UPDATE

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MANSONELLIASIS: A BRAZILIAN NEGLECTED DISEASE

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ABSTRACT

Mansonelliasis is a filariasis whose etiological agents are *Mansonella ozzardi*, *Mansonella perstans* and *Mansonella streptocerca*. Only the first two cited species occur in Brazil. *M. ozzardi* is widely distributed in Amazonas state and it is found along the rivers Solimões, Purus, Negro and their tributaries while *M. perstans* is restricted to the Upper Rio Negro. In this update, we report the occurrence of *M. ozzardi* in Amazonas since the 1950s, and we show that over the years this filariasis has been sustained with high prevalence, while maintaining a constant cycle of transmission in endemic areas due to the lack of treatment and control policies. *M. perstans* has so far only been recorded in indigenous populations in the Upper Rio Negro. However, the continuous flow of migrants to other regions may cause an expansion of this infection.

KEY WORDS: Filariasis; *Mansonella ozzardi; Mansonella perstans;* Amazonas state.

RESUMO

Mansonelose: Uma doença brasileira negligenciada

A mansonelose é uma filariose cujos agentes etiológicos são *Mansonella ozzardi, M. perstans e M. strepotcerca*. Somente as duas primeiras ocorrem no Brasil. *M. ozzardi* apresenta ampla distribuição no estado do Amazonas sendo encontrada ao longo dos rios Solimões, Purus e Negro e afluentes, ao passo que *M. perstans* possui distribuição restrita à região do Alto Rio Negro. Nesta atualização, é relatada a ocorrência de *M. ozzardi* no Amazonas desde a década de 1950 e, ao longo dos anos,

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esta filariose tem sustentado elevadas prevalências, mantendo um ciclo constante de transmissão nas áreas endêmicas em virtude da falta de políticas de tratamento e controle. Até o momento, *M. perstans* só foi registrada nas populações indígenas da região do Alto Rio Negro, mas, em razão da existência de um fluxo migratório contínuo para outras regiões, existe a possibilidade de sua expansão.

DESCRITORES: Filariose; *Mansonella ozzardi; Mansonella perstans;* Amazonas.

INTRODUCTION

Mansonelliasis is a neglected tropical filarial disease caused by three species of parasite from the genus *Mansonella*: *M. perstans*, *M. ozzardi and M. streptocerca. Mansonella streptocerca* is only found in Africa, *M. perstans* may be found in Africa and in the Americas and *M. ozzardi* is autochthonous in America. *M. ozzardi* is endemic in disperse foci, from Mexico to the North of Argentina and the number of infected people is unknown. In some South American countries, such as Colombia and Venezuela, *M. ozzardi* infection is found simultaneously with other filariae, such as *Onchocerca volvulus* and/or *M. perstans* (Beaver et al., 1976; Kozek et al., 1983; Formica & Botto, 1990; Medrano et al., 1992).

Mansonella ozzardi infection was considered a typical rural disease, in riverine populations that live near the breeding sites of black flies. However, urban foci were found in some municipalities of Amazonas state in Brazil (Martins et al., 2010). *Mansonella ozzardi* infection is more frequently found in adults and in men rather than women (Batista et al., 1960a; Botto et al., 1983; Kozek et al., 1983; Medeiros et al., 2009a). People who work in the field as farmers or fishermen are more exposed to the infection, however, it may be found in students or housewives (Batista et al., 1960a; Shelley, 1975; Medeiros et al., 2009a).

STATUS OF MANSONELLIASIS IN BRAZIL

In Brazil, *M. ozzardi* has a broad geographic distribution in Amazonas state, while *M. perstans* co-exists with *M. ozzardi* in the region of the upper Rio Negro River (Medeiros & Py-Daniel, 2009). In the 1960s *M. ozzardi* was also recorded in the states of Mato Grosso and Roraima (Oliveira, 1963; D'Andretta et al., 1969); however, there is currently no information about the occurrence of *M. ozzardi* in these states, although recently new cases were found in Acre state (Adami et al., 2008). A recent study, carried out by Basano et al. (2011), after examining 4,452 inhabitants of the main rivers of Rondônia state, did not find the disease in this region.

In the 1950s a broad haemoscopic survey for *M. ozzardi* in Amazonas state revealed its wide distribution in the rivers Solimões, Purus, and Negro, with a higher prevalence in the municipalities along the Solimões River (Codajás, 23.9%; Fonte Boa, 17.6%; São Paulo de Olivença, 12.6%; Uaupés, 10.5% and Coari 10.0%) in relation to other regions, such as Negro River (Barcelos, 1.1% and Cucuí, 5.0%),

Purus River (Canutama, 0.5%; Lábrea, 0.4% and Boca do Acre, 0.2%) and Juruá River (Eirunepé, 0.3%) (Rachou, 1957). The indigenous communities were also affected, with a high prevalence (28.6%) for the Ticuna ethnicity (Rachou, 1957).

The current status in Amazonas state is not significantly different. Abrahim (2004) observed that up to 15.0% of the total blood bags in some municipality banks were contaminated with *M. ozzardi.* This is of extreme importance because there is no screening of blood for this parasite. Abrahim also emphasized that the microfilariae remained viable in the blood bags for 15 days; although it is known that the infective forms need to pass part of their life cycle in the dipteran vectors in order to develop into adults and become infective. In the riverine communities of the Purus River in the municipalities of Lábrea, Pauini and Boca do Acre, the prevalence of *M. ozzardi* was 20.7%, 24.2% and 27.3%, respectively (Medeiros et al., 2009a; 2009b; 2011). In the region of Ituxi River, Lábrea, 30.2% of the population had *M. ozzardi* infections (Medeiros et al., 2008). This prevalence was approximately 5 times greater than the values obtained in the past in Lábrea and Ituxi River (Shelley, 1975; Tavares, 1981). In Coari ("Médio Solimões") the prevalence is high, both in urban (10.2%) and rural areas (18.2%) (Martins et al., 2010). In the urban area of Coari, vectors with the infective stage of *M. ozzardi* (L3) have been identified, confirming the trend of urbanization of this filaria (Martins et al., 2010). Partial data collected by our research team have shown that filariasis has a high prevalence in Codajás (9.4%) and Tefé (13.5%). In the region of "Médio Solimões," there is concern about the possibility of filariasis expansion because there are people from other states who work in companies involved in oil and natural gas exploitation.

The lack of specificity for symptoms of *M. ozzardi* infection remains controversial. The main reported symptoms of *M. ozzardi* infection are fever, arthralgias, headache, and inguinocrural adenitis (Batista et al., 1960b; Tavares, 1981). In the interior of the Amazon, fever and chills are also reported by people infected with *Plasmodium* spp., the etiologic agent of malaria. Recent studies indicate the presence of ocular lesions possibly associated with *M. ozzardi* infection (Cohen et al., 2008; Vianna et al., 2013).

The most common technique for diagnosing this filariasis is the thick blood smear; however, false negative diagnoses are still occurring in the most isolated communities of Amazonas state where health workers do not diagnose filariasis because they are only trained to look for *Plasmodium* spp.. *Plasmodium* spp. are observed at a magnification of 100 times while *Mansonella* spp. are observed at a magnification of 10 to 40 times.

Ivermectin (0.20 mg/kg in a single dose) eliminates blood microfilariae and is the current treatment for *M. ozzardi* infection (Nutman et al., 1987; Gonzalez et al., 1999). Among individuals with high blood microfilariae loads there might be side effects, such as chills, fever, and sometimes anaphylactic reactions. There is no information available regarding elimination of adult worms by ivermectin; however, preliminary data gathered by us suggest that ivermectin is also able to

eliminate *M. ozzardi* adults in some cases. We recently examined 32 individuals who were diagnosed with *M. ozzardi* and prescribed ivermectin, between 2002 and 2011. Twenty (62.5%) had no more microfilariae; all individuals examined who were positive for *M. ozzardi* and treated, remained in endemic areas, where they had been infected. Basano et al. (2014) observed that 53 patients, after treatment with ivermectin, were microfilariae negative after 12 months.

M. perstans is found in indigenous communities along the Içana, Tiquié, Waupés, Xié, and Negro rivers in the region of "Alto Rio Negro" (Medeiros & Py-Daniel, 2009). In addition to the indigenous communities, *M. perstans* was also diagnosed in members of the Brazilian Army in Maturacá and Tunuí Cachoeira (Py-Daniel, 2012). The severity of symptoms caused by this filaria (Asio et al., 2009) deserves more attention from the health authorities.

There is still no consensus about the treatment for *M. perstans*. In Africa diethylcarbamazine (DEC) is often used to treat *M. perstans*; however, suppression of microfilariae is more efficient with doxycycline (Coulibaly et al., 2009). In the region of "Alto Rio Negro" co-infection with *M. ozzardi* and *M. perstans* is a common diagnosis (Medeiros & Py-Daniel, 2009). In such cases, individualized treatment is required for each species. Incorrect identification of filariae species found in the region, however, has resulted in treatment with ivermectin, which eliminates *M. ozzardi* filariae only and is not effective against *M. perstans*.

The simuliid vectors of *M. ozzardi* are borne in Amazonian rivers (Cerqueira, 1959; Shelley et al., 1980; Medeiros et al., 2009a). Considering that there is no strategy to control the vectors, elimination of *M. ozzardi* and *M. perstans* is only possible through treatment of human beings. In addition to the impact of *M. ozzardi* and *M. perstans* on the health and daily lives of the population, because of the continuous cycle of transmission and the lack of treatment policies, the trend will be to perpetuate, sustaining a large number of microfilaremics with serious risks of urbanization and expansion of the disease to other states of Brazil.

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