Editorial

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# Onchocerciasis and its Impact on the Female Reproductive System: A Neglected Situation?

**Grácio Maria A* and Grácio António JS**

*Instituto de Higiene e Medicina Tropical, Universidade Nova de Lisboa, Rua da Junqueira 100, Lisboa, Portugal.*

***Correspondence:**
Grácio Maria A, Instituto de Higiene e Medicina Tropical, Universidade Nova de Lisboa, Rua da Junqueira 100, 1349-008 Lisboa, Portugal, E-mail: mameliahelm@ihmt.unl.pt.

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Onchocerciasis is a vector borne disease whose etiological agent is the nematode *Onchocerca volvulus* that it is transmitted by insects of the genus *Simulium* (blackflies, and in Brazil also known as "borrachudos"). The disease was recognized for the first time when explorers arrived in Africa and the Arabian Peninsula. Then, the diseased people were observed to experience blindness of unknown cause, as well as scabies itch, nodular skin, which was known as "kru kru" or "craw craw" in West Africa [1]. This author, in a historical note referred in 1874 to John O'Neil, an Irish naval surgeon, who had discovered subcutaneous microfilariae, while examining skin-snips from craw craw patients in Ghana; in 1897, the zoologist Rudolf Leuckart described, for the first time, the morphology of adult worms in subcutaneous nodules; in 1890, Patrick Manson observed and identified the adult worms; in 1904, Emile Brumpt recognized that microfilariae come from the adult worms living in subcutaneous nodules and that the infection occurs most commonly along river banks; in 1917, Rudolf Robles published findings on a "new disease" from Guatemala associated with subcutaneous nodules, anterior ocular lesions, dermatitis, and microfilariae; in 1920, the role of microfilariae in causing lesions was established by A. Lacroix and Jean Montpellier. Lastly, in 1926 B. Blacklock working in Sierra Leone (Africa) demonstrated, for the first time, that *Simulium* species are vectors of *O. volvulus* [2,3]. He successfully infected *Simulium damnosum* adults with microfilariae of *O. volvulus*, and described its development in the insect. This was confirmed by Bequaert [4] in Africa, Hoffmann [5] in Mexico and by Strong (1931) [6] in Guatemala, and lastly, Vargas [7] and Lebied [8] reported other important aspects of the larval development of the parasite in *Simulium*.

*O. volvulus* has a complex life cycle, with one part occurring within blackflies (vectors) and another in the human (definitive hosts). The blackflies become infected when taking a blood meal from an infected person. The larvae (microfilariae) penetrate the gut to reach the flight muscles and there they moult twice. After, they migrate to the head and develop into infective third-stage larvae in about one week and infect a new host when the blackfly takes another blood meal. They enter the wound, migrate to the subcutaneous tissues and develop into adult males and females in around 12 months. Sometimes they live in the deeper tissues. In other cases they are more superficial, becoming enclosed in fibrous capsules or nodules in the subcutaneous tissue (onchocercoma) usually over bony prominences. The adult male worms die shortly after fertilizing females, which then produce large numbers of larvae, which are the important pathogenic agents for the host. The larvae pass into the subcutaneous tissues where they cause pruritus with an itchy rash and lymphadenopathy in the groin or axila. After months or years, this can lead to intradermal oedema with pachyderma ("crocodile skin"). Later, there is loss of the elastic fibers causing hernias or "hanging groin"(hanging lymph glands), atrophy of the skin causing a prematurely aged appearance and in the African patients the skin (particularly over the tibia) may become thin and despigmented, a condition known as "leopard skin".

Blindness is the most important effect of *O. volvulus* and it results from lesions in the eyes caused by microfilariae. This condition is known as "river blindness" because it occurs in areas with fast flowing well-oxygenated river, which are the breeding grounds for the blackflies that transmit the parasite [9]. However, the microfilariae can invade other parts of the body including liver, kidney, lungs, spleen and the cerebrospinal fluid. Pain and weight loss may not be as dramatic as blindness but their contribution to the overall debilitating effects of morbidity should not be ignored. They note that onchocerciasis may be capable of more wide- spread harm than previously thought. Both clinical and cultural clues to

another potential effect of onchocerciasis - involvement with the female reproductive system been mentioned by some authors. Clinical evidence includes microfilariae found in gynaecologic smears [10] and in vaginal irrigation specimens [11]. Intrauterine transmission of onchocerciasis has been postulated when positive skin-snips were taken from new born babies and infants [12,13] on the cultural side, explains that traditional societies living in endemic areas think that onchocerciasis may be responsible for human reproductive problems. In East Africa, the Ugandan people believe onchocerciasis can cause habitual abortion [14]. The Yoruba of Ibarapa District, Oyo State Nigeria, have no doubt that the disease can cause impotence in males and infertility and spontaneous abortions in females [15]. An example is the experience of a village woman that had been trying unsuccessfully to get pregnant for five years. She was found to have a positive skin snip during an epidemiological survey, and was given a course of diethylcarbamazine citrate. She completed the course and six months later was happy to report she was pregnant. She blamed onchocerciasis for her inability to conceive, and felt the drug had made her pregnancy possible [15]. Also, on the other hand, in the same study, women in their reproductive years, aged 15-49, from both the main town and villages were surveyed, and of the 422 woman examined 35.4% had onchocerciasis. Fifty-six percent of the woman believed that onchocerciasis affected menstruation, certainly increasing very significantly with age [15]. Concerning onchocerciasis in Latin America, about 500,00 people have historically, been at risk of infection in 13 foci throughout Brazil, Colombia, Ecuador, Guatemala, Mexico and Venezuela. The disease arrived in the Americas through the slave trade. Starting in the early 26th Century, slaves from the heavily endemic areas of West Africa were brought to Central and South America, bringing with them *O. volvulus* parasites. Slaves, then migrated within the colonies, including between coffee plantations and as suitable *Simulium* species were present, the parasites were also transmitted to the indigenous American population and then spread further through migration, including among certain contiguous border countries like Guatemala and Mexico. The spread of the disease through labor and other migration, and the presence of different vectors in the environment, explains the presence of onchocerciasis in Ecuador, Colombia, Guatemala, Mexico and Northern Venezuela, and genetic testing of parasites confirms this linkage between Old World and New World *O. volvulus* [16].

Actually, transmission of parasite onchocerciasis is still ongoing in Brazil, and southern Venezuela and it has been introduced in Yemen. In July 2016, Colombia, Ecuador, Guatemala, and Mexico were considered free of onchocerciasis after successfully implementing elimination activities for decades [17].

In a retrospective study [18] compared the number of spontaneous abortions in a hyperendemic area for onchocerciasis in Ecuador before and after ivermectin treatment with that of a comparable non-endemic area, has showed that the frequency of spontaneous abortions was associated with the change in the community microfilariae load, suggesting that there may be a relationship between spontaneous abortions with *O. volvulus*. In the endemic area, a significantly greater rate of spontaneous abortions was seen in the period before ivermectin distribution compared to the after the start of ivermectin treatment every six months. In the non-endemic area, no change in the rate of spontaneous abortions was seen over the same time period. The authors have concluded that "in addition to the well-documented improvements in skin and ocular disease, ivermectin may also improve the reproductive health of endemic populations."

In conclusion, the scientific studies, the observations and the reports of woman living in endemic areas are coincident in the attribution of negative effects of the parasite and the disease in the female reproductive system. These effects are namely infertility, spontaneous abortions, which cause strong physical and psychological suffering.

In this context, in the countries where onchocerciasis is or was endemic the health services have to include onchocerciasis in the group of priority disease to be eliminated, so that the elimination of disease can be possible, as shown by the results obtained in several countries. Effectively, in July 2016, Guatemala becomes the fourth country in the world, after Colombia (2013), Ecuador (2014) and Mexico (2015) to be verified free of onchocerciasis after successfully implementing elimination activities for decades [17].

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