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Review of *Mansonella ozzardi* and its Vectors in the Neotropical Region with Emphasis on the Current Situation in Haiti

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Abstract

Mansonella ozzardi (Nematoda: Onchocercidae) is an understudied filarial nematode. This human parasite transmitted by two families of dipteran vectors, biting midges (most of them members of the genus *Culicoides*) and black flies (genus *Simulium*), is endemic to the Neotropic regions of the New World. With a patchy geographic distribution from southern Mexico to northwestern 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 adult worm and permitted to clarify the taxonomic position of this filarial species. In this paper, the author reports the known geographic distribution of *M. ozzardi* in neotropical regions of America and Caribbean, and focuses on the current situation in Haiti where this filariasis remains a completely neglected public health problem.

Keywords: *Mansonella ozzardi*; Neotropic; Haiti

Introduction

Mansonella ozzardi is a filarial nematode from the neotropical region, endemic as small foci in South America (Amazon Basin), Central America and the West Indies. Upon its discovery, *M. ozzardi* was the subject of confusion to some extent. Indeed, Sir Patrick Manson has 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 Guiana. With little research interest, due to the lack of serious pathogenic effects easily recognizable in humans, this filarial nematode has remained not very well-known for a long time, especially as the adult form was difficult to find. In the decade 1974-1984, studies were carried out on this parasite and its vectors in Haiti. They have resulted in the definitive description of the adult form of the filarial nematode [1], which allows to clarify the taxonomic position of the species [2] and to accumulate morphological and biological information on this parasite of the Onchocercidae family [3]. Singularly, *M. ozzardi* has adapted himself to two families of Diptera, possible intermediate hosts or effective vectors, depending on the geographical regions. Furthermore, the blood microfilariae are able to leave the vascular bed to migrate into the dermal interstitial fluid so that they can be detected by skin biopsy as well as by taking venous or capillary blood sample. Thus *M. ozzardi* establishes a kind of link between the human filarial species with blood microfilariae (*M. perstans*) and those with dermal microfilariae (*M. streptocerca*).

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

Historical Review

At the end of the nineteenth century, Manson described *M. ozzardi* under the name *Filaria ozzardi* from blood samples taken from the Indians of Guyana by Ozzard [4,5]. 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 [6,7]. But these adult worms, supposed to belong to the species *M. ozzardi*, were in fact *Wuchereria bancrofti* [8]. The first adult specimens of this new species (five female) were found in 1899 during the autopsy of a Caribbean from Saint Lucia in the Lesser Antilles. The genus *Mansonella* was created in 1929, because the morphological characteristics of the microfilariae and those given by the incomplete description of the adult made it impossible to link this species to any other known genus of the time [9]. Due to the success of experimental infection of the monkey *Erythrocebus patas* with third stage larvae from Haiti [10], the complete description of male and female adult worms was achieved almost a century after discovery of microfilariae [1] and the definitive taxonomic position of this nematode finally established [2].

Taxonomic position

The last review of the genus *Mansonella* [9], which includes low-pathogenic filaria living in subcutaneous tissues and in the muscular fascia of mammals, including humans, transmitted by Ceratopogonidae and/or Simuliidae, and which brings up to date the classification of this group of parasites, makes it possible to definitively classify this species (Table 1) [11]. Its scientific name is: *Mansonella* (*Mansonella*) *ozzardi* (Manson, 1897) Orihel & Eberhard, 1982 [1,4].

Geographical Distribution

Mansonella ozzardi is strictly a neotropical filaria. Since its discovery in Guyana and St. Vincent Island in the Caribbean, its presence has been reported in almost all Latin American countries,

from southern Mexico to northern Argentina, and in some fifteen islands of the Caribbean archipelago [12,13].

Class	Nematoda
Subclass	Secernentea
Order	Spirudida
Suborder	Camallania
Super-family	Filarioidea
Family	Onchocercidea [8]
Subfamily	Onchocercinae [8]
Genus	*Mansonella* [9]
Subgenus	*Mansonella* [2]
Species	*ozzardi* [1,4]

Table 1: Classification of *Mansonella ozzardi*.

In fact, the actual distribution of the parasite in the Western Hemisphere is only partially known because of the immensity of the territories concerned, access difficulties, the relatively limited number of epidemiological surveys carried out, limited interest raised by this low or non-pathogenic parasite, precarious and sometimes non-existent health infrastructures in some regions still underserved. Moreover, geographical distribution deserves to be periodically updated due to the spontaneous or induced disappearance of certain foci and the emergence of other foci due to migrations of infected populations. Three main endemic areas persist, or have existed in the Neotropical area where the importance of source of infection is not always well-known.

On the South American continent

M. ozzardi is located in the forest areas of the Amazon Basin [14] and the Orinoco Basin [15] where there are small foci scattered along the banks of the rivers. The countries concerned are Northern Brazil [16-33], the three Guianas : French Guiana [34], Surinam [35] and Guyana [36,37], Venezuela [15,38-41], Eastern Colombia [42-45], and Northeastern Peru [46,48].

Three other forest regions relate to this important group:

In the North, the focus straddling Northwestern Colombia and Eastern Panama with extensions to the Atlantic and Pacific coastal regions of Colombia. Information about this endemic area is old [49] and deserves to be verified and updated.

In the center of Brazil exist some foci that go up along the Xingu River in the North of Mato Grosso [50].

In the South, the focus straddling Southern Bolivia and Northern Argentina is still active, as illustred by recent publications [51-54].

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

In Central America

The foci of the Yucatan peninsula in Mexico has been known since 1930 [55] and carriers of microfilariae *M. ozzardi* have been reported at the same time in Panama among the Indians of the province of Darien, near the Colombian border [56]. *Mansonella ozzardi* has been reported in the three Mexican regions of Campeche, Yucatan and Quintana Roo [57-59]. No recent information relates to these Mexican foci which may have disappeared. The presence of *M. ozzardi* would also have been reported in Guatemala by O'Connor in 1937 [60]. An update of the situation in Central America and Mexico is therefore necessary.

In the Caribbean

Small foci have been reported over the last century in almost all the Lesser Antilles from the island of Viéques, East of Puerto [61], to Trinidad on the Northern coast [62-65]. The latter source of contamination was successfully treated with ivermectin [66,67]. In Guadeloupe, it seems that 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 Saint-Vincent [68]. Subsequently, *M. ozzardi* was regularly found in the French West Indies (St. Bartholomew, Guadeloupe, Desirade, Marie-Galante, Martinique) and in the Lesser Antilles (Antigua, Nevis, Dominica, Saint Lucia, Saint Vincent, Grenadine and St. Kitts) [3]. The contamination of a US blood donor returning from a cruise in these popular tourist destinations was also the subject of a report in 1978 [69]. The foci of the Lesser Antilles, particularly in the French departments of Guadeloupe and Martinique, seem to have spontaneously disappeared with the economic development of these islands. The last cases reported go back to about fifty years [70]. In the Greater Antilles, the presence of the parasite has curiously never been reported in Puerto Rico, Cuba, Jamaica, Dominican Republic. It has been reported only in two lepers from the Turks Islands, an archipelago located in the North of Haiti [71]. In Haiti, *M. ozzardi* was reported for the first time by the Rockefeller mission in 1920 [72] and then in an article on lymphatic filariasis in Puerto Rico [61]. Haiti has important foci in coastal areas colonized by the mangroves [3,73], a situation that persists until today [74,75]. A review of cases of carriers of microfilariae - detected between November 1964 and June 1965 (144 blood smears) and February 1969 to February 1976 (280 blood smears) by the Service National d'Éradication de la Malaria (SNEM) and the medical laboratory of the hospital "Le Bon Samaritain", in Limbé, in the North of Haiti, from July 1969 to February 1976 (83 blood smears) - has been carried out by Ripert et al. [76]. Five hundred and seven slides showed microfilariae with the specific morphological characteristics of *M. ozzardi*: absence of sheath, irregular and imbricated nuclei, posterior tapered extremity free of nuclei in its terminal portion. All subjects with microfilariae came from localities on the coast, in a plain or valley close to the coastline at an altitude of less than 100 m. The distribution of the cases is shown on the map of Figure 1. They are grouped into small coastal foci of varying size.

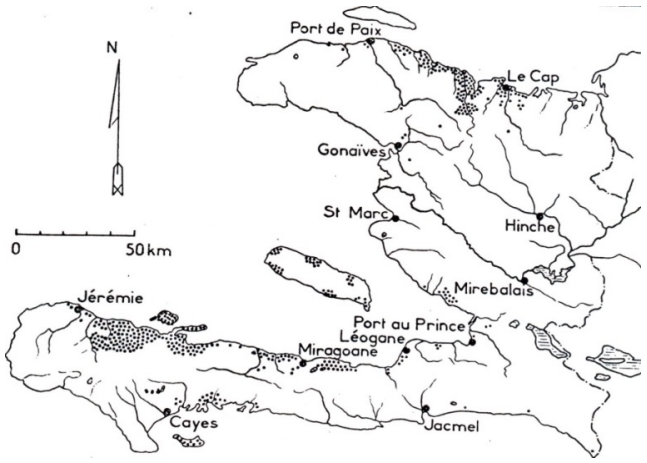

Figure 1: Map of the distribution of *Mansonella ozzardi* cases in Haiti (1964 – 1976) according to C. Ripert, C Raccurt and PL Douyon.

The two main foci are located in the Northern part of Haiti (coastal foci between Port-de-Paix and Cap Haitian, and along the Limbé river valley) and in the South-West of Haiti where numerous cases concentrate 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 coasts of Nippes, around Saint-Louis-du-Sud, and on the island of Ile à Vache.

The two most important foci are found in marshy coastal areas where grown the mangroves, particularly favorable to the proliferation of *Culicoides furens* and *C. barbosai*, vectors of the parasite.

Vectors of *Mansonella ozzardi*

Depending on the region, the vectors of *M. ozzardi* belong to two groups of Diptera (suborder Nematocera). The morphological similarity of adult filariae found at autopsy of monkeys experimentally infected with third stage larvae from the Haitian *M. ozzardi* strain transmitted by culicoides and the Colombian strain transmitted by simulium confirmed that it was indeed a single species of filaria [10]. Similarly, the optical microscopy and electron microscopy studies of *M. ozzardi* microfilariae from Haiti and Colombia [77,78], showed no significant difference in their respective morphology and ultrastructure. We are therefore dealing with only one and the same species of filaria transmitted by two groups of competent vectors belonging to two kinds of Diptera: the Ceratopogonidae and the Simuliidae.

In 1933, a Ceratopogonidae, *C. furens*, was first recognized as vector of the parasite in St. Vincent, in the Caribbean [79,80], while in the Amazon Basin [81], Simuliidae have been recognized as the competent vector of *M. ozzardi*.

Culicoides furens is the main vector of *M. ozzardi* in the Yucatan peninsula in Mexico [59], and in the Caribbean, especially in Haiti [82]. Other culicoides ensure the transmission of the parasite such as *C. phlebotomus* in Northern Trinidad, [63,83,84] or *C. barbosai* in Southern Haiti [85].

At least one species has been identified as valid for larval maturation up to the third stage of *M. ozzardi* in South America: *C. insinuatus* in Colombia [86].

Taxonomic studies of *Simulium* fauna in Amazonia have shown that the species of Simuliidae, intermediate hosts and vectors of *M. ozzardi* in this region, belong to the amazonicum group [87-91].

From the data from the literature, we can list the vectors currently known according to the foci and in which *M. ozzardi* accomplishes larval development up to the infesting stage Table 2. Among the Ceratopogonidae, seven species are currently recognized as vectors, and four among the Simuliidae.

	Ceratopogonidae	Simuliidae	
Culicoides furens	Caribbean, Yucatan	*Simulium gr. amazonicum*	Guyana
Culicoides barbosai	Haiti	*Simulium amazonicum*	Amazon Basin (Brazil, Colombia and Venezuela)
Culicoides phlebotomus	Trinidad	*Simulium argentiscutum*	Brazilian and Colombian Amazon
Culicoides insinuatus	Colombia	*Simulium sanguineum*	Colombia
Culicoides guttatus	Surinam		
Culicoides paraensis	French Guiana, Brazil, Argentina		
Leptoconops bequaerti	Haiti		

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

Current Situation of Mansonellosis in Haiti

A study was conducted in June-July 2013 in the Corail region, in Grande Anse, by Raccurt et al. [75]. Finger-prick blood samples were carried out in 462 people who provided their consent: 76 showed the presence of *M. ozzardi* microfilariae, an overall prevalence of 16.5%. In 70% of infected subjects, microfilaraemia was less than 10 microfilariae

per 20 microliters of capillary blood. The highest microfilaraemia (227 mf/20 µL) was found in a 70-year-old woman. Among adults, males were more frequently infected (23%) than females (21%). These results are quite comparable to those found 35 years ago, in the Bayeux focus located in the Northern part of Haiti [73]. On the other hand, 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 living around and within the mangroves where two efficient vectors are proliferated: *C. furens* and *C. barbosai*.

Conclusion

In 45 years, the situation of Mansonellosis has remained stable in Haiti where *Mansonella ozzardi* persists in localized coastal foci. No action has been taken either to control filariasis by appropriate treatment or to combat culicoides proliferation during this time. Authorities have never paid attention to this filariasis known to be non-pathogenic, while affected individuals complain of fever, headache and chronic pruritus [92]. This situation is also explained by the fact that the economic situation in Haiti is very precarious and has not improved significantly over the last 50 years, especially in peripheral regions where poverty and illiteracy remain at very high levels. As already mentioned Raccurt et al. [74], it would be useful to place this neglected disease on the agenda to the Ministry of Public Health, and to provide ivermectin to the health facilities to treat the inhabitants, fishermen or cultivators, carriers of microfilariae and who complain of chronic symptoms such as fever, headache, pruritus. Surveillance campaigns for *M. ozzardi* among exposed populations should also be carried out to better control this endemic disease. Moreover, following the current efforts to develop tourism in Haiti, it would be urgent to pay serious attention to this completely neglected Filariasis. If tourists come back carrying the parasite after a stay in Haiti, this would undoubtedly have unfortunate consequences for the future of tourism in this country and who knows for potential new additional foci of this Filariasis in other parts of the world.

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