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ONCHOCERCIASIS SEROSURVEILLANCE IN UGANDA

Serosurveillance to Monitor Onchocerciasis Elimination: The Ugandan Experience

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Abstract.

Uganda is the only African country whose onchocerciasis elimination program uses a two-pronged approach of vector control and mass drug distribution. The Ugandan program relies heavily upon the use of serosurveys of children to monitor progress toward elimination. The program has tested over 39,000 individuals from 11 foci for Onchocerca volvulus exposure, using the Ov16 ELISA test. The data show that the Ov16 ELISA is a useful operational tool to monitor onchocerciasis transmission interruption in Africa at the World Health Organization (WHO) recommended threshold of < 0.1% in children. The Ugandan experience has also resulted in a re-examination of the statistical methods used to estimate the boundary of the upper 95% confidence interval for the WHO prevalence threshold when all samples tested are negative. This has resulted in the development of Bayesian and hypergeometric statistical methods that reduce the number of individuals who must be tested to meet the WHO criterion.

INTRODUCTION

Onchocerciasis has historically been one of the most important causes of infectious blindness.[1,2] The disease is caused by the filarial nematode parasite Onchocerca volvulus. It is estimated that 120 million individuals worldwide are at risk of O. volvulus infection, with most residing in rural Africa.[3] Onchocerca volvulus is transmitted by black flies of the genus Simulium, insects that breed in fast flowing water. Thus, the infection is most intense in areas located along rivers, leading to the common name of "river blindness" for the disease. Unfortunately, the areas bordering the river basins contain much of the fertile land found in sub-Saharan African savanna ecosystems. By preventing the agricultural use of the most fertile lands, onchocerciasis has had a significant negative impact on the economic growth of many of the poorest countries of Africa.

The devastating impact that onchocerciasis has historically had upon some of the poorest people on the planet has attracted the attention of the international community, which has supported several programs to control or eliminate the disease. Strategies originally focused on vector control, but this approach has been largely supplanted with the discovery that ivermectin was a safe and effective treatment of human onchocerciasis, having a potent effect on the microfilarial stage of O. volvulus.[4] The offer of Merck & Co, Inc. to donate ivermectin free of charge for the treatment of onchocerciasis for as long as needed resulted in the establishment of two major regional programs, the African Program for Onchocerciasis Control, (APOC) and the Onchocerciasis Elimination Program of the Americas (OEPA). The strategies of these programs are to use population-based chemotherapy (mass drug administration) with ivermectin to control morbidity from onchocerciasis in Africa (APOC) or to completely eliminate the parasite from the Americas (OEPA). It was initially believed that ivermectin distribution alone could not successfully eliminate onchocerciasis in Africa, as a result of the widespread distribution of the infection and the intensity of transmission.5 However, recent data have suggested that this is not the case, and that long-term community wide distribution of ivermectin may be capable of eliminating onchocerciasis in at least some foci in Africa.[6–10] This discovery has resulted in a refocusing of the international community from an emphasis on control of onchocerciasis in Africa toward an emphasis upon possible elimination. [11,12]

Monitoring and evaluation activities are especially necessary in elimination efforts to document the effectiveness of program operations and eventually in showing that transmission had been interrupted. The latter task requires that assays with high negative predictive values be used to test large numbers of samples to verify that transmission has been interrupted. To this end, in 2001 the World Health Organization (WHO) adopted two key criteria for transmission interruption: 1) An absence or near absence of infective stage larvae (L3) in the vector population and; 2) Infection rates of < 0.1% in children residing in the endemic area.[13] Infection rates in children have operationally been measured by detecting the presence of IgG4 antibodies to a parasite-specific 16 kDa antigen (Ov16) using an enzyme-linked immunosorbent assay (ELISA) format. Using conventional statistical methods,[14] the WHO 2001 guidelines noted that it would be necessary to test 3,000 individuals to conclude that the upper bound of the 95% confidence interval (CI) of the prevalence estimate was < 0.1%.

In 2007, Uganda declared a goal of national elimination of onchocerciasis by 2020, becoming one of the first countries in Africa to do so.[15] Uganda contains 18 distinct onchocerciasis transmission zones (foci). With the exception of the Victoria and Mount Elgon foci, all of the

foci are found in the western and northern regions of the country (Figure 1). The vector in the western foci is Simulium neavei, whereas S. neavei and Simulium damnosum sensu lato serve as vectors in the northern foci. [16,17] Onchocerciasis was eliminated by DDT river treatments in the Victoria focus in the 1960s. [18,19] The Ugandan Onchocerciasis Elimination Program (UOEP) is unique in that it is currently the only program that incorporates both mass ivermectin distribution and vector control or local elimination into its strategic plan.[15] This combination of approaches has resulted in the rapid interruption of transmission of O. volvulus in at least two foci in Uganda. [9,20–22]

that many of the seropositive children converted to seronegativity in the 3 years between the two

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Note: Supplemental materials appear at www.ajtmh.org.

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Figures and Tables

FIGURE 1. Map of onchocerciasis foci in Uganda included in this study: The foci included in this study and their current epidemiological status are shown by different color codes. The names of the foci are as follows: 1 = Maracha Terengo; 2 = Mpamba-Nkusi; 3 = Imaramagambo; 4 = Itwara; 5 = Mt Elgon; 6 = Wambabya-Rwamarongo; 7 = Budongo; 8 = Wadelai; 9 = Bwindi; 10 = Kashoya; 11 = Nyamugasani. This figure appears in color at www.ajtmh.org.

FIGURE 2. Prevalence of IgG4 antibodies recognizing Ov16 in children in Ugandan foci of onchocerciasis by age group: Error bars indicate 95% confidence intervals (CIs) for the prevalence estimates.

FIGURE 3. Prevalence of IgG4 antibodies recognizing Ov16 in children in different parishes of the Budongo focus: Error bars indicate 95% confidence intervals for the prevalence estimates.

Table 1. Summary of Ov16 ELISA serosurveys in Uganda

Table 2. Bayesian credibility intervals for the upper limit of the 95% confidence interval (CI) of prevalence for different sample sizes when all samples are negative.

Table 3. Proportion of a finite target population that needs to be tested to conclude that the prevalence in the entire target population is ≤ 0.1% when none of the samples tested are positive.

Supplemental Material S1

OV16 ELISA Protocol

A. Reagents
B.