



onchocerciasis. When used on an individual basis, ivermectin rapidly kills the microfilariae and reduces the fecundity of adult female worms, but does not kill them (Taylor . 1990; Rodriguez-Perez & Reyes-Villanueva 1994; Chippaux . 1995). Therefore, ivermectin must be given repetitively. The frequency and duration of ivermectin administration remains at issue, and is influenced by whether ivermectin mass treatment in a given area can stop new infections (transmission) from taking place.

The Ministry of Health (MOH) onchocerciasis control programmes in Cameroon and Uganda had been assisted by the Carter Center and Lions Clubs since 1996, in partnership with the African Programme for Onchocerciasis Control (APOC) and the affected communities. The goal of the APOC partnership is 'to eliminate onchocerciasis as a disease of public health and socio-economic importance throughout Africa' (Amazigo & Boatin 2006). The strategy is to deliver an annual dose of ivermectin to the entire eligible population of onchocerciasis meso- and hyperendemic villages through community-directed treatment with ivermectin (CDTI) (Molyneux & Davies 1997). M is defined as onchocercal nodule rates  $\geq 20\%$  or microfilaridermia rate  $>40\%$ ; as nodule rates  $\geq 40\%$  or microfilaridermia  $\geq 60\%$  (WHO 1991). CDTI is an approach where community members are educated about onchocerciasis and then allowed to organize and rely upon themselves to provide annual treatment (Katarawa . 2002). Community members called community-directed distributors (CDDs) are selected by the community at large and trained by health workers to carry out periodic household census, health educate and treat their fellow community members. CDDs are also trained to manage minor side reactions, and promptly report to the nearest health facility severe reactions, treatment data and drug utilization.

The APOC approach is to provide core financial support from a World Bank Trust Fund to CDTI projects for a period of 5 years to help establish ivermectin delivery through CDTI with the hope that after building the capacity in the project areas, ivermectin distribution will be sustained; some additional APOC support is provided for replacement of capital items and advocacy for 3 years after the 5-year core period. The duration of treatment required after APOC support ceases to reach the goal of elimination as a public health problem remains an objective of speculation and debate. Some sources suggest that ivermectin distribution should continue for a total of 15 years (Amazigo . 2002), based on the estimate that the adult O. worms live that long. Such a calculation is based on the assumption that transmission of the parasite will be essentially interrupted by annual treatment in meso- and hyperendemic areas. However, studies show that a

single annual dose of ivermectin may reduce but not completely stop onchocerciasis transmission, and that recrudescence could occur after 15 years of treatment (Remme . 1990; Boatin . 1998). Therefore, to prevent recrudescence and maintain the gains made in disease morbidity control, some have argued that ivermectin programmes based on annual doses of ivermectin require indefinite ivermectin distribution (Richards . 2000; Winnen . 2002). To throw more light on this issue, we assessed the impact of single annual dose of ivermectin on onchocerciasis in 'Post-APOC' areas of Cameroon and Uganda after a decade or more of uninterrupted distribution to assess impact on prevalence and transmission of the parasite. Our fundamental question was, 'Are we reaching a point where it would be safe to halt ivermectin treatment?'

## Methods

Pre-treatment (baseline) community level microfilaria and nodule prevalence data were available from 1996 for 10 sentinel communities in West Province, Cameroon, and from 1993 for 20 sentinel communities in several districts in Uganda (Tables 1 and 2). Baseline data for 904 person examinations in Cameroon were obtained from two sentinel communities in each of five health districts: Bangangte, Foubot, Bafang, Kekem and Bandja. There were no baseline data for children from Bangangte and Bandja districts. In Uganda, baseline data for 1767 person examinations were from five districts: Mbale (four communities), Kasese (three communities), Nebbi (four communities), Kisoro (five communities) and Moyo (four communities). WeIn Ug1 0 (Baew336.1(34.8(scamest)-338.villagos)-332.8( sentiner communiti

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Table 1 Cameroon (West Province) and Uganda. Baseline and follow-up data on microfilaria and nodules in children 10 years of age and above and adults

Country	District (No. of communities)	Year	No. assessed	(min	Follow-up		Mean coverage % UTG	Range (min/max)

parents of individual children. Trained MOH personnel carried out the examinations. Participation was voluntary and any individual (or parent of a child) was free to opt out of examination without fear of retaliation from their community leaders and programme personnel.

After name, age (recorded in Cameroon as an age range) and gender were recorded on an individual registration form, each participant was examined in a well-lit private room. Qualified and certified MOH staff performed a palpation examination on the partially disrobed participant, paying particular attention to bony prominences of the torso, iliac crests and upper trochanter of the femurs. Onchocercal nodules (onchocercomas) were identified clinically as being firm, painless and mobile (Albiez 1988; Ngoumou 1994; Katarbarwa 1999). Results were recorded on the form as 'positive' or negative'. Nodule prevalence was expressed as a percent (number positive for nodules divided by number examined  $\times 100$ ) and classified as (nodule rate  $\leq 20\%$ ), (nodule rate  $\geq 20-40\%$ ) or (nodule rate  $\geq 40\%$ ) (WHO Report 1991).

Immediately after the nodule examination, two skin snips were taken from each iliac crest posteriorly (Prost & Prod'hon 1978) as follows: (1) the site was cleansed with an antiseptic, (2) a 2-3 mg sample of skin was taken with the help of disposable sterile dermal hook and scalpel, (3) the skin sample was placed immediately in wells of microtitration plates containing a sterile normal saline solution, (4) another snip was taken from the opposite side following the same procedure (1-3), (5) hook and blade were safely discarded, (6) sterile bandages were applied and (7) the wells used were noted on the patient form. When the plate was full, it was sealed with a transparent adhesive tape. After 12-24 h, the snips were removed and the fluid from each well was examined separately on a glass slide for microfilaria under low (40 $\times$ ) magnification by a trained MOH microscopist. The microfilariae were not counted; results were expressed for each individual as 'positive' or 'negative'. Laboratory results were recorded on the original (field) registration form. Microfilaria prevalence was expressed as a percent (number positive divided by number examined  $\times 100$ ), and classified as (microfilaridermia rate  $\leq 40\%$ ), me (microfilaridermia rate  $\geq 40-59\%$ ) or (microfilaridermia  $\geq 60\%$ ) (WHO Report 1991).

## History

In sentinel communities of four districts in Uganda (Kasese, Mbale, Moyo and Nebbi districts) nodules were offered to a sample of willing adults. The procedures were performed by trained MOH clinicians using sterile technique as described by Albiez (1988). Excised nodules were preserved in 90% ethanol and transported to the Bernhard Nocht Institute for Tropical Medicine in Hamburg, Germany where they were sectioned, stained by H&E and read by an expert (Prof. D.W. Büttner) following criteria for vitality and fertility of female and male *O.* (Duke 2002). The results were compared with findings from an unpublished study of 28 nodules obtained in 1993 and read by the same expert (unpublished results courtesy of Vector Control Division, MOH, Uganda and Prof. D.W. Büttner, Bernhard Nocht Institute).

## Treatment

At the launching of the treatment programme, CDDs in all communities onchocerciasis selected for mass treatment with ivermectin conducted a complete census and results were recorded in a community register. Registers were updated every year by the CDDs, before another round of ivermectin distribution was implemented. We determined treatment coverage of the sentinel communities based on the annual summary treatment statistics kept by the local MOH offices and The Carter Center country office. Treatment

coverage was defined as number of persons treated divided by the eligible population denominator (which is the total population minus children under 5 years of age) determined each year during the treatment exercise. 'Interval treatment coverage' was defined as the average of coverage over the interval (10 years in Cameroon, 13 years in Uganda) for each sentinel village.

## Data

Programme baseline and follow-up nodule and microfilaria prevalence figures for 'Older children and Adults' and 'Young Children' were compared implementing general linear contrasts using Sudaan annualtheih3Aeftwaereoveisiol

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hyperendemic for either or both nodule and microfilaria prevalence, with the exception of Kisoro, which was mesoendemic. All sentinel areas showed a significant

definition, in all cases the APOC goal has been achieved. We note, however, that the 19.5% nodule prevalence in Nebbi district in Uganda and the 16.0% nodule prevalence in Fombot district in Cameroon remain uncomfortably close to the proposed threshold, even after over a decade of



Bangangté health district; Dr Joseph Pouenpène, Medical Officer, Bafang health district; and Dr Abel Fossi, Medical Officer, Bandja health district; Mr Maurice Ngoungoué, Health Bureau chief; and programme coordinators, Mr Leonard Tchana and Mr Demanga Ngangue who participated in the 2005 surveys.

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#### References

- Albiez EJ, Büttner DW & Duke BO (1988) Diagnosis and extirpation of nodules in human onchocerciasis. *T M P* 39(Suppl. 4), 331–346.
- Amazigo U & Boatin B (2006) The future of onchocerciasis control in Africa. *L* 368, 1947.

