

The First Confirmed Elimination of an Onchocerciasis Focus in Africa: Abu Hamed, Sudan

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Abstract. Mass treatment with ivermectin for onchocerciasis was stopped in 2012 in Abu Hamed, an isolated focus on the River Nile in northern Sudan. A 3-year posttreatment surveillance (PTS) ensued, at the end of which an evaluation was conducted in 2015 following the current World Health Organization guidelines for verification of onchocerciasis elimination. Vector black flies were collected from sentinel breeding sites and finger-prick bloodspots were collected from children ≤ 10 years of age resident in 35 communities within the focus. Polymerase chain reaction (PCR) screening of 19,191 flies from four sites for the O-150 parasite-specific marker found no flies carrying *Onchocerca volvulus* larvae (0%, 95% upper confidence limit [UCL] = 0.16), and serological testing of 5,266 children identified only one Ov16 seropositive child (0.019%, 95% UCL = 0.074); whose skin snips were negative when tested by O-150 PCR assay. These results indicate that for the first time in Africa, onchocerciasis elimination has been verified after a successful PTS in Abu Hamed.

Onchocerciasis or river blindness is a major tropical disease currently endemic in Venezuela, Brazil, Yemen, and importantly in 31 African countries where 99% of the estimated 123 million individuals at risk reside.¹ Onchocerciasis is caused by the parasitic filarial nematode *Onchocerca volvulus*, and is transmitted by black flies of the genus *Simulium* that breed in fast-flowing rivers and streams. The disease is manifested in debilitating skin lesions and ocular pathology that can lead to blindness.

Sudan is one of 20 African countries within the former African Program for Onchocerciasis Control (APOC) that covered > 102 million people at risk of this infection.² Currently, the disease remains endemic in four foci located in the north, east, southeast, and in the southwest of the country. The Abu Hamed focus, the northernmost focus in the world, is an isolated site associated with active *Simulium* breeding in the River Nile as it winds through the rocks and sands within the Nubian Desert to the north and east (Figure 1A). The focus is at least 600 km away from the closest existing onchocerciasis focus in Galabat, east Sudan. First reported in 1958,³ the Abu Hamed onchocerciasis focus has been described at times of having infection rates of up to 37%⁴ (Figure 1B), and presenting a nonblinding form of the disease predominated by severe dermal disease, including the characteristic “sowda” form of acute reactive onchodermatitis.⁴ Molecular and cytogenetic studies have identified the presence of unique forms of the parasite and *Simulium damnosum* s.l. vector^{5,6} in this focus and the characteristics of black fly breeding sites and biting in Abu Hamed have been described.^{7,8}

The Abu Hamed focus was the first in the country to undergo rapid epidemiological mapping of onchocerciasis and to begin a control program under auspices of APOC using a mass drug administration (MDA) strategy employing annual community-directed treatment with ivermectin (CDTI) in 1998 (Figure 1B). The isolated nature and the mesoendemic disease status of the Abu Hamed focus led the government of Sudan to declare an official elimination strategy for the first time in

Africa in December 2006 (Figure 1B). As onchocerciasis elimination has now been achieved in Colombia,⁹ Ecuador,¹⁰ and Mexico¹¹ by using a semiannual or quarterly ivermectin treatment regimen, a switch to semiannual CDTI in the Abu Hamed focus was used with the new elimination approach, and detailed parasitological, entomological, and serological assessments of the disease were carried out. The 2007 entomological assessment of more than 29,000 flies by O-150 polymerase chain reaction (PCR)-based enzyme-linked immunosorbent assay showed 0.17 (95% confidence interval [CI] = 0.097–1.88) L3 larvae per 2,000 black flies indicating (according to World Health Organization [WHO] guidelines requiring < 1 L3/2,000¹²) ongoing transmission of infection despite 10 years of annual MDA.¹³

To focus on elimination, the treatment coverage of the target population of about 120,000 in this focus was improved and a second assessment of the disease status was performed in 2011/2012, 5 years after the switch to semiannual CDTI¹⁴ (Figure 1B). In this assessment, no infection was found in > 17,000 black flies screened by O-150 PCR, no antibodies to Ov16 antigen in 6,756 children ≤ 10 years of age, and no signs of infection in 536 adult individuals from seven communities within the focus.¹⁴ This assessment indicated that the disease transmission has been interrupted in Abu Hamed based on the WHO 2001 guidelines for interruption of onchocerciasis transmission.¹¹ Review of these findings prompted the government of Sudan to declare interruption of the parasite transmission, halting mass treatment activities, and beginning a 3-year posttreatment surveillance (PTS) phase in May 2012 (Figure 1B). The PTS period has been marked and celebrated by extensive health education and community mobilization campaigns throughout the focus in 2013 and 2014, led by state ministries of health (MOHs) and community partners, to educate the local population about the cessation of the disease transmission, the stoppage of treatment, and the next steps toward successful elimination of this infection.

Both the 2012 and the assessments described in the present report have taken into consideration some of the important recent environmental developments in the area. The Merowe hydroelectric dam, about 30 km downstream of the western limit of the Abu Hamed focus (Figure 1A), was built and activated in 2009. The artificial reservoir filling as a result of the

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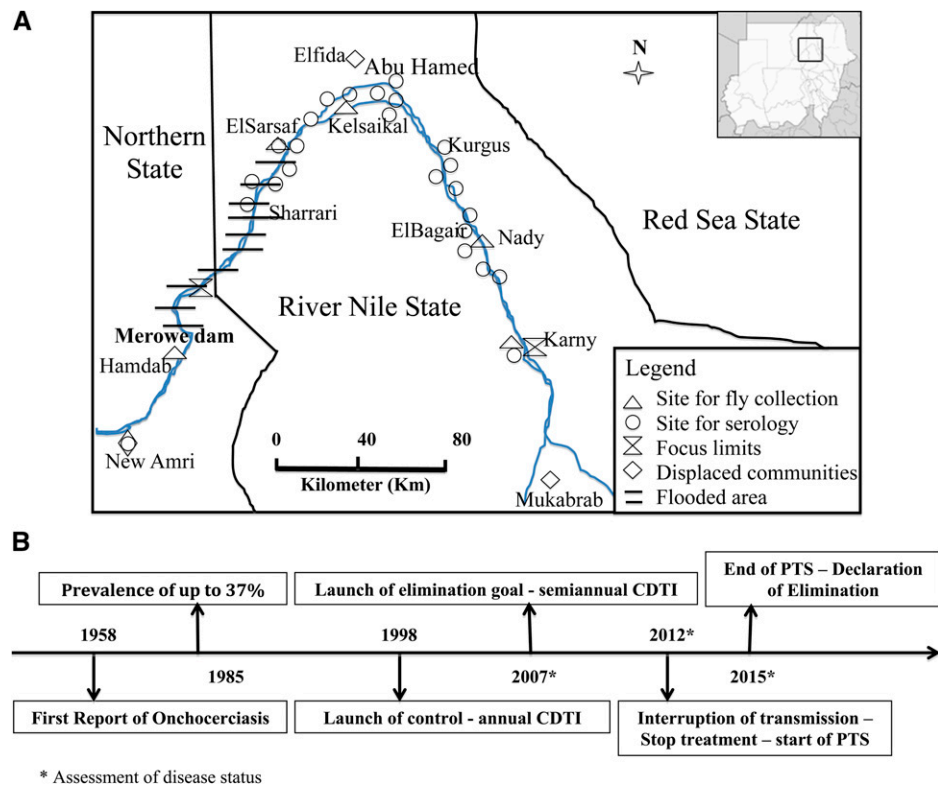


FIGURE 1. (A) Map of the Abu Hamed focus showing black fly collection sites and some serology collection sites in 2014/2015. Also shown is the flooded portion of the focus and some displaced communities. (B) Timeline of onchocerciasis history in Abu Hamed from discovery to elimination.

completion of the dam has gradually flooded a considerable portion of the western part of the focus and displaced some island and shore communities to new locations within and near the focus (Figure 1A).¹³⁻¹⁵ Thus, a new breeding site near Al Sarsaf village west of the flooded area was added to the PTS assessment protocol. In addition, Hamdab Island, downstream of Merowe dam, was also monitored for the possible introduction of new black fly breeding sites due to favorable conditions created by the dam, and two displaced communities were screened in their new locations for any exposure to the infection.

The Abu Hamed PTS assessment followed the criteria and procedures of the 2016 WHO guidelines for stopping MDA and verifying elimination of human onchocerciasis.¹⁶ Black flies were collected from four sentinel breeding sites within the focus (Figure 1A) from November 2014 to June 2015 following standard procedures.¹⁴ Finger-prick sampled blood was also collected on filter papers from children ≤ 10 years of age from 39 schools representing 35 communities within and around the focus including flooded and displaced communities (Figure 1A) in July 2015. Black flies and sera extracted from filter paper were processed and tested for *O. volvulus* infection using the O-150 pool screening PCR and the Ov16 serological assays, respectively, as previously described.¹⁴ All communities included in the study were informed of the purpose and procedures of the monitoring process and necessary ethical approvals were obtained from federal and state MOHs, and all individuals involved in the study, or their guardians/headmasters. In addition, the study protocols were reviewed by the Emory University Institutional Review Board, which classified them as nonresearch routine program evaluation.

PCR screening of 19,191 black fly bodies collected from four sites throughout the focus in the 2014/2015 breeding season showed no parasite-specific DNA (point prevalence of flies carrying *O. volvulus* of 0%, with an upper limit of the 95% CI = 0.16/2,000 flies) (Table 1). No flies were detected in the Hamdab Island site downstream of the Merowe dam (Table 1). Testing black fly bodies allows for detection of all larval stages of the parasite rather than only L3 larvae that are detected in black fly heads. Screening of blood spots from 5,266 children ≤ 10 years of age from 33 communities within the focus and residing in two displaced communities, showed one child positive for Ov16 IgG4 antibodies (0.019% prevalence; 95% CI = 0.00003–0.074) (Table 2). As soon the Ov16 serological test results became known, the assessment team conducted an epidemiological investigation. The child was a

TABLE 1
Prevalence of *Onchocerca volvulus*-infected black flies in Abu Hamed from November 2014 to June 2015 based on O-150 pool screening polymerase chain reaction

Breeding site	No. of flies/pools analyzed	No. infected	Prevalence of flies carrying <i>O. volvulus</i> (any stage) per 2,000 flies*
Kelsakel	5,664/58	0	0 (0–0.72)
Nady	3,550/38	0	0 (0–1.12)
Karny	2,245/24	0	0 (0–1.6)
AlSarsaf	7,732/82	0	0 (0–0.52)
Hamdab Island	0	N/A	N/A
Abu Hamed total	19,191/202	0	0 (0–0.16)

N/A = not applicable.

*Upper number represents the estimated point prevalence (95% confidence interval).

TABLE 2

Prevalence of Ov16 IgG4 antibodies in school children ≤ 10 years of age in Abu Hamed focus on July 2015

Site (no. of communities)	No. examined	No. positive (prevalence %)	95% CI (%)
Within focus (33)	4,987	1* (0.02)	0.00003–0.075
Displaced (2)	279	0 (0)	0–0.68
Abu Hamed total	5,266	1* (0.019)	0.00003–0.074

CI = confidence interval.

*O-150 polymerase chain reaction on skin snips showed no current infection.

9-year-old female from the Kurgus community who had no history of travel or clinical history or symptoms of onchocerciasis infection. Two skin snips obtained from the left and right posterior superior iliac crest tested negative for parasite-specific DNA by the O-150 PCR assay. The number of samples collected and screened in this study complies with the limits set by WHO guidelines of at least 6,000 black flies and 2,000 blood spots per transmission zone.¹⁶

Previously we reported the first evidence of interruption of *O. volvulus* transmission in Africa achieved with annual and semiannual ivermectin mass treatment alone in Abu Hamed in 2012,¹⁴ and now provide evidence for the first elimination of onchocerciasis after PTS in Africa following the new WHO guidelines for verification of onchocerciasis transmission interruption and elimination¹⁶; these guidelines are based on the successes in South America.^{9–11} Our data meets the major recommendation of $< 1\%$ upper limit 95% CI of infection where no black flies screened by the O-150 PCR assay are infected, as well as the upper limit of the 95% CI of 0.1% for the prevalence of infection in children ≤ 10 years of age. In addition, the absence of positive bodies in the flies is strong evidence for the absence of available microfilaria in the human population. Finally, O-150 PCR confirmed the absence of current active infection in skin snips from the single Ov16 seropositive child as recommended in the guidelines. This positive reaction may have been due to a false positive, an exposure without patent infection, or a prepatent infection. The child will be followed up on a later date to determine the latter. Other factors that assisted in the decision to stop treatment in 2012 and achievement of elimination status are the absence of lymphatic filariasis and the negligible chance of infected vectors or people migration into the Abu Hamed area due to its unique location and nature.¹⁴

The onchocerciasis elimination activities in Abu Hamed had its share of challenges represented by displacement of communities impacted by Merowe dam and the potential for creation of new and perennial vector breeding sites in the spillway downstream of the dam. In this and a previous study, we have screened an 8-km area along the River Nile to verify absence of adult and aquatic stages of black flies. The area upstream of the dam was also screened to identify the westernmost breeding sites beyond the flooding impact of the artificial reservoir. Overall, Merowe Dam appears to have had a positive impact on onchocerciasis and its black fly vectors in Abu Hamed focus.¹⁵ This study shows the importance of monitoring the impact of hydropower dams and other environment changes on onchocerciasis elimination activities. It also shows that elimination efforts must face and tackle the unique characteristics of each onchocerciasis transmission zone. The history of the onchocerciasis control and elimination activities in Abu Hamed also highlights the impact of the switch from annual to semiannual mass treatment in completing the

interruption of transmission^{14,17} and ultimate achievement of the disease elimination.

The Abu Hamed success story is an example of sustained commitment and successful collaboration of state governments, international organization, non-governmental organizations, pharmaceutical companies, and the local affected communities to realize the vision of elimination of a major tropical disease in Africa. The PTS assessment data presented here was reviewed in a meeting of the national onchocerciasis elimination program partners in Khartoum, Sudan, in October 2015, at which time the government of Sudan declared elimination of onchocerciasis from Abu Hamed. We presented assessment data for the first PTS and verification of elimination of the disease in Africa based on the 2016 WHO guidelines. Lessons and experience learned from these activities should assist in elimination efforts in the rest of the country and across the continent.

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