocerca*). Schweiz. Med. Wschrft. 95, 1102–1104.

Voung, P.N., Wanji, S., Prod'Hon, J., Bain, O., 1994. Subcutaneous nodules and cutaneous lesions caused by different *Onchocerca* spp. in African cattle. Rev. Med. Vet. Pays Trop. 47, 47–51.

WHO, 2003. Onchocerciasis. Available at http://www.who.int/tdr/dw/oncho2003.htm and http://www.who.int/blindness/partnerships/onchocerciasis_home/en/index.html.

Wright, R.W., Neafie, R.C., McLean, M., Markman, A.W., 2002. Zoonotic onchocerciasis of the shoulder: a case report. J. Bone Joint Surg. 84, 627–629.

Zarfoss, M.K., Dubielzig, R.R., Eberhard, M.L., Schmidt, K.S., 2005. Canine ocular onchocerciasis in the United States: two new cases and a review of the literature. Vet. Ophthalmol. 8, 51–57.