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Mansonella ozzardi and its vectors in the New World: an update with emphasis on the current situation in Haiti

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Review Article

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Abstract

Mansonella ozzardi (Nematoda: Onchocercidae) is a little studied filarial nematode. This human parasite, transmitted by two families of dipteran vectors, biting midges (most of them members of the genus *Culicoides*) and blackflies (genus *Simulium*), is endemic to the Neotropical regions of the New World. With a patchy geographical distribution from southern Mexico to north-western Argentina, human infection with *M. ozzardi* is highly prevalent in some of the Caribbean islands, along riverine communities in the Amazon Basin, and on both sides of the border between Bolivia and Argentina. Studies conducted in Haiti between 1974 and 1984 allowed the first complete description of the adult worm and permitted clarification of the taxonomic position of this filarial species. This paper reports the known geographical distribution of *M. ozzardi* in Neotropical regions of the Americas, and focuses on the current situation in Haiti where this filariasis remains a completely neglected public health problem.

Introduction

Mansonella ozzardi is a filarial nematode endemic as small foci in South America (Amazon Basin), in the isthmian portion of the North American continent (Yucatan, Panama) and in the West Indies (Haiti and the Lesser Antilles). Upon its discovery, *M. ozzardi* was the subject of some confusion. Indeed, Patrick Manson described it under two different names: *Filaria demarquayi*, for the microfilariae found in the inhabitants of Saint Vincent Island in the Lesser Antilles, and *F. ozzardi*, for those found among the Indians of Guyana in South America. With little research, due to the lack of serious pathogenic effects easily recognizable in humans, and the fact that the adult form was difficult to find, this filarial nematode has remained little known for a long time. In the decade 1974–1984, studies were carried out on this parasite and its vectors in Haiti (Ripert *et al.*, 1977; Raccurt *et al.*, 1980, 1982, 1983; Lowrie & Raccurt, 1981, 1984; Orihel *et al.*, 1981; Kozek & Raccurt, 1983; Kozek *et al.*, 1983a; Lowrie *et al.*, 1983; Raccurt, 1984; McNeeley *et al.*, 1989). These studies have resulted in the definitive description of the adult form of the filarial nematode (Orihel & Eberhard, 1982), which allows for clarification of the taxonomic position of the species (Eberhard & Orihel, 1984), and the accumulation of morphological and biological information on this parasite, which is part of the Onchocercidae family (Raccurt, 1984). *Mansonella ozzardi* is singular for two reasons. First, it has adapted to two families of haematophagous Diptera (Ceratopogonidae and Simuliidae), possible intermediate hosts or effective vectors, depending on the geographical regions. Second, the blood microfilariae are able to leave the vascular bed to migrate into the dermal interstitial fluid, so they can be detected by skin biopsy (Moraes, 1976) as well as by taking a venous or capillary blood sample (Nathan *et al.*, 1978). Thus, *M. ozzardi* establishes a kind of link between the human *Mansonella* species with blood microfilariae, such as *M. perstans* in Africa and South America, and those with dermal microfilariae, such as *M. streptocerca* in Central Africa.

This article aims to highlight the knowledge gained on *M. ozzardi* and its vectors in Haiti over the past 40 years, to review the scientific literature, and to generate renewed interest among researchers, policy makers and donors on this filarial nematode, which is still very much neglected.

Historical review

At the end of the nineteenth century, Manson described a new species of filarial nematode under the name *Filaria demarquayi* in blood samples taken from inhabitants of St. Vincent in the Lesser Antilles (Manson, 1897), and under the name *F. ozzardi* in blood samples taken from the Indians of Guyana by Ozzard (Manson, 1897; Ozzard, 1897). Daniels remarked that the microfilariae with tapered posterior extremities were very common among the Indians of this country. By performing autopsies, he thought he had discovered the adult forms

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(Daniels, 1898, 1899). However, these adult worms, supposedly belonging to the species *F. ozzardi*, were instead *Wuchereria bancrofti* (Leiper, 1913). The first adult specimens of this new species (five females) were found in 1899 during the autopsy of a Saint Lucian in the Lesser Antilles (Low, 1902). The genus *Mansonella* was created in 1929, because the morphological characteristics of the microfilariae and the incomplete description of the adult made it impossible to link this species to any other known genus at the time (Faust, 1929). Due to the success of experimental infection of the monkey *Erythrocebus patas* with third-stage larvae from Haiti (Orihel *et al.*, 1981), the complete description of male and female adult worms was achieved for the first time almost a century after discovery of the microfilariae (Orihel & Eberhard, 1982), and the definitive taxonomic position of this nematode was finally established (Eberhard & Orihel, 1984).

Taxonomic position

The last review of the genus *Mansonella* (Faust, 1929), which includes low-pathogenic filariae that live in subcutaneous tissues and in muscular fascia of mammals, including humans, transmitted by Ceratopogonidae and/or Simuliidae, and which updates the classification of this group of parasites, makes it possible to classify this species definitively (Bain *et al.*, 2015) (table 1). Its scientific name is *Mansonella (Mansonella) ozzardi* (Manson, 1897) Orihel & Eberhard, 1982.

Geographical distribution

While *M. perstans* is present both in the large forests of equatorial Africa and South America (Tavares da Silva *et al.*, 2017), *M. ozzardi* is strictly a Neotropical filaria. In the New World, both filarial nematodes are found in sympatry across the Amazon, in western Guyana (Orihel, 1967), southern Colombia (Kozek & Raccurt, 1983) and Venezuela (Formica & Botto, 1990). Since its discovery in Guyana and St. Vincent Island in the Caribbean, the presence of *M. ozzardi* has been reported in almost all Latin American countries, from southern Mexico to northern Argentina, and in 15 islands of the Caribbean archipelago (Sasa, 1976; Hawking, 1979).

A patchy geographical distribution is characteristic of *M. ozzardi* foci in the Amazon Basin as well in the Caribbean region. The environmental factors that limit the spread of *M. ozzardi* beyond well-characterized hotspots along major rivers in the Amazon Basin and in the coastal mangroves in Haiti remain largely undetermined. In fact, the actual distribution of the parasite in the Western Hemisphere is only partially understood because of the immensity of the territories, access difficulties, the relatively limited number of epidemiological surveys conducted, limited interest in this low or non-pathogenic parasite, as well as precarious and sometimes non-existent health infrastructures in some regions that remain undeserved. Moreover, geographical distribution deserves to be updated periodically due to the spontaneous or induced disappearance of certain foci and the emergence of other foci, as a result of migrations of infected populations. Three main endemic areas persist in the Neotropical region, where the source of infection is not always well known.

Table 1. Classification of *Mansonella ozzardi*.

Class	*Nematoda*
Subclass	*Secernentea*
Order	*Spirudida*
Suborder	*Camallania*
Super-family	*Fiarioidea*
Family	*Onchocercidae* (Leiper, 1911) Chabaud & Anderson, 1959
Subfamily	*Onchocercinae* Leiper, 1911
Genus	*Mansonella* Faust, 1929
Subgenus	*Mansonella* Eberhard & Orihel, 1984
Species	*ozzardi* (Manson, 1897) Orihel & Eberhard, 1982

The South American continent

Mansonella ozzardi is located in the forest areas of the Amazon Basin (Shelley, 1975) and the Orinoco Basin (Medrano *et al.*, 1992) where there are small foci scattered along the banks of the rivers. The countries include northern Brazil (Rachou, 1957; Batista *et al.*, 1960; Oliveira, 1963; Lage, 1964; Moraes *et al.*, 1978, 1985; Adami *et al.*, 2008, 2014; Medeiros *et al.*, 2008, 2009, 2011, 2014a, b, c; Martins *et al.*, 2010; Basano *et al.*, 2011, 2014, 2016; Ta-Tang *et al.*, 2016); the three Guianas – French Guiana (Floch & Abonnenc, 1950), Suriname (Bruijning, 1957) and Guyana (Orihel, 1967; Nathan *et al.*, 1982); Venezuela (Beaver *et al.*, 1976; Godoy *et al.*, 1980; Formica & Botto, 1990; Medrano *et al.*, 1992; Gómez & Guerrero, 2000); eastern Colombia (Marinkelle & German, 1970; Kozek *et al.*, 1982, 1983b, 1984) and north-eastern Peru (Marcos *et al.*, 2012; Vargas-Herrera *et al.*, 2013; Vargas *et al.*, 2015).

Three other forest regions relate to this important geographical region: first, in the north, the area straddling north-western Colombia and eastern Panama with extensions to the Atlantic and Pacific coastal regions of Colombia. Information about this endemic area is dated (McCoy, 1933) and deserves to be verified and updated. Second, in the centre of Brazil, some foci have been reported along the Xingu River in the north of Mato Grosso (d'Andretta *et al.*, 1969), but this region is not widely recognized as an endemic area. Third, in the south, the area straddling southern Bolivia and northern Argentina is still active (Shelley & Coscarón, 2001; Dantur Juri *et al.*, 2013; Lima *et al.*, 2016; Veggiani Aybar, 2016).

In these forest regions, the parasite infects predominantly Amerindian populations, which are established along streams in small, scattered communities that are difficult to access. The prevalence is usually very high.

The isthmian portion of the North American continent

The focus in the Yucatan peninsula in Mexico has been known since 1930 (Hoffman, 1930) and carriers of microfilariae of *M. ozzardi* have also been reported in Panama among the Indians of the province of Darien, near the Colombian border (Petersen *et al.*, 1984). *Mansonella ozzardi* has also been reported in the three Mexican regions of Campeche, Yucatan and Quintana Roo (Mazzotti, 1942; Biagi, 1956; Biagi *et al.*, 1958). No recent information relates to these Mexican foci: have they already disappeared? The presence of *M. ozzardi* was also reported in

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Guatemala by O'Connor in 1937 (in Brumpt, 1949). An update of the situation in Mesoamerica is therefore necessary.

The Caribbean

Small foci have been reported over the past century in almost all of the Lesser Antilles, from the island of Viéques, east of Puerto Rico (Hoffman *et al.*, 1932) to the northern coast of Trinidad (Aschcroff, 1965; Nelson & Davies, 1976; Nathan *et al.*, 1979, 1982; Chadee *et al.*, 1994). The latter source of contamination was successfully treated with ivermectin (Chadee *et al.*, 1995; Gonzales *et al.*, 1999). In Guadeloupe, Le Dantec first reported the presence of *M. ozzardi* in 1924. In 1929, in the British Overseas Territories of the Caribbean, the endemic nature of the filaria was confirmed for the first time in St. Vincent (Cameron, 1929). Subsequently, *M. ozzardi* was found regularly in the French West Indies (St. Bartholomew, Guadeloupe, Désirade, Marie-Galante, Martinique) and in the Lesser Antilles (Antigua, Nevis, Dominica, Saint Lucia, Saint Vincent, Grenadine and St. Kitts) (Raccurt, 1984). Additionally, the contamination of a blood donor from the USA returning from a cruise in these popular tourist destinations was reported in 1978 (Weller *et al.*, 1978).

The foci of the Lesser Antilles, particularly in the French departments (Guadeloupe and Martinique), seem to have disappeared spontaneously with the economic development of these islands. The last cases reported in Guadeloupe go back about 50 years (Courmes *et al.*, 1968).

In the Greater Antilles, the parasite has never been reported in Puerto Rico, Cuba or Jamaica. Curiously, *M. ozzardi* has not been described in the Dominican Republic, which shares the island of Hispaniola with Haiti, where numerous foci of mansonelliasis occur (Raccurt, 1984). It has been reported only in two lepers from the Turks Islands, an archipelago located north of Haiti (Stafford *et al.*, 1955). This disparity between the western part and the eastern part of the island of Hispaniola is paradoxical. Have there been any surveys of coastal populations to identify possible carriers of *M. ozzardi* microfilariae in the Dominican Republic? If *M. ozzardi* is truly absent in this country, it is most likely due to the Dominican Republic's much higher level of economic development than Haiti, and a more elaborate habitat. Studies are needed to answer these questions.

In Haiti, *M. ozzardi* was reported for the first time by the Rockefeller mission in 1920 (Raccurt, 1999) and then in an article on lymphatic filariasis in Puerto Rico (Hoffman *et al.*, 1932). In Haiti, foci have been reported in coastal areas populated by mangroves (Ripert *et al.*, 1977; Raccurt *et al.*, 1980; Raccurt, 1984), a situation that persists until today (Raccurt *et al.*, 2014a, b). A revision of blood smears collected in all parts of the country by the Service National d'Éradication de la Malaria (SNEM), and in the north of Haiti by the hospital 'Le Bon Samaritain' in Limbé, has been conducted (Ripert *et al.*, 1977). Five hundred and seven slides showed microfilariae with the specific morphological characteristics of *M. ozzardi*. All subjects with microfilariae came from localities on the coast, in a plain or valley close to the coastline.

In Haiti the two main areas of concentration are located in the northern part of the island (coastal area between Port-de-Paix and Cap Haïtien, and along the Limbé river valley) and in the southwest, where numerous cases are concentrated along the coast between Jérémie and Petit-Trou-de-Nippes, including the Baradères Peninsula and the Cayemittes Islands.

Small foci are observed on the peripheries of the island of La Gonâve; around Cabaret, Gressier, Leogane, in the Gulf of Gonâve; around Miragoâne, from Petit-Goâve to Anse-à-Veau, on the coast of Nippes; around Saint-Louis-du-Sud; and on the island, Île à Vache.

The two most important foci were found in marshy coastal areas where mangroves grow, climates particularly favourable to the proliferation of sandflies, which are intermediate hosts and vectors of the parasite in Haiti (Raccurt, 1984). The endemic foci of mansonelliasis in Haiti are shown in fig. 1.

Vectors of *Mansonella ozzardi*

Depending on the region, the vectors of *M. ozzardi* belong to two groups of Diptera (suborder Nematocera): Ceratopogonidae and Simuliidae. Currently, only *Culicoides* species are known to

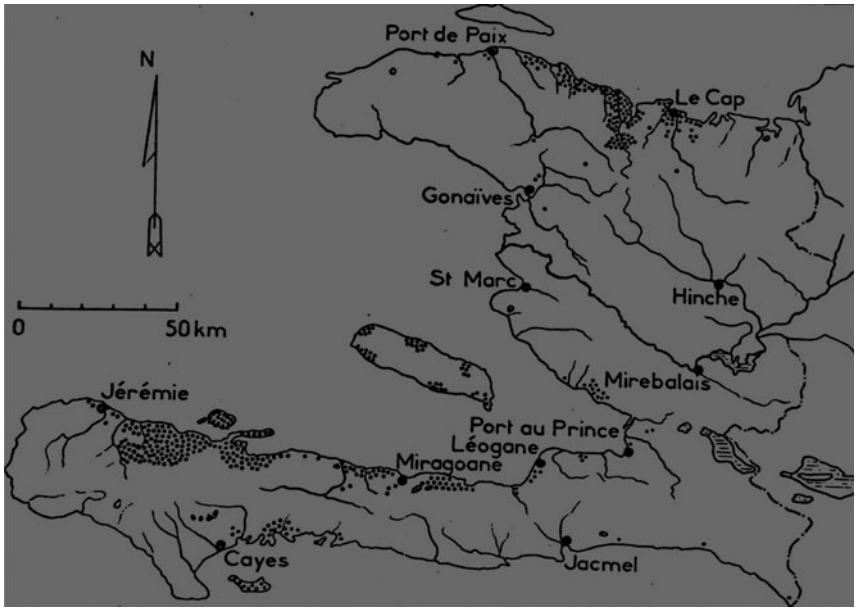

Fig. 1. Distribution of foci of *Mansonella ozzardi* in Haiti, as determineted in 1973–1975 (from Ripert *et al.*, 1977).

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Table 2. Ceratopogonidae and Simuliidae species recognized as vectors of *Mansonella ozzardi* by geographic region.

Ceratopogonidae		Simuliidae	
Culicoides furens	Caribbean Yucatan (Mexico)	*Simulium* gr. *Amazonicum* *Simulium minusculum*	Guyana
Culicoides barbosai	Haiti	*Simulium amazonicum*	Amazon Basin (Brazil, Colombia, Venezuela)
Culicoides phlebotomus	Trinidad	*Simulium argentiscutum*	Brazilian and Colombian Amazon
Culicoides insinuatus	Colombia	*Simulium sanguineum*	Colombia
Culicoides guttatus	Surinam	*Simulium sanguineum*	Panama
Culicoides paraensis	French Guiana	*Simulium sanchezi* *Simulium oyapockense*	Venezuela
Culicoides paraensis *Culicoides debilipalpis*	Bolivia and Argentina	*Simulium amazonicum* *Simulium oyapockense*	Brazil
Culicoides lahillei *Culicoides paraensis*	Argentina	*Simulium exiguum*	Argentina
Leptoconops bequaerti	Haiti		

transmit *M. ozzardi* in the Caribbean islands, but both *Simulium* and *Culicoides* species are vectors in Central and South America. The morphological similarity of adult filariae found during autopsy of monkeys that had been infected experimentally with third-stage larvae from the Haitian strain of *M. ozzardi* transmitted by *Culicoides* species and the Colombian strain transmitted by *Simulium* species confirmed that it was indeed a single species of filaria (Orihel *et al*., 1981). Similarly, the optical microscopy and electron microscopy studies of *M. ozzardi* microfilariae from Haiti and Colombia showed no significant difference in their respective morphology and ultrastructure (Kozek & Raccurt, 1983; Kozek *et al*., 1983a). We are therefore dealing with only one species of filaria transmitted by two groups of competent vectors belonging to two kinds of Diptera: the Ceratopogonidae and the Simuliidae.

In 1933, a member of the Ceratopogonidae, *Culicoides furens*, was first recognized as a vector of the parasite in St. Vincent, in the Caribbean (Buckley, 1933, 1934), while in the Amazon Basin, Simuliidae have been recognized as the competent vector of *M. ozzardi* (Cerqueira, 1959).

Culicoides furens is the main vector of *M. ozzardi* in the Yucatan peninsula in Mexico (Biagi *et al*., 1958) and in the Caribbean, especially in Haiti (Lowrie & Raccurt, 1981; Raccurt, 1984). Other sandflies ensure the transmission of the parasite, such as *Culicoides phlebotomus* in northern Trinidad, (Nelson & Davies, 1976; Nathan, 1978, 1980) or *Culicoides barbosai* in southern Haiti (Lowrie & Raccurt, 1984).

In South America, *Culicoides paraensis* was first reported as a probable vector of *M. ozzardi* in the Tucumán province of northern Argentina (Romaña & Wigodzinsky, 1950). Fifty years later, Shelley and Coscarón reported that, in the Jujuy province of Argentina, *Culicoides lahillei* was the primary vector, while *C. paraensis* and *Simulium exiguum* were secondary vectors (Shelley & Coscarón, 2001). *Culicoides lahillei*, *Culicoides debilipalpis* and *C. paraensis* were recently described as the primary vectors of *M. ozzardi* in north-western Argentina and south-western Bolivia (Veggiani Aybar et *al*., 2016). Other species of biting midges have been identified as valid for larval maturation up to the third stage of *M. ozzardi* in South America: *Culicoides guttatus* in Suriname (Bruijning, 1957) and *Culicoides insinuatus* in Colombia (Tidwell & Tidwell, 1982).

Taxonomic studies of *Simulium* fauna in Amazonia have shown that the species of Simuliidae, intermediate hosts and vectors of *M. ozzardi* in this region, often belong to the *amazonicum* group (Shelley & Luna Dias, 1980; Ramirez Perez & Peterson, 1981; Tidwell *et al*., 1981a, b; Shelley *et al*., 1982). Other species such as *Simulium oyapockense* have been implicated as the main vectors in the Amazon Basin of Brazil (Cerqueira, 1959), *Simulium minusculum* in Guyana (Nathan *et al*., 1982), *Simulium sanguineum* in Panama (Petersen *et al*., 1984) and *Simulium sanchezi* in Venezuela (Yarzábal *et al*., 1985).

From the published data, we can list the currently known vectors according to the foci and manner in which *M. ozzardi* accomplishes larval development up to the infesting stage (table 2). Among the Ceratedopogonidae, seven species of *Culcoides* and one species of *Leptoconops*, *L. bequaerti* (Lowrie *et al*., 1983) are currently recognized as vectors, and seven species among the Simuliidae.

Current situation of mansonelliasis in Haiti

A study was conducted in June–July 2013 in the town of Corail (Grande Anse) and the surrounding area (Raccurt *et al*., 2014b). Finger-prick blood samples were collected from 462 people: 76 showed the presence of *M. ozzardi* microfilariae, an overall prevalence of 16.5%. In 70% of infected subjects, microfilaraemia was fewer than 10 microfilariae (mf) per 20 µl of capillary blood. The highest microfilaraemia (227 mf/20 µl) was found in a 70-year-old woman. These results are comparable to those found 35 years ago in the Bayeux focus, located in the northern part of Haiti (Raccurt *et al*., 1980). The site of Corail, where this infection is developed, is similar to that of the fishing village of Bayeux: the houses are constructed of materials that are permeable to the vectors breeding around and within the mangroves where two main vectors thrive: *C. furens* and *C. barbosai*.

Conclusion

In 45 years, the situation of mansonelliasis has remained stable in Haiti, where *M. ozzardi* persists in localized coastal foci. No action has been taken either to control filariasis by appropriate

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treatment or to combat culicoides proliferation during this time. The authorities have never paid attention to this non-pathogenic filariasis, while affected individuals complain of fever, headache and chronic pruritus (McNeeley *et al*., 1989). This situation is also explained by the fact that the economic situation in Haiti is very precarious and has not improved significantly over the past 50 years, especially in peripheral regions where poverty and illiteracy remain at very high levels. As already mentioned (Raccurt *et al*., 2014a), it would be useful to place this neglected tropical disease on the Ministry of Public Health's agenda, and to provide ivermectin for the health facilities to treat the inhabitants, fishermen or farmers, carriers of microfilariae and those who complain of chronic symptoms such as fever, headache and pruritus. Surveillance campaigns for *M. ozzardi* among exposed populations should also be conducted to better control this endemic disease. Moreover, in line with the current efforts to develop tourism in Haiti, it will be necessary to pay serious attention to this completely neglected filariasis. If tourists return home carrying the parasite after a stay in Haiti, this would undoubtedly have unfortunate consequences for the future of tourism in Haiti, not to mention the potential for new additional foci of this filariasis in other parts of the New World.

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