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INTERRUPTION OF TRANSMISSION OF O. VOLVULUS IN UGANDA

Transmission of *Onchocerca volvulus* by *Simulium neavei* in Mount Elgon Focus of Eastern Uganda Has Been Interrupted

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Abstract.

The study determined that *Simulium neavei*-transmitted onchocerciasis in Mount Elgon onchocerciasis focus had been interrupted. Annual mass treatment with ivermectin changed to two times per year along with vector elimination in 2007. Then, baseline microfilaria (mf) prevalence data of 1994 in five sentinel communities were compared with follow-up data in 2005 and 2011. Blood spots from 3,051 children obtained in 2009 were analyzed for exposure to *Onchocerca volvulus* immunoglobulin G4 antibodies. Fresh water crab host captures and blackflies collected indicated their infestation with larval stages of *S. neavei* and presence or absence of the vector, respectively. Mf rates dropped from 62.2% to 0.5%, and 1 (0.03%) of 3,051 children was positive for *O. volvulus* antibodies. Crab infestation dropped from 41.9% in 2007 to 0%, and *S. neavei* biting reduced to zero. Both remained zero for the next 3 years, confirming interruption of onchocerciasis transmission, and interventions were halted.

INTRODUCTION.

At the 2002 conference on the eradicability of onchocerciasis, global eradicability of onchocerciasis was deemed impossible using currently available tools (ivermectin and vector control) because of the challenges posed

eventual elimination of the parasite and halting of interventions in those foci. The remaining meso- and hyperendemic foci in Africa under the assistance of African Program for Onchocerciasis Control (APOC) were advised to continue annual mass drug administration (MDA) of ivermectin (Mectizan; donated by Merck & Co.) with the goal of reaching a point of high-level control, where the disease resulting from the infection is no longer a public health problem.[2] However, the donation of ivermectin and questions of how long the mass ivermectin treatment programs would be needed in endemic areas have long been a concern to the public health community in endemic African countries, including Uganda.[3]

The immense health challenges of sustaining programs over time given frequent transfers of trained and committed personnel, shifting government policies, donor fatigue, and uncertain long-term political needed to justify long-term investment in

METHODS.

History of recent assessments and treatment activities in the focus.

By 1994, the Mount Elgon focus was comprised of parts of Mbale and Sironko districts; subsequently, two more districts (Bududa and Manafua) were created from Mbale and Sironko districts (Figure 1). Rapid epidemiological assessment (REA) based on community nodule prevalence was done in 1994 in Mount Elgon to target ivermectin MDA.[17] Samples of 30 resident adults ages 20 years and above who had lived in the community for at least 10 years were assessed for nodules.[18] Annual mass treatment was launched in 1994 through community based treat

for at least 1 hour and then immediately examined for crabs carrying larvae and pupae of *S. neavei*.[5,13] The crabs carrying young stages of *S. neavei* were counted, and infestation rate was expressed as a percentage of the total catch. Crabs were returned to the stream immediately after examination. Crab monitoring continued one time per month until October of 2011.

Adult S. neavei *collection.*

Adult *S. neavei* collection following an MOH protocol based on WHO standards for full-day human landing catches of *S. neavei* (0700–1800 hours) were established at four catching sites: one on the Namufumbilo river system, two on the Namatala river system, and one on the Tsutsu river system (Figure 2).[31] Female *S. neavei* seeking a blood meal settled on exposed legs of local collectors, who collected them in tubes before they bit. *S. neavei* collection was 2 days/week and 8 days/month until June of 2011, and the captures were preserved in ethanol. In a small study conducted in 2007, captured *S. neavei* were dissected to determine parous and infection rates before launching two times per year ivermectin treatments. Infection rate was defined as the proportion of S. neavei with all larval stages (L1, L2, and L3).[18, 32]

Larviciding.

Larviciding with temephos was conducted and supervised by expert MOH vector control teams at all sites where infested crabs were observed.[5] First insecticide carry trials were carried out at 27 dosing points from October to November of 2007. During this period, river gauging to establish the discharge and determine dosing and booster points was done. Temephos was applied at a rate of 0.2–0.4 mg/L to reach a concentration of 0.1–0.3 ppm. The insecticide was pre-mixed in a 15-L knapsack sprayer and applied for a period of 30 minutes at established dosing points.

RESULTS.

Mass treatment.

S. neavei *adult fly collection.*

S. neavei collections from April of 2007 show a year-round biting pattern, with a peak biting period between June and October. With the commencement of larviciding in January of 2008, a progressive decline in *S. neavei* collection was observed, and the last *S. neavei* were collected in June of 2008. The mean biting rate in 2007 of five *S. neavei* per man-hour had quickly been reduced to zero after commencement of ground larviciding. The vector population did not recover for a period of 3 years since July of 2008 (Figure 6). The very limited dissections in 2006 of 57 parous *S. neavei* showed an infection rate of 7.0%.

DISCUSSION.

In the Mount Elgon onchocerciasis focus in eastern Uganda, the human adult infection rates in sentinel communities in 2011 averaged below 1%, with only one community being above 1% (1.5% in Buriri). Children under 10 years of age from 17 communities selected from throughout the focus in 2010 show no serological evidence of recent infection or exposure to onchocerciasis. The last crab with larval stages of *S. neavei* was captured in August of 2008, and no infested crab has been captured since that time. Also, no *S. neavei* was collected for 3 years between July of 2008 and July of 2011. Larviciding halted in March of 2009, and therefore, it seems that the *S. neavei* population is incapable of recovering. Absence of the vector (as far as we were able to measure) from the Mount Elgon focus means that onchocerciasis transmission has been interrupted. The Ugandan entomological and epidemiological criteria for interruption of transmission have been met.

In the Mount Elgon focus, communities using the CDTI approach showed that they are capable of distributing ivermectin two times per year while maintaining treatment coverage exceeding 90%. The capacity of CDTI to incorporate (without collapsing) a 6-month treatment strategy in Africa has been debated (Boatin and Richards, unpublished data). This study, however, is the second report from Uganda that documents the ability of a CDTI program to rapidly expand from annual to 6-month treatments (the first being from Wadalai[21]). The debate about two times per year treatment should move away from asking the research question about whether CDTI can tolerate two times per year to an operational/epidemiological question of when and where two times per year treatment needs to be implemented to advance the elimination agenda.

At its fourth meeting in August of 2011, the UOEEAC reviewed and discussed the Mount Elgon focus survey data with respect to national parasitological, serological, and entomological elimination criteria.[22] The UOEEAC concluded that the Mount Elgon focus had met the Ugandan national criteria for transmission interruption and recommended to the MOH that interventions be halted. Subsequently, the MOH's National Certification Committee accepted the UOEEAC recommendation, and in 2012, ivermectin mass treatments in Mount Elgon were halted. If, during a 3-year post-treatment surveillance (PTS) phase, no evidence for renewed transmission is noted, the focus could be declared free of onchocerciasis.[21–25]

The 2009 serological results from the Ov-16 antibody survey among children were discussed by the UOEEAC at length. The national criteria call for < 0.1% seroprevalence, and although the serosurvey found a prevalence of 0.03%, the upper bound of the 95% CI was just above 0.1% (at 0.128%). The UOEEAC concluded, however, that the one positive child was in an age group that likely represented an older transmission event, given the absence of infection in younger children. The UOEEAC unanimously recommended to stop interventions in Mount Elgon, despite the one positive child in the survey, while also urging any subsequent serosurveys to sample only children less than 10 years of age so as to avoid this problem in future.[21,33] The national guidelines now require the seroprevalence of children under 10 years of age to be less than 0.1%.[21]

It was evident that deforestation rendered a large area unsuitable for *S. neavei* breeding and survival, resulting in progressive shrinking of the Mount Elgon focus from 1,500 km^2 in the 1950s to the current 250 km^2.[15,16] In fact, tree felling and bush clearing was used in the 1940s and early 1950s successfully to control *S. neavei* in the Nyanza region of Kenya.[34] Deforestation is an important factor in reducing onchocerciasis in areas where the sole vector is *S. neavei*.[35] Deforestation was exacerbated by the population pressure on land (currently at about 1,315 persons/km^2)in and around Mount Elgon. There was also evidence of declining crab host populations of *P. niloticus* and *P. loven*. Previous studies in western Uganda had implicated deforestation as a major factor driving the decline of the fresh water crab population.[5, 29] Our surveys conducted from 2007 to 2011 documented a dramatic decline in crab populations in both treated and untreated rivers, indicating that the decline that we observed was not related to the larviciding with temephos to control the vector population. On reflection, deforestation in the Mount Elgon focus may have also contributed to the interruption of transmission of onchocerciasis.

CONCLUSION.

Transmission interruption in Mount Elgon validates the Ugandan MOH decision in 2007 to adopt an aggressive tactical approach to onchocerciasis elimination, including semiannual mass treatment of the afflicted communities with ivermectin and vector elimination/control efforts where feasible. Onchocerciasis elimination as a strategy should mean the reconfiguration of static onchocerciasis control programs to more flexible ones in an attempt to speed up the elimination process, and it should convey to all partners that elimination means that it can no longer be business as usual.

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